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Kinetic Studies on Base-Catalyzed Condensation of Benzaldehyde, *p*-Hydroxybenzaldehyde, *p*-Dimethylaminobenzaldehyde and *N,N*-Dimethyl-*p*-nitrosoaniline with 1-Phenyl-3-methyl-2-pyrazolin-5-one

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The condensation reaction of 1-phenyl-3-methyl-2-pyrazolin-5-one (*I*) with benzaldehyde (*II*), *p*-hydroxybenzaldehyde (*III*), *p*-dimethylaminobenzaldehyde (*IV*) and *N,N*-dimethyl-p-nitrosoaniline (*V*) in ethanolic media containing piperidine as base catalyst was investigated spectrophotometrically at 10—50 °C. It was found that these reactions followed over-all second-order kinetics, first-order with respect to each of the reactants. The results suggest that the rate determining step involves the dehydration of the aldol intermediate (*XII*). From the dependence of the rate constants on temperature, the thermodynamic parameters of activation were determined and the mechanism which is consistent with the obtained data is discussed.

INTRODUCTION

Although considerable amount of work was done on the condensation reactions of arylidene and azomethine dyes of pyrazolone,[1-4] due to the wide application of these compounds, no attention was focused on the kinetics and mechanisms of these reactions. In this work the rate constants of the reactions and their energies of activation were determined and discussed in terms of the molecular structure of the aromatic aldehydes (*II—IV*) and the nitroso compound (*V*). The activation parameters ($\Delta G^{\neq}$, $\Delta H^{\neq}$ and $\Delta S^{\neq}$) and frequency factor (*A*) of the reactions were calculated and discussed to gain more evidence concerning the reaction mechanism. The effect of solvents of different dielectric constants, such as chloroform, isopropyl alcohol and ethyl alcohol, on the reaction rate of pyrazolone (*I*) with aldehyde (*IV*) was also investigated.

EXPERIMENTAL

Materials and Method

1-Phenyl-3-methyl-2-pyrazolin-5-one (*I*)[5] and its 4-arylidene (azamethine) derivatives[1] (*VI—IX*) were prepared according to the methods described earlier and recrystallized several times from ethanol. Aromatic aldehydes (*II—IV*), *N,N*-dimethyl-*p*-nitrosoaniline (*V*) and piperidine (BDH) were purified according to the recommended procedures. Spectral grade quality solvents (BDH or E. Merck) were used. The absorption spectra were recorded on a Shimadzu UV-200 S double beam spectrophotometer, using 1 cm matched silica cells. The rate of reaction in all cases was followed up to ≥ 60% of the initial concentrations.

Kinetic Measurements

Equal volumes of freshly prepared solutions (0.1 M) of pyrazolone (*I*), aromatic aldehyde (*II—IV*) or nitrosocompound (*V*) were transferred to a 25 ml dark flask to which piperidine was added and the volume of the reaction mixture was completed to the mark with the spectral grade quality solvent. The initial concentrations of (*I*) and other reactants (*II—V*) were usually 6.0×10^{-3} M whereas piperidine concentration was 0.52 M. The kinetic experiments were carried out in a temperature-controlled (±0.1 °C) water bath and the reaction was followed spectrophotometrically.

TABLE I

The λ_{max} and ε_{max} Values of Different Pyrazolone Derivatives in the Presence, of the Same Amount of Piperidine as in the Reaction Mixture

Derivative	Solvent					
	EtOH		isopropyl alcohol		$CHCl_3$	
	λ_{max} (nm)	ε_{max} (mole^{-1} cm^2)	λ_{max} (nm)	ε_{max} (mole^{-1} cm^2)	λ_{max} (nm)	ε_{max} (mole^{-1} cm^2)
4-(Benzylidene)-1-phenyl-3-methyl-2-pyrazolin-5-one (*VI*)	367	9.411	—	—	—	—
4-(*p*-Hydroxybenzylidene)-1-phenyl-3-methyl-2-pyrazolin-5-one (*VII*)	479	25.144	—	—	—	—
4-(*p*-dimethylaminobenzylidene)-1-phenyl-3-methyl-2-pyrazolin-5-one (*VIII*)	460	70.198	460	27.769	440	49.119
4-[(*p*-dimethyl-amino)phenylimino]-1-phenyl-3-methyl-2-pyrazolin-5-one (*IX*)	519	25.371	—	—	—	—

Aliquots of the reaction mixture were withdrawn at different time intervals and diluted rapidly to the definite volume by adding the same solvent, then the absorption was recorded at λ_{max} of the pyrazolone derivative. The amounts of the produced pyrazolone derivative at different time intervals were evaluated applying Beer's law. The ε_{max} was determined as the slope of the plot of absorbance versus [pyrazolone derivative]. The λ_{max} and ε_{max} values of different pyrazolone derivatives (*VI—IX*) in the presence of the same amount of piperidine as in the reaction mixture are given in Table I.

RESULTS AND DISCUSSION

Effect of Piperidine

The reaction rate of pyrazolone (*I*) with aldehyde (*IV*) at 25 °C was found to be independent of the concentration of piperidine ranging from $(0.6—68) \times 10^{-2}$ M, i. e., the reaction order is zero with respect to piperidine. This indicates that piperidine does not enter into the rate determining step and its concentration is not involved into the rate equation under our experimental conditions. A similar finding was observed by Issa *et al.*[6] in the condensation of α-picoline ethiodide with vaniline, *p*-hydroxybenzaldehyde, *p*-*N*-dimethylbenzaldehyde and salicylaldehyde.

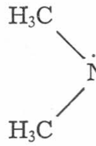
Rate Law

The rate was found to be of the first order in each of the reactants of pyrazolone (*I*) and the aromatic aldehyde (*II*—*IV*) or the nitroso compound (*V*). The initial kinetic data obtained were analyzed using the integrated second order expression:

$$k_{obst} = \left(\frac{1}{(a - x)} - \frac{1}{a} \right) \qquad (1)$$

where k_{obs} are the apparent second order rate constants of such reactions, a is the initial concentration of pyrazolone (*I*) or compounds (*II*—*V*) and $(a—x)$ is the concentration of such reactants at any time t.

Plots of $\left(\frac{(a—x)}{1} — \frac{1}{a} \right)$ against time for these reactions yield straight lines passing through the origin up to the point where the reactions were about $80^{0}/_{0}$ of completion. These linear rate plots indicate that the reactions follow second-order kinetics, being a first-order with respect to each of the reactants. The values of the apparent second-order rate constants k_{obs} were obtained from the slope of these lines. Such plots for different temperatures are shown in Figure 1. In certain cases, slight curvature was noted in the initial stages of the reactions, which may be attributed to inefficient mixing of the reactants. The experiments were performed in duplicate at each temperature and the average rate constants were calculated. The rate constants, k_{obs}, at 30 °C, the activation energies. $\Delta E^{\neq}$, and the frequency factors, *A*, which were determined from the Arrhenius plots, are listed in Table II. The frequency factor values, *A*, are in good agreement with those reported for bimolecular reactions.[7]

The rate of the reaction of pyrazolone (*I*) with aldehyde (*IV*) is much greater than that with the nitroso compound (*V*). This may be attributed to the increased polarization of the carbonyl group relative to the nitroso one, which facilitates the nucleophilic attack of the intermediate (*X*) on the polarized group of the aldehyde (*IV*) more than on the polarized group of compound (*V*) as shown in step (b) of Scheme 1. Furthermore, the reaction rate of pyrazolone (*I*) with p-hydroxybenzaldehyde (*III*) is greater than that with *p*-dimethylaminobenzaledehyde (*IV*). Here, the withdrawing character of (—CHO) group in *p*-hydroxybenzaldehyde may increase the acidity of the phenolic (—OH) group. Then, the presence of piperidine as base catalyst facilitates the deprotonation of such a (—OH) group leaving a negative charge on oxygen. The electron repelling character of the residual negative charge ($O^{\ominus}$—) on compound (*II*) is more effective than that of the dimethyl amino group ( $(H_3C)_2\ddot{N}$—). This is reflected in the higher values of k_{obs} for the reaction (*I*)—(*III*) than those of the reaction (*I*)—(*IV*).

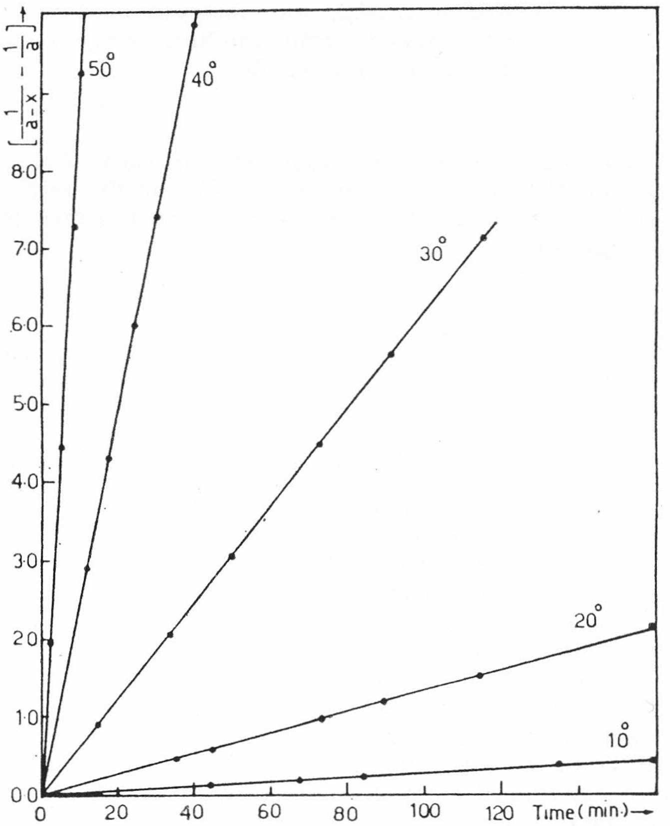


Figure 1. Second order plots of $\left[\frac{1}{a-x}-\frac{1}{a}\right]$ *versus* time for the reaction of pyrazolone (*I*) with *p*-dimethyl-aminobenzaldehyde (*IV*) in EtOH.

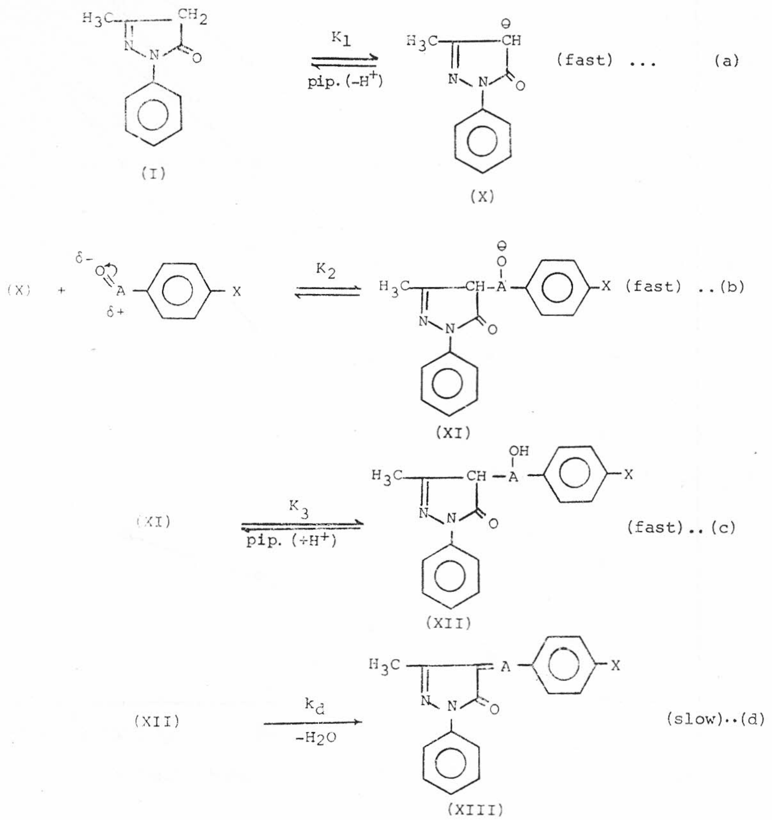
TABLE II

Rate Constants (k_{obs}) *at 30 °C, Activation Energies* ($\Delta E^{\ddagger}$), *Frequency Factors* (A) *and Thermodynamic Parameters of Activation for the Condensation of Pyrazolone* (I) *with Compounds* (II—V)

Compound	Solvent	$k_{obs} \times 10^4$ (litre mole^{-1} sec^{-1})	$\Delta E^{\ddagger}$* (kJ·mole^{-1})	log A*	$\Delta G^{\ddagger}$** (kJ·mole^{-1})	$\Delta H^{\ddagger}$** (kJ·mole^{-1})	$\Delta S^{\ddagger}$** (J·mole^{-1} deg^{-1})
II	EtOH	5.28 ± 0.05	68.29	56.46	92.75	65.60 ± 1.34	—91.12 ± 2.11
III	EtOH	35.21 ± 0.13	103.34	85.23	88.57	100.72 ± 1.98	40.76 ± 0.93
IV	EtOH	10.27 ± 0.20	111.70	88.99	91.90	108.61 ± 2.21	56.10 ± 1.12
	Isopropyl alcohol	12.24 ± 0.15	78.37	65.28	90.81	75.93 ± 1.41	—49.93 ± 0.98
	$CHCl_3$	133.40 ± 1.09	31.53	35.84	84.12	28.77 ± 0.22	—185.76 ± 3.25
V	EtOH	2.06 ± 0.01	71.51	57.04	95.11	69.68 ± 1.31	—85.34 ± 1.98

* Calculated using Arrhenius equation.
** Calculated using Eyring equation.

SCHEME 1



* (A) = (CH) in compounds (*II—IV*);
= (N) in compound (*V*).

** (X) = (H) in compound (*II*);
= in compound (*III*);
= $N(CH_3)_2$ in compounds (*IV* and *V*).

*** pip. = piperidine.

The rate constants for the reactions of pyrazolone (*I*) with different substituted benzaldehyde (k_{obs}) should be related to that for the reaction with unsubstituted benzaldehyde $(k_{obs})_o$ by the Hammett relation — log $[(k_{obs})/(k_{obs})_o] = \sigma_i \rho$[8], where σ_i is a substituent constant characteristic of a substituent i and σ is the reaction constant. The log k_{obs} values of different aldehydes (in ethanol at 30 °C) are plotted against the corresponding σ_i-values[9,10] in Figure 2. The slope of the plot gives a reaction constant value $\rho = -1.58$. The negative ρ value indicates that these reactions are aided by electron donating groups to the benzene ring.[11]

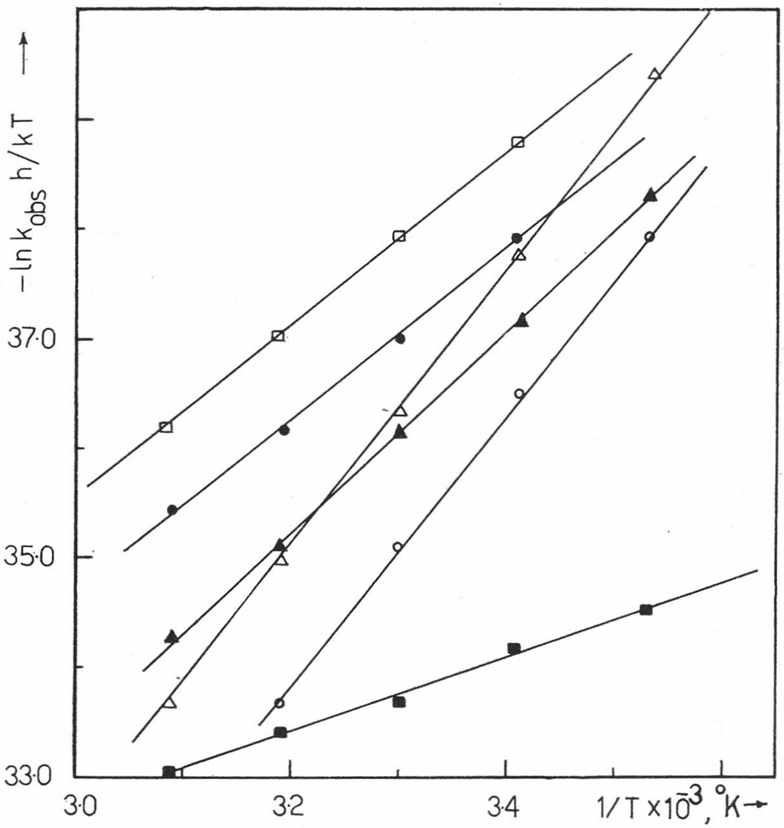


Figure 2. Plot of log k_{obs} *versus* substituent constant (σ).

Reaction Mechanism

It is generally agreed[12,13] that the present reactions proceed through a carbanion intermediate, as shown in Scheme 1. The first step involves the formation of the carbanion (*X*) and such an ionization step is normally fast.[14] The second step involves the addition of the polarized aldehydic carbonyl group (or polarized nitroso group) to the product (*X*), forming the aldol anion (*XI*) and expected to be fast. The third step involves a charge neutralization reaction to yield the aldol intermediate (*XII*) and is also very fast.[13] The last dehydration step involves the cleavage of one C—H and one A—OH bond together with the formation of C=A bond and is expected to require higher energies. Since the last step is the only one involving cleavage of bonds, it is likely to be considered as the rate-determining step and consequently leads to the following rate equation

$$Rate = -\frac{d\,[XII]}{dt} = k_d\ [XII] \tag{2}$$

Substituting the equilibrium constants K_1, K_2, and K_3 defined by Eqs. (a), (b), and (c) in Scheme 1 into Eq. (2), yields

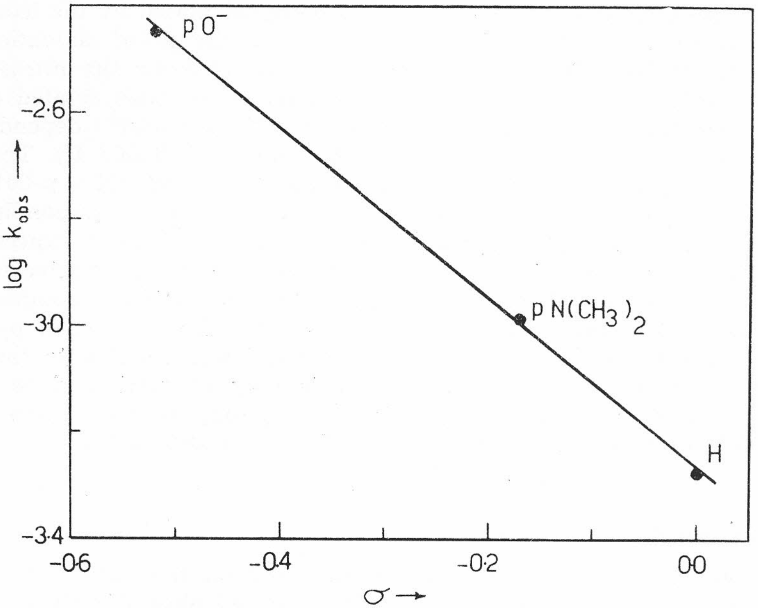


Figure 3. Plots of —ln k_{obs} h/kT *versus* $1/T$.

for *II*, EtOH (●)
III, EtOH (○)
IV, EtOH (△), isopropyl alc (▲), $CHCl_3$ (■)
V, EtOH (□)

$$Rate = k_d K_1 K_2 K_3 \text{ [pyrazolone] [aldehyde/nitroso compound]} \tag{3}$$

From Eq. (3), one can conclude that

$$k_{obs} = k_d K_1 K_2 K_3 \tag{4}$$

Eq. (3) shows that the reaction follows second order kinetics, first order with respect to both pyrazolone and aldehyde or nitroso compound. The apparent second-order rate constant, k_{obs}, is therefore a product of the three equilibrium constants of the first three steps (K_1, K_2 and K_3, respectively) and the rate constant k_d of the fourth step. Unfortunately, the second order rate constant, k_d, could not be evaluated since no data are available for the equilibrium constants K_1, K_2, and K_3. Moreover, many attempts were made to evaluate these equilibrium constants from the experimental data but the results were not encouraging for a satisfactory explanation.

Effect of Temperature

The rate of the reactions was studied over a temperature range from 10 to 50 °C in ethanolic media. The results are summarized in Table II. The experimentally observed rate constants k_{obs} were applied to the rate-determining step because there was no way of calculating k_d in Eq. (4). As shown in Figure 3, the plot of $-\ln \frac{kT}{h} k_{obs}$ versus $\frac{1}{T}$ of Eyring equation,[15] gave straight lines from which the activation parameters were calculated. The values of the activation parameters of k_{obs} were calculated by the least square method, as shown in Table II. The free energy change of activation ($\Delta G^{\neq}$) shows a weak dependence on the nature of aldehyde or the nitroso group, indicating that there is no change in mechanism for such related series of reactions. On the other hand, the entropy of activation ($\Delta S^{\neq}$) depends on the type of substituent at the aldehydic compound (c. f. Table II). The higher $\Delta S^{\neq}$ values for (*IV*) [$X = p\text{-}N(CH_3)_2$] as compared to (*III*) [$X = p\text{-}OH$] or (*II*) [$X = H$], may indicate that the extent of solvation of the corresponding intermediate is less in the former than in the latter ones. This is expected since the higher electron donating character of ($—N(CH_3)_2$) group relative to (p-OH) or (—H) would favour charge delocalization, and the activated complex would be less solvated in this case. Also, $\Delta S^{\neq}$ values for the reaction of pyrazolone (*I*) with the nitroso compound (*V*) were much lower relative to the corresponding aldehyde (*IV*) (c. f. Table II). This may be attributed to the fact that the charge delocalization on [$>C^{+\delta}=O^{-\delta}$]group is more than that on [$—N^{+\delta}=O^{-\delta}$]group and the activated complex for compound (*IV*) is less solvated than that for compound (*V*).

Effect of Solvent

The solvent effect on the reaction rate and on the nature of the transition state was investigated using EtOH, isopropyl alcohol, $CHCl_3$ under the same experimental conditions. The results are also summarized in Table II. It is evident that the activation energy ($\Delta E^{\neq}$) increases with increasing the solvent dielectric constant in the order EtOH $>$ isopropyl alcohol $>$ $CHCl_3$.

The increase in both dielectric constant and solvating power of the medium will stabilize the lone pair of electrons on [$—\ddot{N}(CH_3)_2$]group through the hydrogen bond formed between the aldehyde and the solvent. This effectively depresses the combination rate with the carbanion (*X*) and decreases the formation rate of (*XI*) (c. f. Scheme 1). These factors lead to higher $\Delta E^{\neq}$ values. The high reaction rate observed when carrying out the reaction in $CHCl_3$ may be due to the low dielectric constant of this solvent and its low solvating power. This increases the mobility of the electron pair on [$—\ddot{N}(CH_3)_2$]group and increases the rate of formation of the corresponding derivative.

The thermodynamic parameters of activation $\Delta G^{\neq}$, $\Delta H^{\neq}$ and $\Delta S^{\neq}$ corresponding to the reaction of aldehyde (*IV*) with pyrazolone (*I*) in the various organic solvents used, are also collected in Table II. It is evident that, $\Delta G^{\neq}$ is independent of the solvent used, indicating that the reaction mechanism is also the same. Furthermore, $\Delta S^{\neq}$ values get more negative as the dielectric constant decreases. This may be attributed to the high random distribution of the solvent molecules around the activated complex.

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SAŽETAK

Kinetički studij bazno-katalizirane kondenzacije benzaldehida, *p*-hidroksibenzaldehida, *p*-dimetilaminobenzaldehida i *N,N*-dimetil-*p*-nitrosoanilina sa 1-fenil-3-metil-2-pirazolin-5-onom

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Primjenom UV spektroskopije proučavana je kinetika kondenzacije benzaldehida, *p*-hidroksibenzaldehida, *p*-dimetilaminobenzaldehida i *N,N*-dimetil-*p*-nitrosoanilina s 1-fenil-3-metil-2-pirazolin-5-onom u alkoholnom mediju i uz piperidin kao katalizator. Na temelju određenih kinetičkih i termodinamičkih parametara detaljno je prodiskutiran mehanizam reakcije.