A Mechanistic Approach on the Solvolysis of Cinnamoyl Chloride in the Presence and Absence of Mercuric Chloride Catalyst

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ABSTRACT

The order with respect to water in the solvolysis of cinnamoyl chloride in aqueous acetone and aqueous acetonitrile of lesser water content is H"2.6, favours an addion-elimination mechanism , S_N2 mechanism or a competition between them. Higher enthalpy and lower negative entropy of activation favours S_N2 mechanism. Order with respect to mercuric chloride in the concentration range of 0.001M to 0.0025M is very small, in the range of 0.24, which reveals that mercuric chloride is not involved in the rate determining step of the reaction. The order with respect to water in the presence and absence of mercuric chloride remains the same which indicates that there is no mechanistic change in the presence of the catalyst. The increase in rate of the reaction in presence of catalyst is due to the combined effect of increase in the transition state stabilization and the abstraction of the leaving group from the transition state of the substrate.

Key words: Cinnamoyl chloride, , Solvolysis, Hydrolysis, S_N2, S_N1, Enthalpy and Entropy of Activation. Dipolar aprotic solvents, mercuric chloride catalyst.

INTRODUCTION

Cinnamoyl derivatives are used to produce compounds that have shown promising antifungal, antibacterial and anticancer activity.[1-2].Hence it is important to comprehend the correlations between the chemical structure, chemical reactivity, and solvent effects of such compounds. This knowledge can then be applied to the development of compounds that are designed to either stimulate or block other chemicals from interacting with targeted receptors, resulting in the production of pharmaceutically important products. Although the solvolyses of benzoyl halides have been extensively studied kinetically, less is known about the kinetics and mechanism of the solvolyses of cinnamoyl chloride. Accordingly, a study of the mechanism of the reactions of cinnamoyl chloride under solvolytic conditions is of continuing interest.

The solvolytic reactions on carboxylic acid derivatives can be basically classified from mechanistic point of view into S_N1 and S_N2. Due to the presence of a third reactive centre, the carbonyl oxygen, on which electrophilic reagents can interact preferentially leading to a more complex intermediate 3, the possibility of carbonyl addition-

elimination mechanism in solvents of low water content was suggested by Williams and Douglas 4 which is also called as tetrahedral mechanism. S_N1 mechanism is preferred in highly polar solvents and in the absence of strong nucleophiles5. In less polar solvents whether S_N2 or tetrahedral mechanism may occur will depend on the nature of substrate, nucleophile and the leaving group.

The study on the hydrolysis of benzoyl chloride and its substituted derivative in aqueous acetone by Berger and Oliver 6, Hudson and co-workers.7-12, Zimmerman and Yuan13 reveals that at relatively low concentrations of water/alcohol in a non-reacting solvent, the reaction was second order with respect to water (or alcohol) and first order with respect to acid halide. The order with respect to water is generally 6-7 for S_N1 reactions, 2-3 for S_N2 or addition-elimination reactions. It is seen that the apparent order in water is 2.9 for benzoyl chloride in 2-5 % water- dioxane at 25°C 14, 2.72 in 25 – 40% water-acetone at 25°C, 6.85 in 50-75 % water-acetone and 7.5 in 50-75 % dioxane – water at 0°C. An increase in the activation energy from 11.73 K.Cal in 5% water to 16.11 K.Cal in 33.3% water and variation in the slope of the line obtained for the plot of log k against (D-1)/2 (D+1) (D is the dielectric constant of the medium) above 30 % water shows a change in mechanism.. All these observation leads to the conclusion that in solvents rich in acetone (>80% aqueous acetone) the hydrolysis of benzoyl chloride proceeds by an addition-elimination mechanism while in water rich solvents,(e.g. in 50% aqueous acetone) there is a borderline behaviour in which simultaneous S_N1 and S_N2 process are occurring and the mechanism can shift to S_N1 with further increase in the composition of water.

The electrophilic catalyst generally used in nucleophilic substitution reactions are unionized molecules like halides and ionized salts like perchlorates, nitrates of mercury and silver 15. The cause of electrophilic activity of Hg2+ ion in the salt like mercuric perchlorate is due to the pronounced tendency of divalent mercury to form covalent bond. The electrophilic activity of the covalently bonded divalent mercury is due to its ability to form more covalent bonds through coordination. The linear mercuric chloride molecule (sp hybridized) is less

stable than tetrahedral complex $HgX_4$2- with sp3 hybridisation at the central mercury atom. The catalytic activity of the unionised mercuric chloride is carried out by assisting the ionization of C-Cl bond in alkyl or acyl chloride by pulling away the chloride ion [Bunton, Hughes and Anantharaman (C.K.Ingold, 359)]. The electrophilic activity of Hg2+ ion is much greater than that of the covalently bonded mercury atom because of smaller ionic radius, greater electronegativity and greater stability of covalently bonded mercury atom. The catalytic activity of mercuric chloride will be relatively lower in S_N2 reaction compared to S_N1.16 For reaction proceding through S_N1 mechanism17the order with respect to mercuric chloride is less than unity in 95% aqueous dimethylsuphoxide which is found to increase with increase in water content. This may be due to the dual role of mercuric chloride as an electrophylic catalyst and as a polar solvating agent of the transition state in a highly non polar environment.

RESULTS AND DISCUSSION

In the solvolysis of cinnamoyl chloride in aqueous acetone and aqueous acetonitrile containing 85 to 92.5% of organic component, the order with respect to water is found to be in the range of 2.6 (Table -1) which which is closer to value of 2.7 obtained for benzoyl chloride in aqueous dioxane containing less than 10% water. It favours an S_N2 or addition-elimination mechanism. Here one of the water molecules may be acting as a nucleophile while the remaining acts as a general base to deprotonate H+ ion from the added nucleophile of the transition state complex and/or involved in its stabilization by hydrogen bonding. The transition state may be either the loose complex formed in S_N2 path way or the tight tetrahedral species formed in addition–elimination pathway. Benzoyl choride which favours an addition-elimination mechanism through a tight tetrahedral transition state is charecterised by very high negative entropy of activation of about -170 $JK^{-1}mol^{-1}$ and relatively lower enthalpy of activation of about 47 kj/mole and free energy of activation of about 98 kj/mole. Relatively lower negative entropy of activation of -80 $JK^{-1}mol^{-1}$, higher enthalpy of actvation of 66 kj/mole (Table 2) observed for cinnamoyl chloride favours an S_N2 mechanism in

preference to addition-elimination. This may be be due to the increase in distance of the phenyl group from the reaction center in cinnamoyl chloride by a >C P% C< group which decreases the sterric effect by phenyl group on the reaction center and decreases the extent of conjugation of .>C=O group with the aromatic ring. This is confirmed by the fact that eventhough –COOH group in benzoic acid is meta directing (due to –M effect of the group), -CH=CH-COOH group is mainly ortho, para directing. This decrease in stabilization of the reaction center accounts for the greater reactivity of cinnamoyl chloride compared to benzoyl chloride. Comparison of the rate of the reaction in aqueous acetone and acetonitile of same composition shows that the rate is about 4 times faster in acetnitrile. This may be due to greater polarity in acetonitrile which may increases the stabilization of the transition state and decreases the activation parameter as observed in the table 2.

Table 1: Determination of order 'm' with respect to water inthe presence and absence of added mercuric chloride and the order with respect to mercuric chloride for the solvolysis of cinnamoyl chloride in aq. acetone and aqueous acetonitrile at 283K

Solvent	% of organic component	Rate const $k \times 10^3$ (sec^{-1})					Value of m w.r.t HgCl$_2$
		Conc. of mercuric chloride in molarity					
		0.00	0.001	0.0015	0.002	0.0025	
Aqueous Acetone	85	1.44	1.92	2.10	2.24	2.38	**0.23**
	87.5	0.817	1.15	1.24	1.32	1.41	**0.22**
	90	0.418	0.616	0.664	0.712	0.761	**0.23**
	92.5	0.236	0.369	0.30	0.412	0.458	**0.22**
Value of 'm' w.r.t H$_2$O	2.6	2.4	2.5	2.4	2.4		
Aqueous Acetonitrile	85	5.79	8.58	9.38	9.63	11.0	**0.25**
	87.5	3.62	6.06	6.64	7.16	7.76	**0.27**
	90	1.78	3.08	3.41	3.64	3.93	**0.26**
	92.5	0.856	1.72	1.91	2.05	2.21	**0.27**
Value of 'm' w.r.t H$_2$O	2.7	2.5	2.4	2.3	2.4		

Table 2: Comparison of activation parameters for the hydrolysis of cinnamoyl chloride in aqueous acetone and aqueous acetonitrile in the presence and absence of mercuric chloride

Solvent	[HgCl$_2$]	Rate Constants $k \times 10^3$ sec-1 at				ΔE^* (kj/mol)	ΔH^* (kj/mol)	ΔS^* (jK-1 mol-1)	ΔG^* (kj/ mol)
		283K	288K	293K	298K				
92.5% aq. Acetone	0.00	0.236	0.367	0.618	0.991	67.2	64.8	-85.2	90.2
	0.0025M	0.458	0.736	1.22	1.77	64.2	61.8	-89.9	88.6
	0.005M	1.73	3.01	5.05	7.31	61.9	59.5	-86.7	85.3
87.5% aq. acetone	0.00	0.827	1.34	2.40	3.57	65.0	62.6	-82.3	87.1
	0.0025M	1.41	2.09	3.49	5.09	61.5	59.1	-90.5	86.1
92.5 aq. acetonitrile	0.00	0.876	1.53	2.28	3.36	62.2	59.8	-91.3	87.0
	0.0025M	2.24	3.28	5.36	7.63	58.5	56.0	-97.3	850
	0.005M	3.89	5.85	9.12	13.1	57.3	4.9	-96.6	83.6
87.5% aq. acetonitrile	0.00	3.62	6.03	8.97	13.2	60.0	57.6	-87.3	83.8
	0.0025M	7.96	1.38	1.87	2.81	57.4	55.0	90.0	81.8

To study the effect of electrophilic catalyst on the solvolysis of cinnamoyl chloride, hydrolysis is carried out in aqueous acetone and aqueous acetonitrile in the composition range of 85 to 92.5% organic component in presence of mercuric chloride. The concentration of mercuric chloride used is in the range from 0.001M to 0.005M at different temperatures. In this range of solvent composition the electrophilic catalytic activity is solely due to unionized mercuric chloride molecule. The order with respect to mercuric chloride both in aqueous acetone as well as in aqueous acetonitrile are found to be very small in the range of only 0.25 (Table -1). The order with respect to water remains unchanged (~2.6) in presence and absence of mercuric chloride which reveals that there is no mechanistic change in presence of mercuric chloride. Very low order with respect to mercuric chloride confirms an S_N2 mechanism as already mentioned for the solvolysis. In addition mercuric chloride may not be involved in the rate determining step of the reaction. Therefore the catalytic activity is due to the increase in the extent of solvation of the transition state thus lowering the activation parameters mainly the enthalpy and free energy of activation. This is in agreement with the observed decrease in the enthalpy and free energy of activation (Table 2). The interaction of $HgCl_2$ molecule with the ClÉ end of the substrate molecule further loosen the loose transition state complex formed in the S_N2 path thus lowering the activation parameters. This interaction also enhances the detachment of the leaving group from the substrate. Thus the increase in rate of the reaction in the presence of catalyst is due to the combined effect of increase in the transition state stabilization and the abstraction of the leaving group from the transition state of the substrate.

Even though the order with respect to mercuric chloride is almost the same both in aqueous acetonitrile and acetone, the extent of increase in presence of mercuric chloride is greater in acetonitrile (Table 2). The extent of increase in rate in 85% aqueous acetone in presence 0.001M mercuric chloride is only 33% while in corresponding acetonitrile solution the extent of increase is about 56%. Similarly in presence of 0.0025M mercuric chloride the extent of increase is from 65% in 85% aqueous acetone to 100% in

Table 3: Effect of added mercuric chloride on the rate of solvolysis of cinnamoyl chride in aqueous acetone and aqueous acetonitrile at 10°C

Solvent	% composition of organic componenet	Rate constant and the percentage increase[HgCl₂]								
		0.00	0.001M		0.0015M		0.002M		0.0025M	
		$k\times10^3$ sec^{-1}	$k\times10^3$ sec^{-1}	increase	$k\times10^3$ sec^{-1}	increase	$k\times10^3$ sec^{-1}	increase	$k\times10^3$ sec^{-1}	increase
Aqueous acetone	85	1.44	1.92	33	2.10	46	2.24	56	2.38	65
	87.5	0.817	1.15	41	1.24	52	1.32	62	1.41	73
	90	0.418	0.616	47	0.664	59	0.712	70	0.761	82
	92.5	0.236	0.369	56	0.390	65	0.412	75	0.458	94
Aqueous acetonitrile	85	5.49	8.58	56	9.38	71	9.63	75	11.0	100
	87.5	3.62	6.06	67	6.64	83	7.16	98	7.76	114
	90	1.68	3.08	83	3.41	103	3.64	117	3.93	134
	92.5	0.876	1.72	96	1.91	118	2.05	134	2.21	152

acetonitrie solution.. The extent of solvation of HgCl$_2$ in solution alters its extent of interaction with the substrate and the stabilization effect in the initial and the transition state. The initial state being the loose complex between the nucleophile and substrate, its charge transfer will be favoured by less solvated catalyst. In aqueous acetonitrile due to greater polarity of the medium the extent of solvation of mercuric chloride may be lesser compared to solvation in aqueous acetone, which leads to greater extent of transition state stabilisation and greater decrease in the activation parameters compared to that in aqueous acetone. Similarly both in aqueous acetone and aqueous acetonitrile with decrease in water content of the medium the catalytic activity is found increase. Increases in water content increases the polarity of the medium which may increase the transition state stabilization and hence the increase in transition stabilization by the catalyst will be diminished which accounts for the decrease in rate increase. All these increase in rate can be accounted by the decrease in free energy whose main contribution is from the decrease in the enthalpy of activation. The entropy of activation does not show considerable variation in presence of mercuric chloride.

MATERIALS AND METHODS

To get a clear picture on the mechanism of hydrolysis of cinnamoyl chloride in aqueous organic solvents and the effect of electrophilic catalyst on it, kinetic studies were carried out in aqueous acetone and acetonitrile with percentage of water varying from 7.5 to 15. To study the effect of electrophilic catalyst the substance chosen is mercuric chloride, whose composition is varied from 0.0.001M to 0.0025M. Acetone used is BDH sample which is further purified by Conant and Kirner method. Cinnamoyl chloride used is Aldrich sample. Mercuric chloride used is also BDH (A.R.) sample For determining the rate constant, the course of the reaction is followed by measuring the conductance of the reaction mixture at regular intervals of time, using a digital conductivity bridge at the desired temperature. All runs were conducted at least in duplicate and the concordant values of the rate constants were used for discussion.To determine

the activation parameters the rate of the reaction were measured at four different temperatures ranging from 283K to 298K. and calculated using Eyring's equation. For determining activation parameters log k vs 1/T and log (k/T) vs1/T were plotted. For determing the order with respect to any one of the component in excess in the medium log k was plotted against log C and the slope is determined.

CONCLUSION

The aim of this work is to establish a clear picture regarding the mechanism of solvolytic reactions of cinnamoyl chlorides, in aqueous organic solvents like acetone and acetonitrile containing limited amount of water. The order with respect to water in the solvolysis of cinnamoyl chloride in aqueous acetone and aqueous acetonitrile in the composition range of 85% to 95% is H"2.6 which supports either an addition-elimination or S$_N$2 mechanism or a competition between them. Relaltively greater enthalpy of activation in the range of 61-66 kj/mole, low negative entropy of activation in the range of -80 to -88 jK-1mol-1 favours an S$_N$2 mechanism than addition-elimination mechanism for cinnamoyl chloride in this solvent range. The order with respect to water in presence and absence of mercuric chloride remain the same which indicates that there is no mechanistic change in the presence of the catalyst. Order with respect to mercuric chloride in the concentration of 0.001M to 0.0025M is very small, in the range of 0.24, which reveals that mercuric chloride is not involved in the rate determining step of the reaction. Its catalytic activity is due to the direct interaction with the ClÉ end of the substrate molecule thus loosening the C-Cl bond which accelerates the departure of the leaving group. In addition ,the catalytic activity is due to the increase in the extent of solvation of the transition state thus lowering the activation parameters mainly the enthalpy and free energy of activation. Thus the increase in rate of the reaction in the presence of catalyst is due to the combined effect of increase in the transition state stabilization and the abstraction of the leaving group from the transition state of the substrate.

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