Kinetics and Mechanism of Certain Benzoylation Reactions under Vilsmeier–Haack Conditions Using Benzamide and Oxychloride in Acetonitrile Medium

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Received 20 August 2011; revised 6 December 2011, 28 February 2012; accepted 2 March 2012

DOI 10.1002/kin.20740
Published online 18 December 2012 in Wiley Online Library (wileyonlinelibrary.com).

ABSTRACT: Vilsmeier–Haack (VH) benzoylation reactions with benzaldehydes and acetophenones in acetonitrile medium obeyed second-order reaction kinetics. Under kinetic conditions, the reactions afforded benzoyl derivatives irrespective of the nature of oxychloride ($POCl_3$ or $SOCl_2$) used for the preparation of VH reagent along with benzamide. The present finding is advantageous to understand the nature of reactive species as well as the mechanism of benzoylation. © 2012 Wiley Periodicals, Inc. Int J Chem Kinet 45: 69–80, 2013

INTRODUCTION

The Vilsmeier–Haack (VH) reaction is one of the mildest methods for the introduction of a formyl or acetyl group to various aromatic and heteroaromatic compounds [1–3]. The Vilsmeier and Haack reagent (VHR) is basically a halomethylene iminium salt, prepared from equimolar oxychloride ($POCl_3$) and N-N'-dimethyl formamide (DMF) under chilled conditions (at $-5^{\circ}C$ temperature) in 1927 by Vilsmeier and Haack [1]. Later on, it was also shown that a similar type of VH adducts could be obtained from N-N'-dimethyl acetamide or analogous N-N'-dialkyl amides along with oxychloride. This reagent has attracted the attention of chemists since its discovery due to simplicity in its preparation and utility to synthesize a variety of organic carbonyl compounds that are being used as intermediates and/or starting materials in several synthetic

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protocols [4–14]. For instance, formylated anilines are used for the synthesis of di- and polyamines of the diphenyl methane derivatives [10]; formyl phenols are used as prodrugs for the drug formyl phenyl aspirins [11], whereas formyl quinolines are known to exhibit antibacterial [12] and antifungal activity [13]. Over the past two decades, our group is also actively working on exploiting the use of a variety of ecofriendly materials such as surfactants and nonconventional energy sources for triggering VH reactions [14]. Earlier publications from our laboratory reported kinetics and mechanism for the formylation of coumarin derivatives and orthohydroxy acetophenones (OHAP) under VH conditions [9]. The present investigation is one such exercise, which is aimed to explore the mechanism of benzoylation reactions with aromatic aldehydes and ketones under VH conditions by studying the kinetics of certain organic compounds, such as benzaldehydes and acetophenones.

EXPERIMENTAL

The chemicals used in the present study, viz. aromatic aldehydes, acetophenones, and oxychloride ($POCl_3$, $SOCl_2$), were procured from either Aldrich or Merck. The solvents acetonitrile (ACN), dichloromethane (DCM), tetrahydrofuran (THF), benzene, and dichloroethane (DCE) were either HPLC grade or purified according to standard literature reports.

General Procedure for Preparation of VHR

The VH adduct is prepared afresh before use from equimolar oxychloride ($POCl_3$ or $SOCl_2$) and benzamide using standard literature procedures [9,14]. To a chilled (at –5°C) benzamide solution prepared in DCE or ACN, calculated amount of $POCl_3$ was slowly added dropwise and stored under cold conditions.

Kinetic Method

The method that is followed for the kinetics of the VH reaction is by and large similar to that reported in our earlier paper [9]. Athermostat (Toshniwal, India) was adjusted to desired reaction temperature. Two different flasks, one containing known amount of VHR and the other with the substrate solution, were clamped in the thermostatic bath for about half an hour. A reaction was initiated by adding requisite amount of substrate solution to the reaction vessel containing VHR and other contents of the reaction mixture. The entire reaction mixture was stirred until the end of the reaction. Aliquots of the reaction mixture were withdrawn into a conical flask, containing about 50 mL of hot distilled water, at regular time intervals. The unreacted VH adduct underwent hydrolysis and gave a mixture of hydrochloric and sulfuric acids in the case of [benzamide/$SOCl_2$] and a mixture of hydrochloric and phosphoric acids in the case of [benzamide/$POCl_3$] reagent. The acid content was estimated against standard NaOH solution to bromocresol green end point.

Product Analysis under Kinetic Conditions

After completion of the kinetic study, remaining part of the reaction mixture was refluxed further until the reaction was over (as ascertained by TLC). The solution was then transferred into a beaker containing excess of water with vigorous stirring and kept aside for about 2 h. The resultant solution was neutralized by sodium hydrogen carbonate. The organic phase was extracted with DCE, dried with $MgSO_4$, and the solvent evaporated. The reaction times and percentage yields of the products are compiled in Table I. The products were characterized by IR, ^{1}H NMR, mass spectra, and physical data with authentic samples and found to be satisfactory. Spectroscopic data (^{1}H NMR, and mass spectra) for certain representative

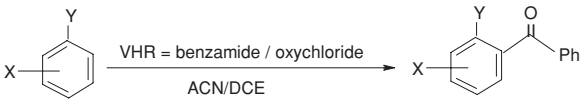
Table I VH Benzoylation Reactions of Carbonyl Compounds with (Benzamide + $SOCl_2$) and (Benzamide + $POCl_3$)

		(Benzamide + $SOCl_2$)		(Benzamide + $POCl_3$)	
Entry	Substrate	RT (h)	Yield (%)	RT (h)	Yield (%)
1	Benzaldehyde	12	65	11	69
2	Salicylaldehyde	12	70	12	70
3	4-OH benzaldehyde	11	80	11	83
4	4-OMe benzaldehyde	13	67	12	67
5	4-Cl benzaldehyde	13	63	11	75
6	Cinamaldehyde	13	62	13	73
7	Acetophenone	12	74	12	77
8	2- OH acetophenone	12	80	11	76
9	4-OH acetophenone	12	71	11	75
10	3-OH acetophenone	11	69	11	70

Table II Spectroscopic Data for VH benzoylation of Aromatic Carbonyl Compounds

			Spectral data	
Entry	Substrate	Product	m/z	^{1}H NMR
1	Benzaldehyde	3-Benzoyl benzaldehyde	210	δ 7.35 (m, 4H, Ar); δ 7.65 (d, 2H, Ar); δ 8.0 (d, 2H, Ar) δ 8.37 (s, 1H, Ar); δ 10.05 (s, 1H, Ar-CHO)
2	Salicylaldehyde	3-Benzoyl salicylaldehyde	258	δ 7.35–7.92 (m, 8H, Ar); δ 10.1 (s, 1H CHO); δ 10.7 (s, 1H, Ar-OH)
3	4-OH benzaldehyde	3-Benzoyl 4-OH benzaldehyde	258	δ 7.3 (m, 4H, Ar); δ 7.6 (d, 1H, Ar); δ 8.0 (d, 2H, Ar) δ 8.3 (s, 1H, Ar); δ 9.95 (s, 1H, Ar-CHO); δ 10.95 (s, 2H, Ar-OH)
4	4-OMe benzaldehyde	3-Benzoyl 4-OMe benzaldehyde	240	δ 3.7 (s ,3H, OCH_3); δ 7.4 (m, 4H, Ar); δ 7.75 (d, 1H, Ar) δ 7.9 (d, 2H, Ar); δ 7.75 (d, 1H, Ar); δ 7.9 (d, 2H, Ar) δ 8.2 (d, 1H, Ar); δ 10.05 (s, 1H, Ar-CHO)
5	4-Cl benzaldehyde	3-Benzoyl 4-Cl benzaldehyde	244	δ 7.4 (m 4H, Ar); δ 7.7 (d 1H, Ar); δ 8.3 (d 2H, Ar) δ 8.45 (s 1H, Ar); δ 10.0 (s 1H, Ar-CHO)
6	Cinamaldehyde	3-Benzoyl cinamaldehyde	235	δ 6.75 (d,1H, =CH); δ 7.4 (m, 1H, Ar); δ 7.45 (d, 1H, Ar) δ 7.5–7.8 (m, 7H, Ar); δ 8.05 (d, 1H, =CH); δ 9.9 (s, 1H, Ar)
7	Acetophenone	3-Benzoyl acetophenone	224	δ 2.8 (s, 3H, CH_3); δ 7.8 (m, 5H, Ar); δ 7.6 (m, 1H, Ar), δ 7.95 (d, 2H, Ar); δ 8.45 (s 1H, Ar)
8	2-OH acetophenone	3-Benzoyl chromone	250	δ 6.34 (s, 1H, Ar); δ 7.4 (m, 6H, Ar); δ 7.65 (d, 2H, Ar), δ 7. 9 (d, 1H, Ar)
9	4-OH acetophenone	3-Benzoyl 4-OH acetophenone	240	δ 2.9 (s, 3H, CH_3); δ 7.3 (m, 3H, Ar); δ 7.6 (d, 2H, Ar), δ 8.45 (m, 2H, Ar); δ 8.8 (s, 1H, Ar);δ 10.9 (s, 1H, Ar-OH)
10	3-OH acetophenone	3-Benzoyl 3-OH acetophenone	240	δ 2.8 (s, 3H, CH_3); δ 7.45 (s, 1H, Ar); δ 7.6–7.8 (m, 5H, Ar), δ 7.95 (s, 2H, Ar); δ 10.05 (s, 1H, Ar)

compounds are given in Table II. Aromatic compounds such as aldehydes and ketones generally underwent benzoylation even under kinetic conditions with VHR and afforded good yields of products. It is of interest to note that only OHAP underwent cyclization followed by benzoylation and afforded benzoyl chromone derivatives. Meta and para hydroxy benzophenones (3-OHAP, and 4-OHAP) did not undergo cyclization but afforded benzoyl derivatives. The difference in the reactivity of OHAP from 3-OHAP and 4-OHAP could be attributed to the fact that the –OH group is far from the carbonyl (main) functional group, which is favorable to form a stable ring through cyclization. A general VH benzoylation reaction is presented in Scheme 1.



Scheme 1 VH benzoylation of benzaldehydes and acetophenones, where VHR = benzamide/$SOCl_2$ or benzamide/$POCl_3$; Y = CHO, $COCH_3$; X = electron-donating or -withdrawing groups.

RESULTS AND DISCUSSION

Salient Features of the Kinetic Study

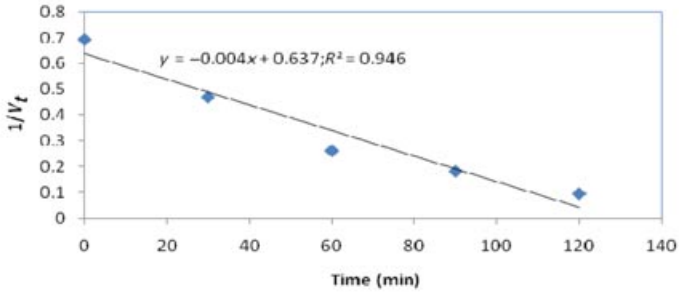
Under pseudo–first-order conditions, viz., [VHR] << [substrate], plots of ln V_t vs. time have been found to be linear with negative slope indicating first order with respect to [VHR] (Fig. 1A). From the slopes of the plots k' was calculated. However, under equimolar conditions ([VHR] = [substrate]), the plots of $1/V_t$ vs. time have been found to be linear with positive slopes and an intercept on the ordinate depictingover all second-order reaction (Fig. 1B). Activation parameters for these reactions are computed from Eyring's plots (Fig. 1C) and presented in Tables III and IV. (The rate constant data for the first-order kinetics are presented in Tables S.1 and S.2, and the data for the evaluation of second-order rate constants at various temperatures are compiled in Tables S.3–S.10 as Supporting Information.)

Formation and Reactive Species of VH Adduct

Reaction kinetics could be used as one of the most efficient tools to propose the mechanism of a

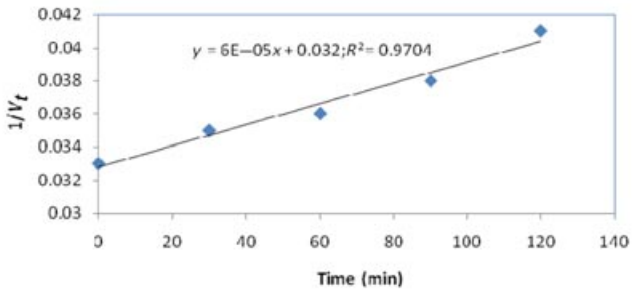
Time (min)	Titer (mL)	$\ln V_t$
0	2	0.693
30	1.6	0.470
60	1.3	0.262
90	1.2	0.182
120	1.1	0.095

(A)



Time (min)	Titer (mL)	$1/V_t$
0	30.1	0.033
30	28	0.035
60	27.3	0.036
90	25.9	0.038
120	24	0.041

(B)



$10^3/T$	$\ln(k'/T)$
3.300	−15.1495
3.195	−14.4476
3.096	−13.7859
3.003	−13.3911

(C)

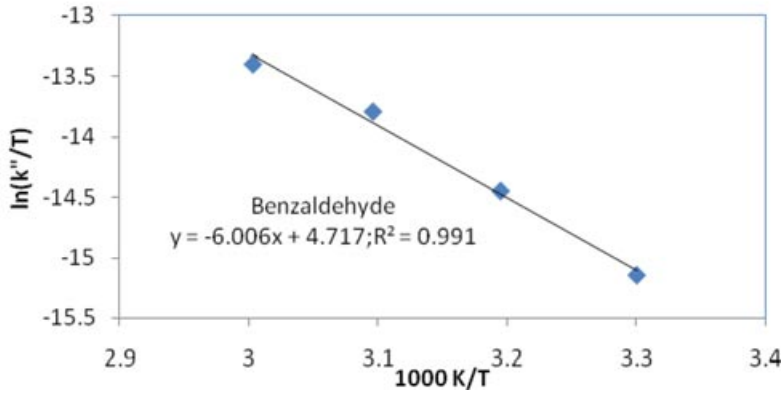


Figure 1 Kinetics and Eyring plots for VH benzoylation of benzaldehyde using (benzamide + $SOCl_2$). (A) [VHR] = 0.010 mol dm^{-3}; [Benzaldehyde] = 0.100 mol dm^{-3}; solvent = MeCN; temperature = 300 K; (B) [VHR] = 0.100 mol dm^{-3};[benzaldehyde] = 0.100 mol dm^{-3}; solvent = MeCN; temperature = 300 K; (C) the temperature effect.

chemical reaction. However, it is essential to gain an insight into the nature of reactive species that are present in the reaction mixture during the course of study to propose the mechanism. On the basis of elemental analysis [1a], Vilsmeier and Haack indicated that 1 mol of oxychloride [$POCl_3$] reacts with one of the amides to form an intermediate adduct, which is responsible for formylation. Since then different opinions prevailed for the formulations of the reactive VH adduct species [4–9]. Infrared spectroscopic studies of Arnold and Holy

Table III Temperature-Dependent Rate Constants and Activation Parameters for VH Benzoylation Reactions with Benzaldehydes Benzamide + $POCl_3$

		k'' (10^5 mol dm^{-3} s^{-1})		Benzamide + $SOCl_2$			Benzamide + $POCl_3$		
Substrate	Temperature (K)	Benzamide + $SOCl_2$	Benzamide + $POCl_3$	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta G^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (JK^{-1}mol^{-1})	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta G^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J K^{-1}mol^{-1})
Benzaldehyde	303	7.80	7.99	49.9	38.1	39.2	49.4	38.1	37.6
	313	16.5	16.7						
	323	33.3	33.8						
	333	51.0	50.1						
Salicylaldehyde	303	10.0	9.90	55.6	36.8	62.8	30.6	37.7	−23.5
	313	26.7	13.3						
	323	51.0	18.7						
	333	83.4	33.3						
4-OH benzaldehyde	303	6.67	8.34	19.1	38.1	−63.4	48.2	37.9	34.3
	313	11.7	16.7						
	323	13.3	33.3						
	333	15.0	50.0						
4- OMe benzaldehyde	303	5.02	5.00	50.0	39.5	35.1	49.4	39.4	33.2
	313	8.99	10.0						
	323	16.7	16.7						
	333	33.3	33.5						
4-Cl benzaldehyde	303	5.33	5.67	66.9	39.2	92.4	35.3	31.9	−11.3
	313	16.7	11.7						
	323	33.3	15.2						
	333	66.7	23.3						
4-Br benzaldehyde	303	7.99	3.33	49.4	38.3	37.1	41.2	40.4	2.60
	313	15.0	5.45						
	323	28.7	8.33						
	333	51.0	16.7						
4-Nitro benzaldehyde	303	5.33	6.67	60.3	39.0	71.1	61.1	38.7	74.8
	313	16.7	16.7						
	323	33.3	33.3						
	333	51.0	66.7						
Cinamaldehyde	303	9.33	10.0	51.8	37.9	46.2	54.3	39.0	51.1
	313	18.3	16.7						
	323	33.3	50.0						
	333	66.7	66.7						

Table IV Temperature-Dependent Rate Constants and Activation Parameters for VH Reactions with Acetophenones

		k'' (10^5 mol dm^{-3} s^{-1})		Benzamide + $SOCl_2$			Benzamide + $POCl_3$		
Substrate	Temperature (K)	Benzamide + $SOCl_2$	Benzamide + $POCl_3$	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta G^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (JK^{-1}mol^{-1})	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta G^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J K^{-1}mol^{-1})
Acetophenone	303	26.7	3.34	23.9	35.0	−37.1	61.1	40.0	69.1
	313	33.3	8.33						
	323	51.0	16.7						
	333	66.7	33.3						
2-hydroxy acetophenone	303	5.79	3.56	44.6	39.1	18.3	74.1	40.2	113
	313	10.0	10.0						
	323	15.0	33.3						
	333	33.3	50.0						
4-hydroxy acetophenone	303	5.67	4.34	67.6	39.4	94.1	30.4	21.3	30.2
	313	12.5	6.67						
	323	33.3	11.7						
	333	66.7	13.4						
4-methyl acetophenone	303	13.3	10.0	72.1	37.9	114	48.3	38.0	34.3
	313	16.7	11.7						
	323	66.7	13.4						
	333	166.	15.0						
3-hydroxy acetophenone	303	8.34	8.37	64.8	38.5	87.7	29.1	19.1	33.3
	313	18.0	16.7						
	323	33.3	33.3						
	333	100.	50.1						
4-Bromo acetophenone	303	13.3	4.76	36.8	37.1	−1.00	8.60	37.2	−95.2
	313	16.7	8.33						
	323	33.3	11.7						
	333	51.0	15.2						
4-Nitro acetophenone	303	7.56	7.89	38.4	38.2	0.500	49.8	38.2	38.7
	313	13.4	16.7						
	323	20.7	33.4						
	333	33.4	50.1						

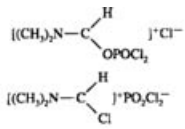
[5a], electronic spectroscopic and ^{31}P NMR spectroscopic studies results of Alunni, Marino, Martin, and others [6–8], together with the kinetic studies reported from our laboratory [9] on VH adducts revealed that a number of covalent, ionic, and ion-pair species of VH-adduct ((I)–(VI)) could exist in solution. The species are given by taking DMF and $POCl_3$ as a specific example:

$[(CH_3)_2N{=}CHCl]^+[OPOCl_2]^-$ (I)

$[(CH_3)_2N{=}CH{-}OPOCl_2]^+Cl^-$ (II)

$[(CH_3)_2N{-}CHClOPOCl_2]$ (III)

$[(CH_3)_2N{=}C^+HCl]$ (IV)



(V)

(VI)

Mechanism of Benzoylation Reactions Involving Benzamide–Oxychloride [$POCl_3$ or $SOCl_2$] Adduct

Benzamide being a Lewis base is capable of forming VH adduct due to the interaction with Lewis acids such as $POCl_3$ or $SOCl_2$. In view of this, the reaction mechanism operating with benzamide/$POCl_3$ may not differ much from that with DMF/$POCl_3$. Accordingly important VH species with benzamide /$POCl_3$ could be written as shown in (VII)–(X):

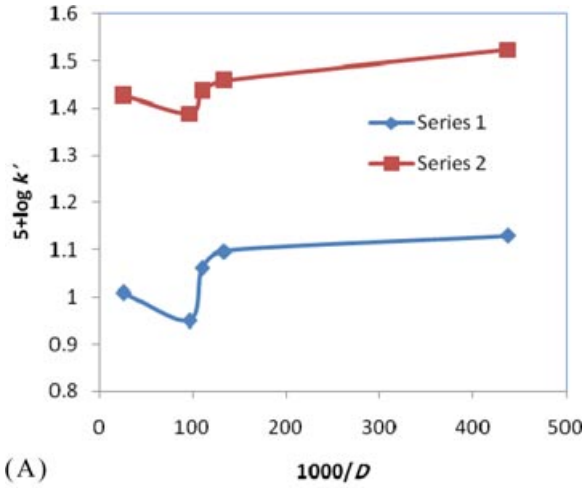
$$[H_2N = CPhCl] + [OPOCl_2]^- \quad \text{(VII)}$$

$$[H_2N = CPh - OPOCl_2] + Cl^- \quad \text{(VIII)}$$

$$[H_2N = CPhClOPOCl_2]^+ \quad \text{(IX)}$$

$$[H_2N = CPhCl]^+ \quad \text{(X)}$$

From the effect of dielectric constant (D) on the reactivity studies, we have noticed that the second-order rate constants followed an irregular trend with a variation of dielectric constant. The rate constants followed an order: benzene > ACN > THF > DCE > DCM. The rate constant data were cast into semi-quantitative plots as suggested by Amis [15a] and Kirkwood [15b] to have an insight into the nature of reactive VH species, taking part in the slow step. The plots of log rate constant (log k'') as a function of (l/D), (D – 1)/ (2D + I) have been found to be nonlinear (Figs. 2A and 2B) with "well"-shaped curves. These findings are similar to our earlier kinetic observations obtained for VH formylation reactions [9]. Therefore, the results could be interpreted in similar lines. The relatively higher rates in DCE medium than those of MeCN medium could be reasonably explained by considering $[H_2N{=}CPhCl]^+$ as reactive species in low dielectric DCE medium since the cationic VH species was electrophilically more reactive than ion pair ($[H_2N{=}CPh{-}OPOCl_2]^+$ Cl^-) VH species. Recent theoretical calculations (ab initio and DFT) of Clark et al. [16] revealed that a cationic form of VH species is more reactive than other forms of VH species. Thus, on the basis of the foregoing discussion coupled with the ab initio and DFT calculations of Clark et al. [16], a general mechanism could be given as shown in the following steps:



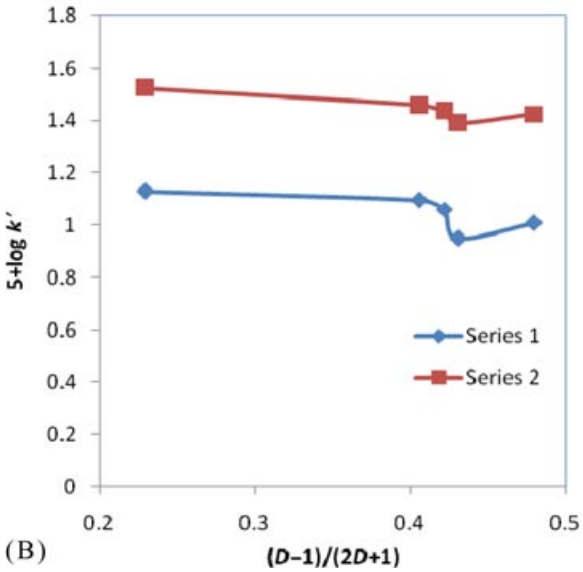
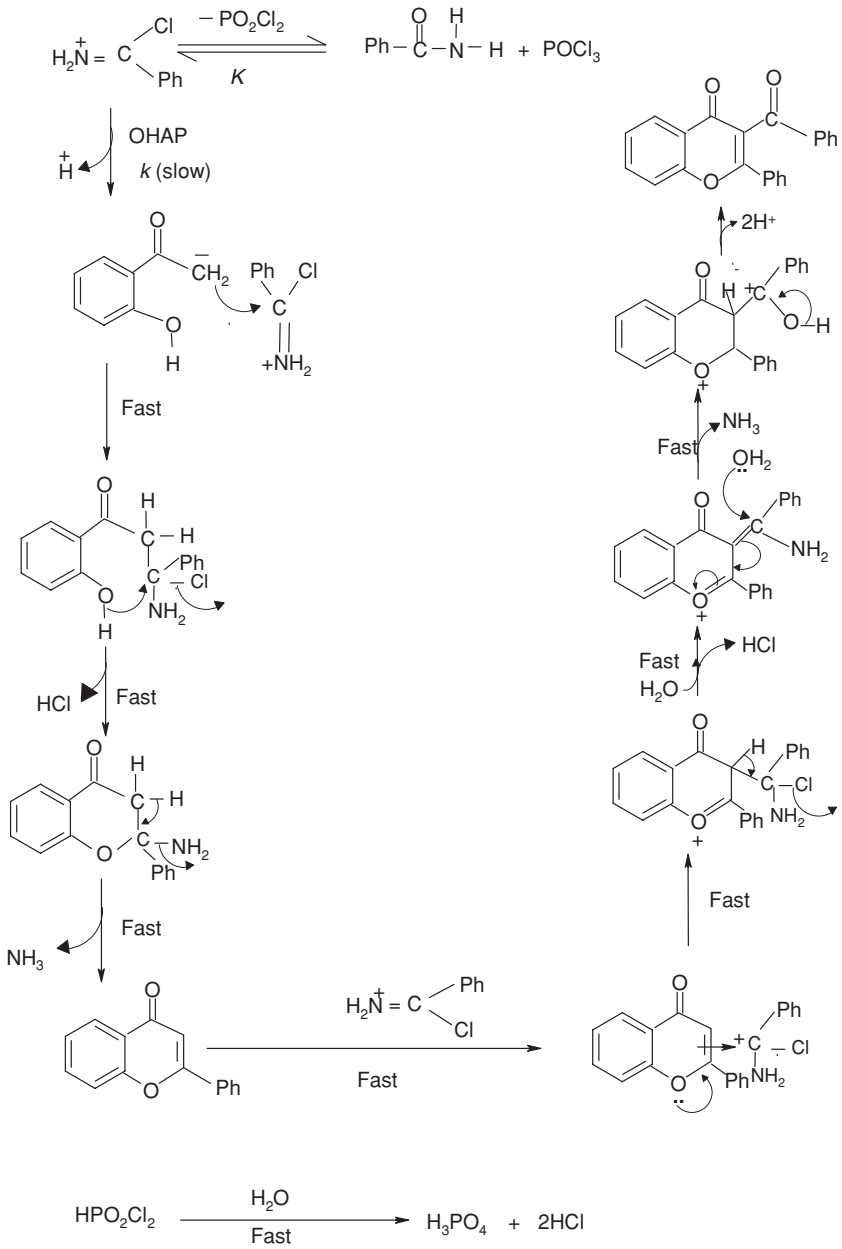


Figure 2 (A) Plots of log k'' vs. (1/D) for VH benzoylation reactions. (B) Plots of log k'' vs. (D − 1)/ (2D + 1)) for VH benzoylation reactions.

$$\text{Benzamide} + POCl_3 \rightleftharpoons \text{VH adduct}$$

$$\text{VH adduct} + \text{Substrate} \xrightarrow[\text{Slow}]{k} \text{Products}$$

where VH adduct represents $[H_2N{=}CPhCl]^+$ in DCE (low dielectric medium) and ion pair



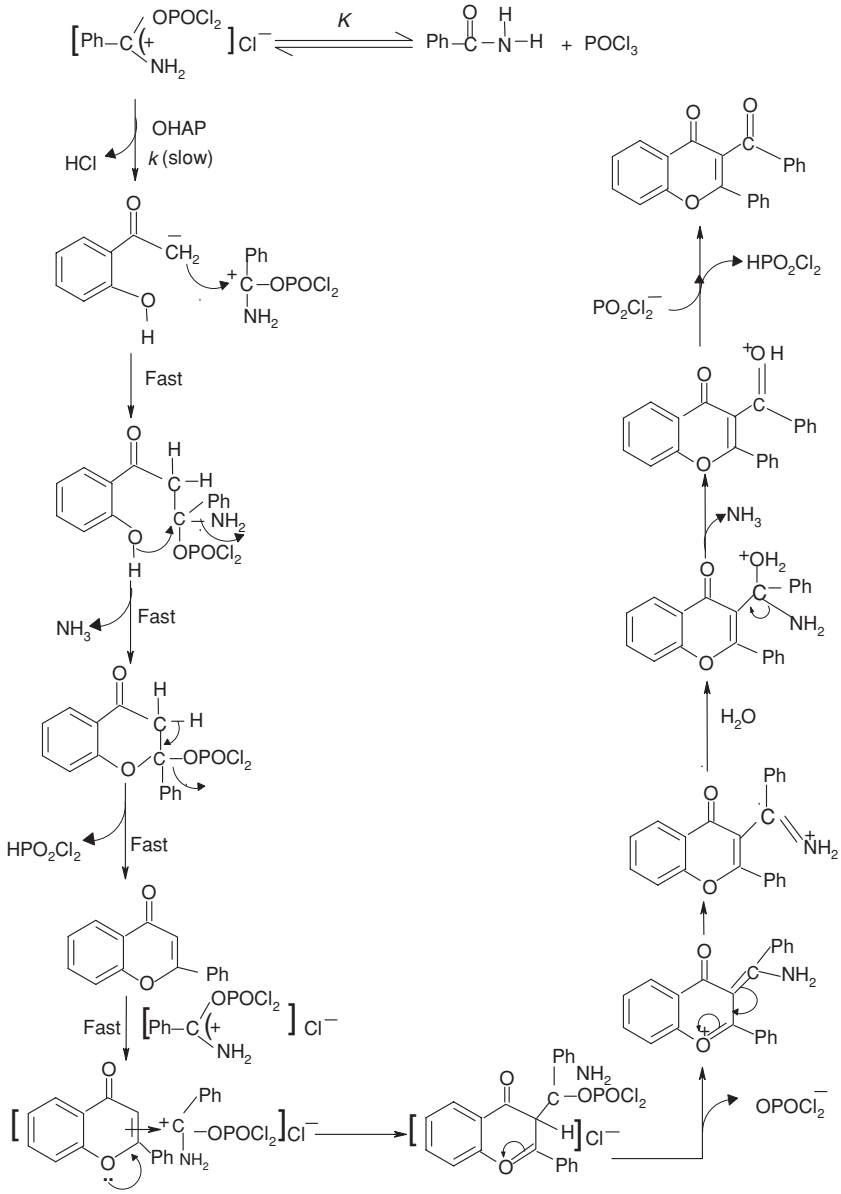
Scheme 2 Mechanism of VH cyclization of 2-hydroxy acetophenones followed by benzoylation.

($[H_2N{=}CPh{-}OPOCl_2]^+ Cl^-$) in MeCN (high dielectric medium).

Products of the reaction have been isolated under kinetic conditions and analyzed by standard spectroscopic procedures. Benzoyl derivates have been found to be the products irrespective of nature of VHR used. For the above scheme, the rate law comes out as

$$\frac{-\mathrm{d}\,[\text{Substrate}]}{\mathrm{d}t} = k\,[\text{Substrate}]\,[\text{VH adduct}]$$

This rate-law shows second-order kinetics with a first-order dependence on [substrate] and also on [VH adduct] and is in accordance with the proposed mechanism. It is of interest to note that OHAP underwent cyclization followed by benzoylation to afford benzoyl chromone. A detailed mechanism of VH reactions with OHAP is given in Schemes 2 and 3. With other substrates, the mechanistic path is shown in Scheme 4. It is of interest to note that free energies of activation ($\Delta G^{\ddagger}$) for a series of substrates (benzaldehydes and acetophenones) show by and large similar magnitude and thus indicate a similar type of mechanism to be operative. Data presented in Tables III and IV reveal either positive or small negative entropies of activation ($\Delta S^{\ddagger}$),

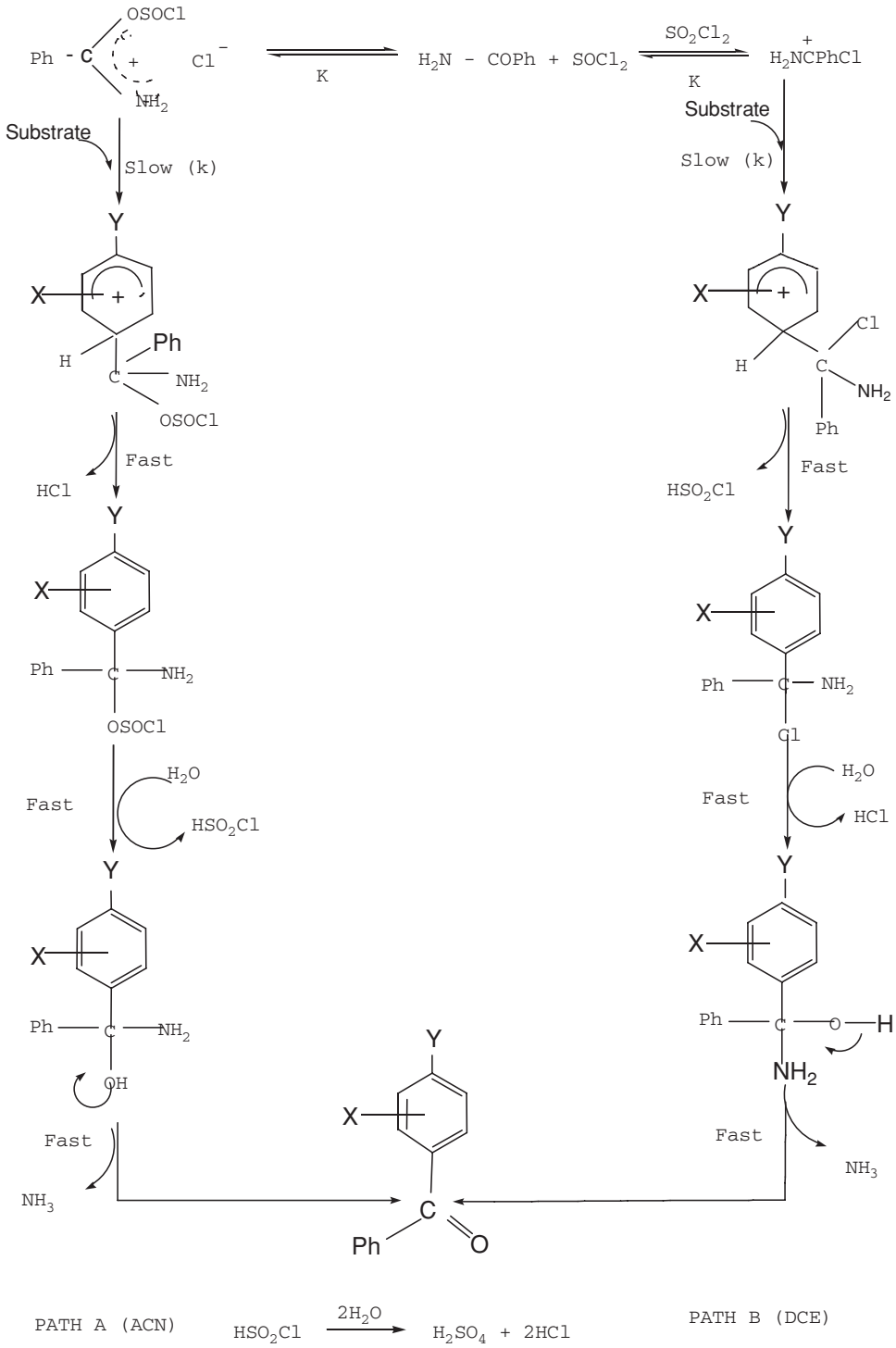


Scheme 3 Mechanism of VH cyclization of 2-hydroxy acetophenones followed by benzoylation.

which may probably indicate greater rearrangement in the transition state. The plots between ($\Delta H^{\ddagger}$) vs. ($\Delta S^{\ddagger}$) for both (benzamide/$SOCl_2$) and (benzamide/$POCl_3$) systems were perfectly linear with good to excellent correlation coefficients (R^2 values), which could be seen from Figs. 3–6. According to Leffler's theory [17] such linearity indicates compensation of both enthalpy and entropy factors in controlling the reactions in a series of structurally related substrates that undergo the same change or when the reaction conditions for a single substrate are changed in a systematic way. Quantitatively, the *enthalpies* and *entropies of activation* sometimes are said to satisfy the following equation (Leffler's equation):

$$\Delta H^{\ddagger} = \beta \Delta S^{\ddagger} + \Delta H_0{}^{\ddagger}$$

The slope of the Leffler's plot represents the "isokinetic temperature" (β, the temperature (T)) at which all members of a series obeying the isokinetic relationship react at the same rate. However, the supposed isokinetic relationships as established by direct correlation of $\Delta H^{\ddagger}$ with $\Delta S^{\ddagger}$ are often spurious, and the calculated value of β is meaningless, because errors in



Scheme 4 Mechanism of VH benzoylation of benzaldehydes and acetophenones, where R = C_6H_5 when VHR = (benzamide + $SOCl_2$ or $POCl_3$); Y = CHO, $COCH_3$; X = electron-donating or electron-withdrawing groups.

$\Delta H^{\ddagger}$ *lead* to compensating errors in $\Delta S^{\ddagger}$.· Evaluation of isokinetic temperature (β' from Leffler's theory has been criticized by Exner, Peterson, Cornish-Bowden, and others [18–20]. In view of this large criticism, we can at best say that the linearity of Leffler's plots coupled with almost similar magnitude of free energies of

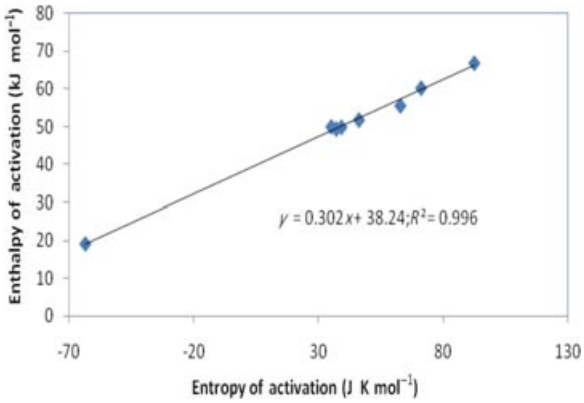


Figure 3 Leffler's plots of $\Delta H^{\ddagger}$ vs. $\Delta S^{\ddagger}$ for VH benzoylation of benzaldehydes using benzamide and $SOCl_2$.

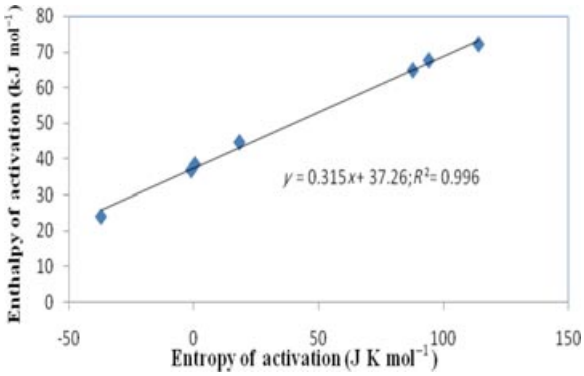


Figure 4 Leffler's plots of $\Delta H^{\ddagger}$ vs. $\Delta S^{\ddagger}$ for VH benzoylation of acetophenones using benzamide and $SOCl_2$,

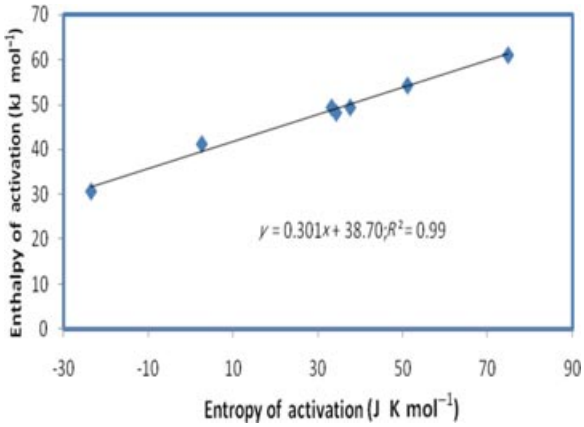


Figure 5 Leffler's plots of $\Delta H^{\ddagger}$ vs. $\Delta S^{\ddagger}$ for VH benzoylation of benzaldehydes using benzamide and $POCl_3$.

activation ($\Delta G^{\ddagger}$) presented in Tables III and IV indicate a similar type of mechanism is operative in the present study.

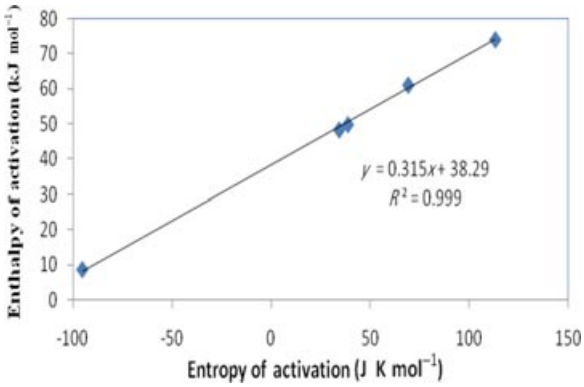


Figure 6 Leffler's plots of $\Delta H^{\ddagger}$ vs. $\Delta S^{\ddagger}$ for VH benzoylation acetophenones using benzamide and $POCl_3$.

CONCLUSIONS

In summary, the authors have successfully demonstrated the VH reaction with benzaldehydes and acetophenones in ACN medium. Kinetics of the VH benzoylation reactions follow the second-order reaction kinetics and afford benzoyl derivatives under kinetic conditions also irrespective of the nature of oxychloride used for the preparation of VHR along with benzamide. The present finding is advantageous to understand the nature of reactive species as well as the mechanism of benzoylation.

The authors thank CSIR, New Delhi, India, for financial support in the form of the emeritus scientist award to Professor P. K. Saiprakash.

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