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Kinetic study for formation of thiazole by cyclisation

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The kinetic study of 3-chloroacetyl acetone with various thioureas has been carried out in ethanol. In this study thioureas used are m-methyl phenylthiourea, m-methoxy phenylthiourea, m-ethoxy phenylthiourea and m-chlorophenyl thiourea. The kinetic study reports second order rate constants for these reactions. The rate of reaction is first order with respect to thioureas and first order with respect to 3-chloroacetyl acetone. The effect of substituents on the rate of reaction is also studied. Thermodynamic parameters are used to explain the nature of reactions. The proposed reaction mechanism and details of Kinetics for various reactions were studied.

Keywords: Kinetics, Thiazole, Cyclisation

INTRODUCTION

Sulphur and nitrogen containing organic compounds are gaining importance in synthetic and pharmaceutical fields. Thiourea and their derivatives are well known intermediates in the synthesis of clinically important heterocycles like thiazoles, 4-thiozolidinones and benzothiozoles. Thioureas are commercially used in photographic films, plastics and textiles. Certain thiourea derivatives are insectides, rhodenticides and pharmaceuticals. Some of the thioureas are screened for anticancer activity. Thioureas have shown antibacterial [1], antipyretic [2], hypnotic [3] and fungicidal [4] activity. Thiazoles are found in medicaments [5] like vitamin-B, sulphathiozoles, promizole, niridazole, aminotrizole and tetramisole. Kinetics and mechanism of reaction between thiourea and iodate in buffer medium has been studied [6]. The kinetic study of reaction of thiourea with formaldehyde is also reported [7]. Reaction kinetics of gold dissolution in acid thiourea solution using ferric sulphate as oxidant was investigated with rotating disk technique [8]. The kinetics of formation of chromium(III) – iminodiacetic acid complex has been studied in temperature range 35 – 55 ^{0}C spectrophotometrically. The study shows rate of reaction is first order with respect to chromium(III) and rate of increases with increase in temperature [9]. The kinetics of oxidation of thiourea and *N*-substituted thioureas and the corresponding formamidine disulfides by sodium *N*-chloro-*p*-toluenesulfonamide or chloramine-T (CAT) in the presence of $HClO_4$ has been studied at 278 K [10]. The kinetics of the reaction between vitamin C (L-ascorbic acid) and ferric chloride hexahydrate was investigated in acidic medium at pH 3 spectrophotometrically. The order of the reaction was established by applying different methods. The order of the reaction with respect to each reactant was found was first and the overall second order was recommended for the reaction [11]. Kinetic investigation in rhodium(III) catalyzed oxidation of D-Mannitol in an acidified solution of potassium bromate in the presence of $Hg(OAc)_2$ as a scavenger, have been studied in the temperature range of 300 - 450 ^{0}C [12]. Kinetic and thermodynamic study on the adsorption behavior of Rhodamine B dye on Duolite C-20 resin has been reported. The effects of various experimental factors; sorbent amount, contact time, dye concentration and temperature, were studied by using the batch technique [13].

We have reported kinetic study of reaction of chloroacetone with p-substituted phenyl thioureas [14]. We have also reported kinetics of reaction of 3-chloroacetyl acetone with p-substituted phenyl thioureas [15]. Literature survey reveals that there is no work on kinetic study of reaction of 3-

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chloroacetyl acetone with m-substituted phenyl thioureas.

EXPERIMENTAL

Apparatus

The pH of thiazole hydrochloride solution was measured by digital pH meter. (EQUIPTRONICS, EQ-614A)

Reagents

All the reagents used were of analytical reagent grade unless otherwise stated; double distilled water was used throughout the experimental work.

Aryl thioureas were prepared by Frank and Smith method [16]. The 3-chloroacetyl acetone (Merck India), diethyl ether (Qualigens) were used for this work. The standard solutions of 3-chloroacetyl acetone and thioureas were prepared in double distilled absolute alcohol.

General procedure

Kinetic measurements were carried out at different concentrations of reactants and temperatures. A solution containing appropriate amount of thiourea which is thermostated at particular temperature was added in the solution containing appropriate amount of 3-chloroacetyl acetone at same temperature. At different time intervals definite volume of aliquot was added to a mixture of diethyl ether and water. It was shaken immediately and aqueous layer containing thiozole hydrochloride was separated, diluted to definite volume with distilled water. The pH of thiazole hydrochloride solution formed was measured by digital pH meter. Equal amounts of thiourea and 3-chloroacetyl acetone were mixed under the similar experimental conditions and kept overnight. The reaction mixture was then cooled and poured on crushed ice. It was extracted with ether to remove the unreacted reactants. The aqueous layer was neutralized by sodium hydroxide. The white solid obtained was crystallized from ethanol.

RESULTS AND DISCUSSION

The stoichiometric study indicates that one mole of thiourea reacts with one mole of 3-chloroacetylacetone. The rates of reaction were measured at different concentration of thioureas at constant concentration of 3-chloroacetylacetone. The plot of log (dc/dt) against log [3-chloroacetylacetone] is also straight line by keeping concentration of thioureas constant. The slope of the graph is 1.0 (Fig. 1).

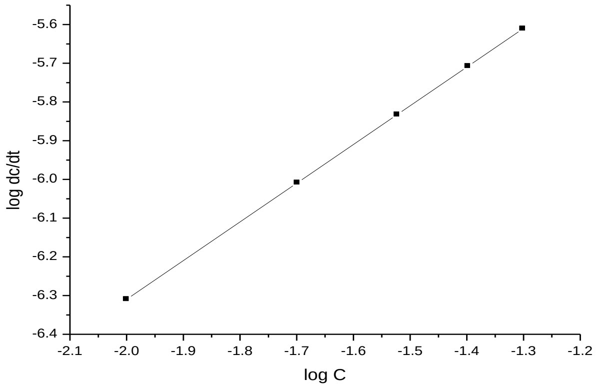

Fig. 1. Variation of log dc/dt with Log C

The plot of log (dc / dt) against log [thioureas by keeping concentration of 3-chloroacetylacetone constant it is also strate line and slop of the plot is one. The overall order of reaction is 2.

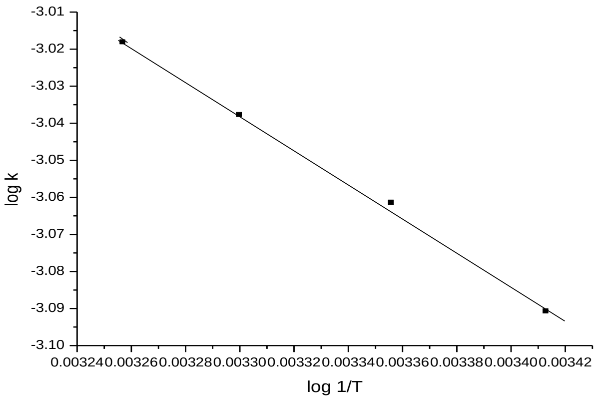

Fig. 2. Variation of log k with 1/T

By using Van't Hoffs differential method [17] the order of reaction with respect to 3-chloroacetylacetone and thioureas was also determined. Second order rate constants were determined at five different temperatures. The energy of activation (Ea*) was determined by plotting graph of log k verses 1/T (Fig. 2) and other thermodynamic parameter were calculated, [Table.1].

Table 1. Thermodynamic parameters for reaction of 3-chloroacetyl acetone with thioureas.

Thioureas	Ea* kJmol^{-1}	ΔH* kJmol^{-1}	-ΔS* kJ K^{-1}mol^{-1}	ΔF* kJ mol^{-1}
m-methyl phenyl & thiourea	30.17	28.67	0.043	20.14
m-mthoxy phenylthiourea	35.40	32.78	0.466	22.41
m-ethoxy phenylthiourea	37.47	35.76	0.0511	26.19
m-chloro phenyl thiourea	34.49	31.87	0.0501	23.32

The entropies of activation (ΔS*) of these reaction are negative indicates rigid nature of the transition state. The negative value of entropies of activation (ΔS*) also indicates that less stable noncyclic reactant convert into stable cyclic products [18]. Almost equal values of free energy of activation (ΔF*) for all thioureas indicates that probably a similar type of mechanism prevails in all cases [18]. When rate constant for the reaction are compared, the thiourea is found to be more reactive than the substituted phenyl thiouras. This may be due to the presence of II-electron in benzene ring. The phenyl thiourea and m-methyl phenyl thiourea show nearly same rate constants. This may be due to small effect of methyl group due to hyper conjugation and inductive effect. The m-ethoxy phenyl thiourea shows higher rate of reaction due to mesomeric effect. The m-chlorophenyl thiourea shows lower rate of reaction due to negative inductive effect of chloro group [19-20]. It is found that, the reaction is second order, first order with respect to thioureas and first order with respect to 3-chloroacetylacetone. The rate constants calculated from second order rate law are fairly constant [Table. 2].

Table 2. Second order rate contents for reaction of 3-Chloroacetyl acetone with thioureas
Thiourea = 0.05 mol dm^{-3} Temp = 313 ^{o}K

Thiourea	10^3 dm^3 mol^{-1} S^{-1} at 3-chloroacetylacetone mol dm^{-3}			
	0.05	0.04	0.03	0.02
m-methyl phenyl thiourea	0.96	0.98	0.94	0.99
m-methoxy phenyl thiourea	1.25	1.27	1.24	1.28
m-ethoxy phenyl thiourea	2.75	2.69	2.72	2.77
m-chloro phenyl thiourea	0.23	0.26	0.21	0.24

Based on these facts, the following general mechanism and rate expression is proposed.

$$S_1 + S_2 \underset{k_{-1}}{\overset{k_1\ \text{Slow}}{\rightleftarrows}} [\text{Intermediate}] \xrightarrow[k_2]{\text{Fast}} \text{products} \qquad (1)$$

S_1 stands for 3-chloroacetylacetone and S_2 stands for thioureas.

$$\text{Rate of reaction} = k_1\,[S_1]\,[S_2] - k_{-1}\,[\text{Intermediate}] \qquad (2)$$

On applying steady state approximation.

$$d / dt\,[\text{Intermediate}] = o = k_1\,[S_1]\,[S_2] - k_{-1}\,[\text{Intermediate}] - k_2\,[\text{Intermediate}] \qquad (3)$$

$$[\text{Intermediate}] = \frac{k_1\,[S_1]\,[S_2]}{k_{-1} + k_2} \qquad (4)$$

Substituting the value of [Intermediate] in equation (2)

$$\text{Rate of reaction} = k_1\,[S_1]\,[S_2] - \frac{k_1\,k_{-1}\,[S_1]\,[S_2]}{k_{-1} + k_2} \qquad (5)$$

$$\text{Rate of reaction} = \left\{ k_{-1} - \frac{k_{-1}\,k_1}{k_{-1} + k_2} \right\} [S_1]\,[S_2] \qquad (6)$$

The order of reaction is two (Reaction mechanism). The derived rate law explains all the observed experimental facts.

CONCLUSION

The order of reaction between 3-chloroacetylacetone and thiourea is found to be two.

The proposed rate law also shows that the rate of reaction is two.

Nearly equal values of free energy (ΔF*) indicates that same type of reaction mechanism prevails.

Decrease in entropy (ΔS*) indicates that, from open chain reactants the cyclic product is formed.

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КИНЕТИЧНО ИЗСЛЕДВАНЕ НА ОБРАЗУВАНЕТО НА ТИАЗОЛ ЧРЕЗ ЦИКЛИЗАЦИЯ

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(Резюме)

Извършено е кинетично изследване на взаимодействието на 3-хлороацетилацетон с различни производни на тиокарбамида в етанол. Производните на карбамида са m-метил-фенилкарбамид, m-метоксифенилкарбамид, m-етоксифенилкарбамид и m-хлорофенилкарбамид. Порядъкът на реакциите е първи по отношение на тиокарбамидните производни, както и за 3- хлороацетилацетон. Изследван е и ефектът на заместителите върху скоростта на реакциите. Използвани са термодинамични параметри за обяснението на природата на реакциите. Изследван е предложеният механизъм на реакциите и подробности за кинетиката им.