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Original Article

MICELLAR EFFECTS ON THE VILSMEIER-HAACK FORMULATION REACTIONS WITH ANILINES IN NONAQUEOUS SOLVENTS – A KINETIC APPROACH

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ABSTRACT

Vilsmeier-Haack (VH) Reaction with Anilines afforded formyl derivatives with DMF/$SOCl_2$. The reactions obeyed second order kinetics with a first order dependence on each [Reactant]. A remarkable rate enhancement was noticed when micelle-forming surfactants such as cetyl tri methyl ammonium bromide (CTAB), sodium dodecyl sulphate (SDS) and triton-X 100 (Tx) were use as catalysts. Rate ($k\Psi$) versus [Surfactant or CD] profiles were generally wavy in nature with all the surfactant systems. The rate profiles of micelle-mediated reactions were categorized into different types and were interpreted using Menger-Portnoy's enzymatic model or Pizkiewicz's modified Cooperativity model.

Key words: *Vilsmeier-Haack (VH) Reaction, cetyl tri methyl ammonium bromide (CTAB), sodium dodecyl sulphate (SDS) and triton-X 100 (Tx)*

INTRODUCTION

Recent studies on Vilsmeier-Haack (VH) reactions revealed that organic compounds in general and hydrocarbons with excess pi-electrons in particular undergo formulation very easily on synthetic scale [1-10]. Formamide, N, N'-dimethyl formamide (DMF), N, N'-diethyl formamide (DEF), were used along with oxy halides such as $POCl_3$ and $SOCl_2$ for the preparation of VH reagents. Surfactants are less expensive, operationally simple and easily available compounds, which form micelles. Micelles are amphipathic species, which possess the hydrophilic polar head groups occupying the surface while the interior of micelle is occupied by hydrophobic alkyl groups. These micelles are known to reverse their characters i.e., the polar heads protrude into the interior part and the substrate directs towards the micelle-solvent interface in non-polar solvents [11-15]. In recent past micelles were found to be very attractive reactions because of a well documented analogy between micellar mediated and enzymatic reactions [11]. Even though many results have been published in the literature showing the catalytic effects of micelles in a variety of chemical reactions such as acid catalysed hydrolysis,

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base catalysed hydrolysis, substitution and oxidation reactions [12, 13], such studies are less known in Vilsmeier-Haack reactions [14]. In view of this, in the present investigation we have tried to explore the catalytic activity of micelles in VH FORMULATION reactions. Phenols and aromatic amines are important group of organic compounds, which have been their use in a number of industrially important and biologically important compounds. Formyl phenol acts as a prodrug for the drug formyl phenyl aspirins [16]. Formyl anilines are used for the synthesis of Di- and polyamines of the diphenyl methane derivatives [17]. The study is also aimed at exploring the similarities and dissimilarities in the mechanistic aspects and the nature of reactive species and also the transition state when different VH adducts are used as reagents for FORMULATION reactions.

EXPERIMENTAL DETAILS

Organic substrates such as phenols, anilines and their substituted compounds were undertaken for kinetic studies of VH reactions in ACN and DCE. Thermostat (Toshniwal, India) was adjusted to desired reaction temperature. Two different flasks, one containing known amount of Vilsmeier- Haack reagent in a suitable solvent and the other with the substrate solution, were taken and clamped in the thermostatic bath for about half-an-hour. Reaction was initiated by adding requisite amount of substrate solution to the reaction vessel containing the other contents of the reaction mixture. The entire reaction mixture was stirred till the end of the reaction. The unreacted VH reagent was estimated as a function of time according to standard literature procedures [14,15]. Aliquots of the reaction mixture were withdrawn into a conical flask, containing considerable (known) amount of hot distilled water, at different time intervals. The unreacted VH adduct underwent hydrolysis and gave a mixture of hydrochloric and sulfuric acids. The acid content was estimated against standard NaOH solution to bromocresol green end point.

Products of the reaction were isolated under kinetic conditions. To the Vilsmeier-Haack complex prepared from DMF and SOCl2 (0.02 moles each) in DCE (100 ml), 0.02 moles of substrate were added with constant stirring. The reaction mixture was refluxed for 4 to 5 hand left aside over night. The solution was poured into ice-cold water with vigorous stirring and kept aside for about 2 h. The resultant solution was neutralized by sodium hydrogen carbonate. Organic phase was extracted with DCE and dried (with MgSO4,) and the solvent evaporated. TLC pure formyl derivative was characterized by spectroscopic methods. The reactions afforded fairly good yields of end products.

RESULTS AND DISCUSSION

Under pseudo first order conditions i.e. [Sub]o<< [VH] o, the plots of ln(Vt) versus time were linear with negative slope with definite intercept on ordinate depicting first order dependence on [Substrate] (i.e., n1 = 1). Slopes of these plots afforded Pseudo first order rate constant (k') values. (2) The First-order rate constant (k') values presented in table indicated that k' is proportional to the first power raised to [VH Reagent] indicating first order kinetics in [VH reagent]. This could also be confirmed from the plots of k' versus [VH reagent] using the presented in table 5.3. (3) Rates of reaction changed significantly when the reaction medium is from a high dielectric ACN to low dielectric DCE medium with the trend: ACN > DCE. These observations may suggest the possibility of a change in the reactive species passing from higher dielectric acetonitrile to low dielectric dichloroethane medium.

The kinetic features observed in the present work are by and large similar to those reported from earlier from our laboratory using DMF/POCl3 as VH reagent [14,15]. A perusal of these publications from our laboratory [14,15] couple with other literature reports [2-5] suggest that VH reagent, in solution, is present in a number of covalent, ion-pair, and cationic forms [DMF/SOCl2] reagent in the lines of [DMF/POCl3] reagent. On the basis of these similar experimental observations, similar type of reactive species could be proposed for [DMF/SOCl2] and [DMA/ SOCl2] systems as shown in structures I to VI. It has also been mentioned that the participation of an individual species in the reaction depends on the nature of substrate and solvent used in the system and also on electrophilic properties of the reacting species.

(I) $[(CH_3)_2 N- C (R) Cl O SOCl]$	**(II) $[(CH_3)_2 N^+ = C (R) Cl][OSOCl]^-$**
(III) $[(CH_3)_2 N^+= C (R)-OSOCl][Cl]$	**(IV) $[(CH_3)_2 N^+---C(R) Cl] [SO_2Cl]^-$**
(V) $[(CH_3)_2 N^+---C (R) OSOCl] [Cl]^-$	**(VI) $[(CH_3)_2 N---C^+ (R) Cl]$**

As mentioned in earlier publications from our laboratory and other literature reports [23] these observations suggests a change in the nature of the reactive species on passing from high dielectric constant (ACN) to less polar DCE. These deviations could also be due to solvent–solute or solvent-co solvent interactions. In ACN (high dielectric media) participation of ion-pair species of VH adduct (V) and substrate was proposed in the slow step to give phosphorousoxy chloromethyleniminium intermediate (B) followed by elimination of HCl. This was supported on the basis of spectroscopic and thermodynamic evidence [17-23]. However, in DCE (low dielectric medium) cationic form of VH adduct (VI) and substrate participated in the rate-determining step to give choloromethyleniminium intermediate (A). These intermediates species (A or B) upon hydrolysis yield the end products. The over all order of the reaction was found to be two with a first order dependence on [Substrate] and [VH reagent] in presence of cationic (CTAB), anionic (SDS) and non ionic (TX) micelles. Rates were generally enhanced in micellar media.

The factors, which determine the size of reversed micelle in non-aqueous solvents, are surfactant structure, nature of the solvent and the presence or absence of solubilizate. Water (solubilizate) was generally found to affect the properties of micelles in apolar solvents. Micellization occurred when water was used as additive in non-aqueous media. It could be therefore concluded that different types of reactive species get distributed in various types of micellar aggregates at different stages of the surfactant concentrations. The crests and troughs could be interpreted as follows:

i) According to the findings, ths abrupt changes in physical properties above the "normal" CMC could be explained in terms of second and third CMC values. Thus the observed crests and troughs in the present study could probably be due to the second and third CMC values. The aggregation number of surfactant monomer differs at these CMC points in the rate-[Surfactant-CD] profile. This contention was earlier supported from the conductivity studies of micelles done earlier in our laboratory. It is of interest to note that plots of conductivity Vs [Surfactant- C_D] indicated a number of crests and troughs suggesting that more than one CMC corresponding to more than one type of micelles could possibly exist in surfactant solutions.

ii) A decreasing trend from maxima to minima in Rate versus C_D profiles could be either due to dilution effects or by formation of new micellar aggregate. The solublization is also affected by the concerted action of several small micelles, whose lypophilic surface interacts with the hydrophobic regions of the substrate or VH reagent. The ion - polar interactions between the charged head groups of the surfactant and the ionized portion of the catalyst are also responsible for the solublization. The wave like curves of dipeptidyl peptidase in Triton-X medium. The kinetic data of micellar catalysis are being generally analyzed and interpreted by enzymatic models in view of the observed close parallelism of micellar systems with globular proteins. Even though many micellar models are proposed earlier in the micellar mediated reactions (i) Menger & Portnoy's saturation kinetics and (ii) Pizkiewicz's cooperativity models are generally used for interpretation of kinetic data. Simple cooperativity model is useful to explain sigmoidal type curves while the extended co-operativity model formed a basis to explain bell (hill) type, valley type and more complicated wavery curves observed in k_ψ–C_D profiles. The observed k_ψ–C_D profiles are classified into the following categories (Type A to F)

The k_ψ–C_D profiles fig 5.9 to 5.20 indicated different trends depending on nature of substrate, surfactant and organic solvent used. Depending on the shape of the profile the plots are classified into the following six types viz., Type –A to Type-F:

Type A: Sigmoid type k_ψ Vs C_D profiles are considered as Type-A curves.

Type B: The k_ψ Vs C_D profiles which were hill (bell) passing through rate maximum k_ψ are classified as Type –B curves.

Type C: In this type k_ψ Vs C_D profiles k_ψ decreases to a minimum at higher concentration of surfactant. These curves are in contrast with Type A profiles.

Type D: Type –D k_ψ Vs C_D profiles are wavery type with one or more maxima and minima i.e with number of crests and troughs.

Type E: This type of k_ψ Vs C_D profiles are valley or well type curves in contrast to hill type curves.

Type F: The plots of k_ψ Vs C_D indicated a continuous increase of k_ψ Vs C_D without any limiting rate maximum. The plots yielded straight lines with positive slope.

TYPE OF PLOTS FOR k_ψ Vs C_D OF FORMULATION REACTIONS:

S.No.	Substrate	ACN			DCE		
		CTAB	Tx	SDS	CTAB	Tx	SDS
1.	Aniline	A	D	E	C	B	E
2.	3-Chloroaniline	E	B	E	B	D	B
3.	4-Nitroaniline	E	D	C	A	A	D
4.	o-Toluidine	A	E	F	B	F	D

Model-I: Menger & Portnoy's Limiting Rate Model

Model-II: Pizkiewicz's model for the quantitative Treatment of k_ψ Vs CD Profiles

CONCLUSIONS:

The results of present study clearly indicate direct FORMULATION can be achieved successfully in CTAB, SDS and / or Tx100 mediated VH reactions, which are sluggish under classical conditions. This method is also useful for synthesis of formyl derivatives with phenols, anilines and acetanilides, which have potential biological activity.

REFRENCES:

1. Olah G.A., and St. Kuhn J., Friedls Craft's and related reactions, Olah G.A., Ed., Vol. III, Part-2, John Wiley and Sons, New York, 1964, p.1211; (b) Ulrich, H., The Chemistry of imidoyl halides, Plenum Press, New York, 1968, Vol. 83, p. 97; (c) Bonnet, R., "Imidoyl halides", The Chemistry of the Carbon Nitrogen double bond, S. Patai, Ed., John Wiley and sons, New York, 1970; (d) Bredereck H., Gompper R., Klemni K., and Remfer H., Chem. Ber., 1959, Vol. 92, p.937; (e) E. Compaigne E., and Archer W.L., Organic Synthesis John Wiley and sons, New York, 1953, Vol. 33, p.27.

2. Smith G.F., J. Chem. Soc., 1954, p.3842; (b) Silverstein R.N., Ryskiewez C., Willert C., and Kocher R.C., J. Org. Chem., 1955, Vol. 20, p. 668.

3. Lorenz A., Winzinger R., Helv Chem Acta., 1945, Vol. 28, p.600; (b) Boshard H.H., and Zollinger H., 1959, Vol. 42, p.1659.

4. Alumi S., Linda P., Marino G., Santine S., and Salvelli G., J. Chem. Soc., Perkin, 1972, Vol. 2, p.2070; (b) Linda P., Lucccarelli A., Marino G., and Savelli G., Perkin, 1974, Vol. 2, p. 1610.

5. Arnold Z., Holy A., Collection Czech. Chem. Commun., 1962, Vol.27, p.2886 and references therein; (b) Smith T.D., J. Chem. Soc. A., 1966, p. 841; (c) Lieoscher and Hartman, Coll. Czech. Chem. Commun., 1976, Vol. 41, p.1565; (d) Anderson A.G., Owen N.E.T., Franon F.J., And Ereckson D., Synthesis, 1966, p. 398.

6. Martin G.J., Poignant S., Filleux M.L., and Quemeneeuer, Tetrahedron Letters, 1970, Vol.58, p. 5061; (b) Martin G., and Martin M., Bull. Soc. Chem., France 1963, p. 1637; (c) Martin G.J., Poignant S., J.Chem. Soc., Perkin, 1972, Vol. 2, p. 1964; 1974, Vol. 2, p. 642.
7. Rajanna K.C., Soloman F., Ali M.M., Saiprakash P.K., Tetrahedron Letters, 1996, Vol. 52, p. 3669; Int. Natl. J. Chem. Kinet., 1996, Vol. 28, p.865.

8. Dingwall,J.G., Reid D.H., and Wade K., J.Chem. Soc. C., 1969, p.913.

9. Davis T.L., and Yelland W.E., J. Am. Chem. Soc., 1937, Vol. 59, p.1998.

10. Cipiciani A., Clementi S., Linda P., Marino G., Savelli G., J. Chem. Soc., Perkin, 1977, Vol. 2, p. 1284.

11. Fendler J. H., and Fendler R.J., "Catalysis in Micellar and Micromolecular Systems", Academic Press, New York, 1975; (b) Vold R.D., and Vold M.J., Colloid and Interface Chemistry, Addison-Wesley Publishing Comp., 1983; (c) Kunitake T., Shinkai S., Adv. Phys. Org. Chem., 1986, Vol. 22, p.213; (d) Christain S.D., and Scamehorn J.F., "Solubilization in Surfactant Aggregates", Marcel Dekker Inc., New York, 1995.

12. Mittal K.L., (Ed.), (a) Micellization, Solubilization and Micro Emulsions, Plenum Press, New York, 1977; (b) Solution Chemistry of Surfactants, Plenum Press, New York, 1979;(c) Mittal K.L., and Lindman (Ed.), "Surfactants in Solution", Plenum Press, New York, 1984.

13. Matha M., Sundari L.B.T., Rajanna K.C., and Saiprakash P.K., Int. Natl. J. Chem. Kinet., 1996, Vol. 28, p.637; Rajanna K.C., Narsi Reddy K., Umesh Kumar U., and Saiprakash P.K., Int. Natl. J. Chem. Kinet., 1996, Vol. 28, p.153; Jhansi Lakshmi P., Channamallu K., Rajanna K.C., and Saiprakash P.K., J. Mol. Catal., 1996, Vol. 108, p. 63.

14. Rajanna K.C., Ali M.M., Tasneem, Sana S., and Saiprakash P.K., Synthetic Letters, 2001, p. 251.

15. Ali M.M., Kinetic and Mechanistic Aspects of Ultrasonically Assisted and Micellar Catalysed Vilsmeier-Haack reactions, Thesis, 2002.

16. Marino G., Adv. Hetrocyclic Chem., 1971, Vol. 13, p. 235.

17. Filleux-Blanchard M.I., Quemeneur M.T., and Martin G.J., Chem. Commun., 1968, p. 836.

18. Fendler J.H., Accts Chem Res, 1976, Vol. 9, p.153; Connor C.J.O., and Ramage R.E., Aust. J. Chem., 1980, Vol.33, p. 695,757,771,779; Connor C.J.O., and Mollett K.J., J. Chem. Soc. Perkin. Trans, 1976, Vol.2, p.369.

19. Ekwall P., Holmberg, Acta Chem.Scand, 1965, Vol.19, p.455.

20. Kodama M., Miura M., Bull. Chem. Soc., Japan, 1972, Vol.45, p.2265; (b) Kodam M., Kubota and Miura M., Bull. Chem. Soc., Japan, 1972, Vol, 45, p.2953.

21. Erikson R.H., and Kim Y.S., Biochem. Biophys., Acta, 1980, Vol. 614, p. 210.

22. Menger F.M., and Portnoy C.E., J.Am. Chem Soc., 1967, Vol. 89, p.4698.

23. Rajanna K.C., Ali M.M., Tasneem, Sana S., and Saiprakash P.K., Synthetic Letters, 2001, p. 251.

24. Roopa Redamala, Ramchander Merugu, K.C. Rajanna. A Comparative study of Vilsmeier-Haack FORMULATION Reactions With Phenols Under Solvent Less And Solvent Conditions. Asian J. Research Chem. 2018; 11(2):409-412. doi: 10.5958/0974-4150.2018.00074.3.

25. R. Roopa, Ramchander Merugu and Rajanna K. C. Journal of Chemical and Pharmaceutical Research, 2015, 7(12):279-283.

26. Mohammed, T., Khan, A.A., Iqubal, S.M.S. et al. Micellar effects on kinetics and mechanism of Vilsmeier–Haack FORMULATION and acetylation with Pyridines. Chem. Pap. 76, 2615–2621 (2022). https://doi.org/10.1007/s11696-022-02066-7.

27. Mohammed, T., Khan, A.A., Iqubal, S.M.S. et al. Micellar effects on kinetics and mechanism of Vilsmeier–Haack FORMULATION and acetylation with Pyridines. Chem. Pap. 76, 2615–2621 (2022). https://doi.org/10.1007/s11696-022-02066-7

Table 1: Effect of Variation of [VH Reagent] (k’) in Formulation Reactions in Presence of CTAB

10^3 [S] = 4.00 mol dm^{-3}; Temp = 323 K; Solvent: (A) ACN; (B) DCE

[VH Reagent] mol dm^{-3}	Solvent	Pseudo first rate constant (k’hr-1)			
		aniline	m-chloroaniline	P-nitroaniline	O-toulidine
0.025	A	0.018	0.026	0.023	0.014
0.050	A	0.037	0.050	0.047	0.028
0.100	A	0.075	0.101	0.094	0.057
0.150	A	0.166	0.151	0.145	0.094
0.250	A	0.194	0.264	0.024	0.145
0.025	B	0.068	0.037	0.036	0.023
0.050	B	0.141	0.075	0.072	0.047
0.100	B	0.275	0.150	0.145	0.095
0.150	B	0.414	0.236	0.216	0.155
0.250	B	0.693	0.384	0.374	0.244

Table 2: Effect of Variation of [CTAB] on the Rate of VH Formulation Reactions:

[VHR] = 0.100ol dm-3 ; 103 [S] = 4.00 mol dm-3; Solvent = ACN; Temp = 323 K.

Substrate	Pseudo first rate constant (k’hr-1)													
	(A) [CTAB] (mM) in ACN							(B) [CTAB] (mM) in DCE						
	0.0	0.25	0.5	1.25	2.50	3.75	5.00	0.0	0.25	0.5	1.25	2.50	3.75	5.00
aniline	0.114	0.098	0.094	0.036	0.037	0.039	0.026	0.156	0.156	0.144	0.138	0.184	0.201	0.178
m-chloraniline	0.057	0.067	0.138	0.102	0.083	0.081	0.095	0.104	0.102	0.099	0.095	0.094	0.192	0.098
P-chloroaniline	0.136	0.129	0.111	0.117	0.107	0.090	0.100	0.140	0.137	0.139	0.140	0.143	0.139	0.144
o-toulidine	0.192	0.250	0.260	0.237	0.233	0.229	0.178	0.127	0.132	0.138	0.128	0.132	0.130	0.135
p-aminophenol	0.185	0.145	0.191	0.293	0.231	0.227	0.181	0.121	0.125	0.127	0.129	0.126	0.125	0.127

Table 3: Effect of Variation of [TX] on the Rate of VH Formulation Reactions: [VHR] = 0.100ol dm-3; 103 [S] = 4.00 mol dm-3; Solvent = ACN ; Temp = 323 K.

Substrate	Pseudo first rate constant (k'hr-1)													
	(A) [Tx] (mM) in ACN							(B) [Tx] (mM) in DCE						
	0.0	0.25	0.50	1.25	2.50	3.75	5.00	0.0	0.25	0.50	1.25	2.50	3.75	5.00
aniline	0.046	0.105	0.114	0.124	0.092	0.130	0.122	0.182	0.178	0.185	0.215	0.173	0.190	0.190
m-chloraniline	0.095	0.088	0.084	0.093	0.075	0.064	0.061	0.114	0.113	0.116	0.108	0.111	0.103	0.109
P-chloroaniline	0.148	0.140	0.100	0.083	0.064	0.066	0.087	0.138	0.144	0.134	0.141	0.139	0.138	0.138
o-toulidine	0.210	0.116	0.152	0.108	0.102	0.116	0.104	0.133	0.132	0.138	0.128	0.132	0.130	0.144
p-aminophenol	0.203	0.212	0.200	0.155	0.110	0.120	0.145	0.124	0.122	0.114	0.120	0.126	0.125	0.127

Table 4: Effect of Variation of [SDS] on the Rate of VH Formulation Reactions:

[VHR] = 0.100ol dm-3 ; 103 [S] = 4.00 mol dm-3; Solvent = ACN ; Temp = 323 K.

Substrate	Pseudo first rate constant (k'hr-1)													
	(A) [SDS] (mM) in ACN							(B) [SDS] (mM) in DCE						
	0.0	0.25	0.50	1.25	2.50	3.75	5.0	0.0	0.25	0.50	1.25	2.50	3.75	5.0
aniline	0.026	0.051	0.075	0.045	0.067	0.083	0.070	0.177	0.178	0.185	0.179	0.170	0.184	0.184
m-chloraniline	0.071	0.076	0.083	0.053	0.032	0.021	0.085	0.117	0.111	0.117	0.100	0.104	0.113	0.114
P-chloroaniline	0.097	0.100	0.105	0.137	0.049	0.053	0.078	0.144	0.124	0.130	0.147	0.153	0.158	0.164
o-toulidine	0.094	0.091	0.064	0.069	0.037	0.014	0.022	0.142	0.142	0.153	0.182	0.142	0.181	0.134
p-aminophenol	0.112	0.029	0.079	0.050	0.028	0.022	0.022	0.127	0.130	0.132	0.134	0.138	0.147	0.141

Table 5: Kinetic features in the form of equations obtained from the Plots of ln (Vt) Vs Time for Formulation reactions in ACN solvent

y =mx + c; R2 = Correlation Coefficient; y = lnVt; x = Time (hr)

Surfactant	Substrate	Equation y = mx + c	Correlation Coefficient R2
CTAB	aniline	y =-0.0937+ 2.6153	0.9999
	m-chloraniline	y =-0.0562+ 2.7023	0.9988
	P-chloroaniline	y =-0.0136+ 2.6999	0.9921
	o-toulidine	y =-0.2374+ 2.9504	0.9941
	p-Aminophenol	y =-0.2929+ 3.2379	0.9960
Tx	aniline	y =-0.1241+ 3.0733	0.9968
	m-chloraniline	y =-0.0954+ 2.7719	0.9993
	P-chloroaniline	y =-0.1481+ 2.8282	0.9992
	o-toulidine	y =-0.1528+ 2.9005	0.9967
	p-Aminophenol	y =-0.2062+ 3.0344	0.9955
SDS	aniline	y =-0.0445+ 2.2743	0.9973
		y =-0.0825+ 2.4237	0.9962
	m-chloraniline	y =-0.1372+ 2.7714	0.9994
	P-chloroaniline	y =-0.0937+ 2.5709	0.9963
	p-Aminophenol	y =-0.0503+ 2.4473	0.9980

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