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QUANTITATIVE KINETIC STUDY OF SALICYLIDENE-*p*-AMINOSALICYLIC ACID FORMATION

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The rate of formation of salicylidene-*p*-aminosalicylic acid has been investigated in the absence and presence of piperidine as a basic catalyst in ethanol medium. The reaction rate is followed spectrophotometrically by measuring the absorbance at $^{\lambda}$max. of the formed product. The rate-determining step is suggested to be the attack of amine on the aldehyde and not the elimination of water as previously suggested. The quantitative addition of piperidine, the buffer solutions and the temperature effect on the reaction rate were investigated and discussed.

Key words: Kinetic study. Salicylidene, *p*-Amino salicylic acid.

INTRODUCTION

The formation mechanism and the application of the Schiff bases derived from alphatic or aromatic amines with aldehydes are interesting and greatly understood by several investigators [1-5]. In the absence of a catalyst it is suggested that the mechanism follows the second-order kinetics and it occurs in two steps. The first is the addition of the aldehyde to the amine to give the unstable carbinolamine intermediate, the second step is the elimination of water to form the Schiff base and this is suggested to be the rate determining step [6-8].

Scanning the literature reveals a little information concerning the quantitative effect of piperidine as a basic catalyst in the formation of the Schiff bases. Thus, the experiments reported here are aimed to investigate the effect of piperidine concentration on the order and the rate of the reaction. The study is extended to illustrate the effect of universal buffer solutions and temperature on the reaction rate.

EXPERIMENTAL

Material and solution. chemicals used in all experiments were of A.R. grades. The ethanol used was of spectral grade (merck). The universal buffer series was prepared according to Britton [9].

Stock solutions (0.5 mol.l^{-1}(1) of each of salicylaldehyde, *p*-aminosalicylic acid and piperidine were prepared by dissolving accurately weighed amounts in ethyl alcohol.

Procedures

Reaction rate measurments. Appropriate amounts of salicylaldehyde, *p*-aminosalicylic acid and piperidine were introduced into three glass-stoppered test tubes. Then the tubes were placed in an Ultrathermostat (HAAK NB2) until the temperature of the solutions and that of the thermostat attained a constant within ± 0.2°. The required volumes of reactants were mixed rapidly in a 25 ml measuring flask and completed with ethanol. The instant of mixing was taken as the zero time.

The reaction was followed spectrophotometrically by measuring the absorbance of the Schiff base formed at intervals time at its $^{\lambda}$max. = 450 nm. The amounts of the Schiff base produced in the reaction were calculated by applying Beers law, where $^{\in}$max. = 520 l.mol. $^{-1}$ cm.

The effect of salicylaldehyde and *p*-aminosalicylic acid concentration on the reaction rate was studied, by varying the initial concentration of both from $2x10^{-3}$ to $1x10^{-1}$ mil.l^{-1}. Piperidine as a reactant or basic catalyst was carried out from $1x10^{-4}$ to $1x10^{-3}$ mol.l^{-1} piperidine concentration. In all cases, the rate of the reaction was followed kinetically up to about 50% of initial concentration.

Reaction order determination. The order of the reaction with respect to each reactant in the absence of piperidine was determined applying the initial rate as a function of initial concentration method (10). This can be done by changing the concentration of the order reactant while the concentration of the other ones are constant and vice-versa. The order with respect to p-aminosalicylic acid was determined by keeping the salicylaldehyde concentration constant at $1x10^{-2}$ mol.l^{-1}, while varying the initial concentration of *p*-aminosalicylic acid from $2x10^{-3}$ to $2x10^{-2}$ mol.l^{-1}. The same technique was applied to determine the order of salicylaldehye. The effect of piperidine on the order and the rate of the reaction was

studied by keeping the concentration of the two reactants constant at $8x10^{-3}$ mil.l^{-1}, while the concentration of piperidine was changed from $1x10^{-4}$ to $1x10^{-3}$ mol.l^{-1}.

The absorbance measurements were carried out on a Shimadzu U.V. and visible recording-240 digital spectrophotometer. The pH values were measured with MV 87 digital pracitronic pH-meter accurate to ± 0.005 unit.

RESULTS AND DISCUSSION

Second-order rate plots for the reaction of *p*-aminosalicylic acid with salicylaldehyde in the absence of piperidine in ethanol medium at 25°C are linear passing through the origin. This behaviour indicates that the reaction follows second-order kinetics. Moreover, the second order character of the reaction has been cleared from the initial concentrations 2,4,6,8, and $10x10^{-3}$ mol.l^{-1} of both reactants (Fig.1). This figure shows that the $8x10^{-3}$ mol.l^{-1}

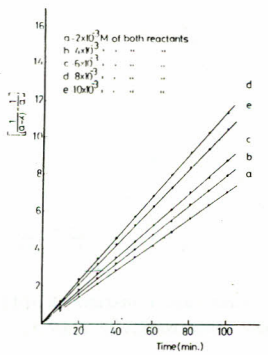
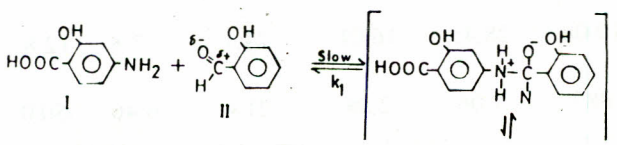
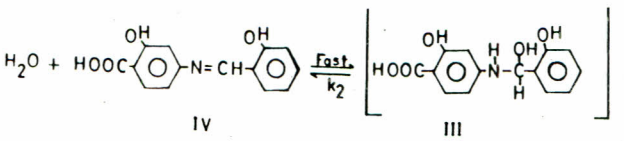


Fig. 1. Second-order plots of reaction between *p*-aminosalicylic acid and salicylaldehyde at different concentration at 25°

is the most suitable concentration for studying the reaction under the temperature range 20-40°C. The second-order rate constant (k) at the different temperatures studied was calculated from the slope of the [1/(a-x) – 1/a] versus (t) plots. The activation energy of the reaction was obtained from Arrhenius plots of the logarithms of the reaction rate constants against the reciprocal of the absolute temperature which yields a satisfactorily straight line from which the activation energy is evaluated. The other activation parameters are calculated (11) and listed in Table 2.

The following mechanism can be proposed for the formation of salicylidene-*p*-aminosalicylic acid in the absence of piperidine.





It was known that the carbon of the partially polarized aldehyde is sufficiently positive to undergo attack by the nucleophilic amine. The rate-determining step is suggested to be the attack of the basic amine on the aldehyde forming unstable carbinolamine anionic intermediate 111. The last step is the Schiff base formation after proton transfer and water elimination, such steps as these are expected to be fast (12–14). According to the above mechanism the rate of the reaction under investigation obeys the following equation'-

$$d[11]/dt = k_1[1][11] = k_{obs.}\ [p\text{-aminosalicylic acid}][\text{salicylaldehyde}].$$

Effect of piperidine. The formation of salicylidene-*p*-aminosalicylic acid was studied in a series of piperidine concentrations varied from $1x10^{-5}$ to $1x10^{-3}$ mol.l^{-1} in ethanol medium at 25°C. The order with respect to piperidine was determined and the rate of the reaction was calculated at each piperidine concentration. The results obtained (Table 1) show that the order is first at low

Table 1. Effect of [piperidine] on the order and the rate of the reaction of $8x10^{-3}$mol.l^{-1} of both *p*-aminosalicylic acid and salicylaldehyde at 25°

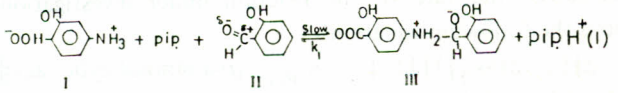
[Pip.]$x10^{-4}$mol .l^{-1}	The order	Initial rate $x10^{4}$M $s.^{-1}$
0.1	0.99	0.45
0.3	0.90	0.76
0.5	0.85	1.01
0.7	0.60	2.05
1.0	0.43	4.43
2.0	0.38	7.75
3.0	0.32	12.33
4.0	0.15	15.00
6.0	0.05	16.92
8.0	0.008	17.45
10.0	0.00	17.41
10.5	0.00	17.40

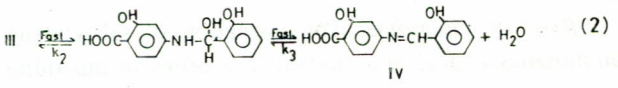
concentration ($1x10^{-5}$) and decreased to zero-order at $1x10^{-3}$ mol.l^{-1} concentration. On the other hand, the rate of the Schiff base formation is increased by increasing the concentration of piperidine until a maximum rate is reached at $0.8x10^{-3}$mol.l^{-1}. This behaviour indicates that the piperidine has a special catalytic role in such types of reaction. In the presence of low concentration, the pipe-

ridine takes place as one of the reactants. Accordingly, the rate question of the reaction can be represented as follow :

$$\text{Rate} = k_{obs.}[1][11][\text{piperidine}]$$

In contrast, in the presence of $\geqslant 0.8\text{x}10^{-3}$mol.l^{-1} piperidine the order of the reaction is independent of piperidine concentration and its role as a basic catalyst. Accordingly, the second-order rate plots for the reaction in presence of $0.8\text{x}10^{-3}$mol.l^{-1} [piperidine] at temperature range 20–40^{o}C are obtained. The specific rate constants and the activation parameters are calculated and listed in Table 2. In the presence of piperidine the reaction is expected to proceed via the following mechanism.





The first step involves the addition of polarized aldehyde to the more basic amine, where the piperidine increases the basic strength of amine by picking up a proton from 1. On the basis of Schiff bases formation, one can deduce that formation of the carbinolamine intermediate is the activated complex state and may be the slow and the rate-determining step. This paper affirms the above suggestion of the rate-determining step for the formation of salicylidene-*p*-aminosalicylic acid. The second step of the mechanism represents the proton transfer and the expulsion of the water molecule to form the Schiff base product IV, which is expected to be fast [14-15].

The thermodynamic parameters data (Table 2) indicate that the activation energy (E_a) as well as the free energy change ($\Delta G^{\ddagger}$) of catalytic reaction are lower than that of non-catalytic one. This indicates that more solvation should be expected in the presence of piperidine due to the solute-ethanol hydrogen bonding. This causes a reduction in E_a. Such behaviour leads to a decrease in $\Delta G^{\ddagger}$ i.e. higher reaction rate. Also, the lower values of the entropy change of activation ($\Delta S^{\ddagger}$) and collision factor (log. A) for the catalytic reaction, indicate that the rate determining step involves the formation of a transition state with less freedom than that for a non-catalytic mechanism (15). This may be attributed to the increase the orientation of the solvent molecules around the more polarized carbinolamine. This leads to lower $\Delta S^{\ddagger}$ and consequently lowers log. A. In addition, the positive values of $\Delta H^{\ddagger}$ indicate that the formation reaction under study is endothermic and more favourable at high temperature.

Effect of universal buffer solution. The formation of the Schiff base under investigation was studied in a series of universal buffer solutions of pH varying from 2.5 to 11.05 with a constant ionic strength of 0.04 mol.l^{-1} at 25^{o}C. The observed second-order rate constants for the reaction are plotted against pH (Fig. 2).

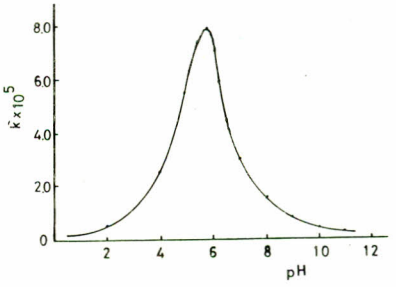


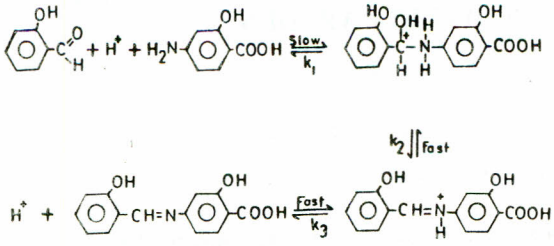
Fig. 2. The second-order rate constant (k)-pH plots for the formation of salicylidene-*p*-aminosalicylic acid at $1\text{x}10^{-2}$mol.l^{-1} of both reactant at 25^{o} .

It is well known that the mechanism of the condensation reaction between amines and aldehydes in acidic medium starts with the protonation of the aldehydic oxygen atom, which is attacked by the nucleophilic amine. This is the first and slow step, which is suggested to be the rate-determining step of the reaction [15-18]. The other two steps, the water and proton elimination are easy and fast steps. According to the above suggestion, the mecha-

Table 2. Specific rate constant and the activation parameters for the reaction of $8\text{x}10^{-3}$mol.l^{-1} of both p-aminosalicylic acid and salicylaldehyde in the absence and presence of $8\text{x}10^{-4}$mol.l^{-1} [pip]

	k' x $10^5$5mol.l^{-1}sec.$^{-1}$					E	log. A	$\Delta G^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$
	20^{o}C	25^{o}C	30^{o}C	35^{o}C	40^{o}C	k.cal. mol.l^{-1}		at 25^{o}C	at 25^{o}C	at 25^{o}C
Absence of Absence of pip.	0.75	1.90	2.97	6.32	10.08	28.45	16.01	24.1	27.8	12.8
[pip.] $8\text{x}10^{-4}$mol.l^{-1}	100	172	309	548	887	7.06	2.38	21.4	6.46	-50.0

nism of salicylidene-p-aminosalicylic acid formation at lower pH's can be written as follow :



From the behaviour of salicylidene-*p*-aminosalicylic acid rate formation under different pHs (Fig. 2), two comments can be made:-

(i) The Schiff base formation is very slow and low values of the specific rate constants are obtained in high basic medium pH's ⩾8. This can be explained on the principle that, in this pH's range the hydrogen ion concentration is small and the fraction of protonated aldehyde existing in this medium is not pronounced. The rate of the attacking step and Schiff base formation are expected to be extremely slow.

(ii) At pH<8, the rate of the Schiff base formation increases with an increase in the acidity of the medium until pH=4, and then decreases. Very slow rate formation is measured at pH<3. This behaviour can be interpreted as follows:- The high specific rate constant is measured at pH range from 8 to 4 due to the extensive presence of protonated aldehyde and the fast attack of the nucleophilic amine. Low measurable formation rate observed at pH<3 is attributed to the transition in the rate-determining step from the formation of the carbinolamine at pH>4 to the elimination of the proton and the water molecule, where this step becomes more difficult in such a medium. The above discussion is in accordance with the suggested mechanism in both of weakly basic (piperidine) and acidic media.

REFERENCES

1. L.T. Taylor, S.C. Vergez and D.H. Bush, J. Am. Chem. Soc., **88**, 3170 (1966).
2. P.A. Vigato, S. Degetto, M. Vidali and L. Cottalini, TV Conv. Naz. Chim. Inorg. Venezia, Comm., F3 (1971).
3. I.M. Issa, E.M. Defallah, M.R. Mahmoud and R. Abdel-Hamide, Indian J. of Chemistry, **14** 296 (1976).
4. M.T. El-Haty and F.A. Adam, Bull. De La Frenc. Chem. Soc., **11**, 253 (1983).
5. M.R. Mahmoud, A.A. El-Samahy, M.A. Hamed and A.M. Shaker, Soc. Chim. Italiana, **115**, 217 (1985).
6. D.S. Auld and T.C. Bruice, J. Am. Chem. Soc., **89**, 2083) (1967).
7. I.L. Shresta and M.N. Das, Anal. Chim. Acta, **60**, 135 (1970).
8. M.R. Mahmoud, A.K. El-Shafei and F.A. Adam, Soc. Chem. Italiana, **110**, 221 (1980).
9. H.T. Britton *Hydrogen Ions* (Chapman and Hall, London, 1952), 2nd ed.
10. A.A. Forst and R.G. Person, *Kinetics and Mechanism* (John Wiley & Sons Inc., New York, London, 1961), 2nd ed.
11. R.K. Chatuirvedi and E.H. Coordes, J. Chem. Soc., **89**, 1230 (1967).
12. E.F. Pratt and M.J. Kamiet, J. Org. Chem., **26**, 4029 (1961).
13. D. Pites, G. Favini and D. Grosso, J. Chem. Soc., Perkin, **11**, 1595 (1974).
14. R. J. Fessenden and J.S. Fessenden, *Organic Chemistry* (Boston, 1979).
15. Patai, *The Chemistry of the Carbon Nitrogen Double Bond* (1970).
16. Parton, *Comprehensive Organic Chemistry* (1979), Vol. 2.
17. C.V. Mcdonnell, Jr. M. Michailidis and R.B. Martin, J. Phys. Chem., **74 26 (1970).**
18. T.C. French, D.S. Auld and T.C. Bruice, J. Am. Chem. Soc., **4** 77(1965).