Review Of Research
Vol. 3 | Issue. 9 | June. 2014
Impact Factor : 2.1002 (UIF)
ISSN:-2249-894X
Available online at www.ror.isrj.net

ORIGINAL ARTICLE

# THE KINCTICS OF FORMATION OF BENZOTHIAZOLCS FROM ARYLTHIOUREAS

**S.L. Padwal**

Karmveer Bhaurao Patil Mahavidyalaya, Pandharpur. India

**ABSTRACT**

The kinctics of formation of benzothiazolcs by carrying cyclacondensation of aryl thioureas using molecular bromine as reagent in chloroform has been investigated. The order of reaction, thcrmodynamic parameters, probable mechanism and rate expression arc reported.

The kinctics of formation of 2-amino-O-substituted benzothiazolcs has been investigated. The cyclocondensation of arylthioureas in the presence of bromine in chloroform medium was found to yield the title 2-aminobenzothiazoles. The Older of the condensation was found to be second order i,e. first order with respect to thioureas and first order with respect to bromine. The effects of substituents on the rate of the condensation have also been investigated.

## INTRODUCTION

The thermodynamic parameters are evaluated and the rate expression is derived on the basis of suggested mechanism. benzothiazoles exhibit wide biological and pharmacccutical activities and hence occupy prominent position in the field of medicinal chemisty[1,'']. The use of benzothiazoles as vulcanizing accelerators and dye intermediates has been reported[4]. The use of thioureas in the synthetic and industrial field is well explored.

There are various conventional methods to synthesize benzothiazole derivatives[4]. The widely used synthetic strategy to obtain 2-amino benzothiazoles is by carrying cyclocondensation of aryl thioureas in presence of oxidizing agents like sulphuryl chloride / bromine by following 1 luger Scholls synthetic method. Recently Varma **el al[5].** have modified the- Huger-Schoffs procedure to obtain 2-amino benzothiazoles with quantitative yields. Recently attention is directed towards the investigation of new synthetic strategies and on the modification of the conventional synthetic routes to obtain commercially important benzothiazoles[6]. Literature reveals that there is scanty information on the kinetic study of formation of benzothiazoles from arylthioureas.

In continuation of our work on thioureas[4-7] and in view of above the significance of benzothiazoles herein we report the kinetics of formation of benzothiazoles by following cyclocondensation of aryl thioureas in presence of bromine in chloroform medium.

**Materials and Methods**

All the aryl thioureas were synthesized by known method[8].The solutions of arylthioureas and bromine (AR grade) were prepared in chloroform. Potassium iodide (10%). sodium thiosulphate (0,1 N). sodium hydroxide (0 1 N) were prepared in glass distilled water, the solvents and reagents used in the work were ol AR grade Stoichiomctry and product analysis

The solutions of aiylthiouieas (50 mmoles) and biomine (50 mmoles) were mixed and the reaction mixture was allowed to reflex for an hour. It was then cooled, To this reaction mixture, 50 ml distilled water was added, content was shaken in separating funnel and the separated aqueous layer was collected. Unreacted bromine present in aqueous layer was neutralized by adding sodium metabisulphide in portions. Then the layer was neutralized by ammonia and the solid obtained was filtered. sucecssively washed with water and dried. The crude product was crystallized from alcohol and authenticity of this obtained 2 amino 6 substituted benzothiazole was confirmed with the help of their melting points. The melting points of these products were found to be good agreement with those reported in literature[9-10]. Yield of benzothiazole observed were in the range of 85% to 90% under the 1:1 stoichiometric conditions.

**Kinetic measurements**

Kinetics of reactions of arylthioureas and bromine was studied by measuring the amount .of amino benzothiazole hydrobromides, formed as acids by titrating against standard NaOH (aq. solution) using literature procedure. The solutions of desired concentration of aryl thioureas and bromine were mixed, After certain time intervals the reaction was ceased by adding 10 ml potassium iodide (10%), 10 ml sodium thiosulphate solution (0.1 and chloroform 25 ml was added. The reaction content was transferred to separating funnel and was thoroughly shaken. The separated aq. layer was collected and

it was diluted to 50 ml using distilled water, then 10 ml of the diluted aq.. Solution was titrated against standard NaOH solution using phenol phthalein as an indicator. .The measurements were carried out at equal concentrations of aryl thioureas and brome at different temperatures.' Also kinetic measurements were recorded at unequal concentrations of arylthioureas and bromine.

**Result and Discussion**

The stoichiometric study indicates that one mole of thiourea reacts with one mole of bromine. The reaction rates were determined at different concentrations of thioureas by keeping concentration of bromine constant (Table I). Similarly the rates were determined at different concentrations of bromine by keeping the concentrations .of thioureas constant (Table II). The order of reaction was also determined with respect to thioureas and bromine by using vant hoff's differential method. Kinetic measurements were carried out at five different temperatures (Table III). The activation energy (Ea) was determined from the slope of Arrhenius plots of log k vs T and other thermodynamic parameters were computed in Table III.

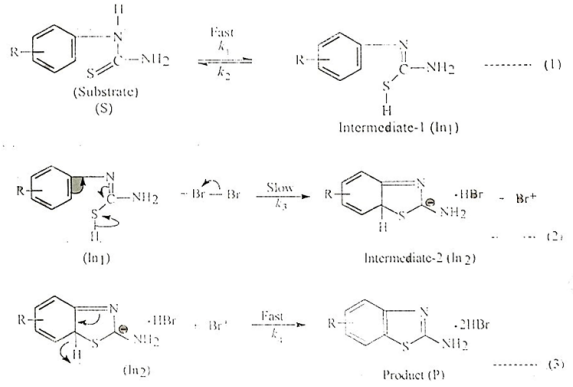
The entropies of activation $(\Delta s)$ for the reaction are all negative, suggesting rigid nature of transition state and lower frequency factor (Ea) shows that the conversion of thiourea into the cyclic products. Almost equal values of free energy of activation $(\Delta G)$ indicate that probably a similar type of mechanism prevails in all the cases.

When the rate constant for the reactions were compared, the order observed was $\rho$ —ethoxy phenylthiourca > $\rho$ mcthyl phenyl thiourea > phenyl thiourea > $\rho$ -bromophenyl thiourea > $\rho$ -chlorophcnyl thiourea. This may be explained on the basis of mesomeric effect of ethoxy group, hyper conjugation effect of methyl group and inductive effect of bromo and chloro group and this is expected as per substitution of the groups present in benzene ring.

It is found that order of reaction is two, first order with respect to thiourea and first order with respect to bromine. The rate constant calculated from second order rate law arc fairly constant (Table II).

Review Of Research
Vol. 3 | Issue. 9 | June. 2014
Impact Factor : 2.1002 (UIF)
ISSN:-2249-894X Available online at www.ror.isrj.net

On the basis of these results the mechanism of cyclocondcnsation of bromine has been proposed as in Scheme 1.




Schcme I

Consistent with above proposed mechanism the rate expression for the cyclo- condensation has been derived.

The product is formed in step (3). Hence the rate of the reaction is given by equation (4)

$$\frac{dx}{dt}\alpha[ln_2][Br]$$

$$\frac{dx}{dt} = k_4[ln_2][Br]$$

It is difficult to determine the concentration of $ln_2$ ∴ It should be expressed in terms of measurable quantities. Hence applying steady state conditions to $ln_2$ which is formed in step 2 and removed in step i.e. rate of formation of $ln_2$ Rate of removal of $ln_2$

I Ience it can be neglected, thus liqn (10) becomes

$$\frac{dx}{dt} = \frac{k_1 k_3}{k_2}[Br_2]\,[S] \qquad \text{....(11)}$$

Where $\frac{k_1 k_3}{k_2}$ is constant k'

$$\therefore \frac{dx}{dt} = k'[Br_2]\,[S] \qquad \text{.....(12)}$$

Or $\frac{dx}{dt}$ $\alpha[Br_2]\,[S]$

Total order of reaction = 1 + 1 = 2.

Hence, theoretically derived rate law expression is in good agreement with the experimental results.

**Acknowledgement**

Authors are thankful to Prof. D B Ingle for his invaluable guidance. One of the authors (SLP) is thankful to the UGC, New Delhi for providing Teacher Fellowship.

$\therefore k_3[In_2]\,[Br_2] = k_4[In_2]\,[Br']$

$$In_2 = \frac{k_3[In_2]\,[Br_2]}{k_4[Br']}$$

Substituting the value of $\tau n_2$ in cqn. (4) we get,

$$\frac{dx}{dt} = k_3[In_2][Br_2] \qquad \text{....(6)}$$

It is difficult to determine the concentration of intermediate-1($\tau n_1$) experimentally. Therefore applying the steady state conditions to $\tau n_1$. which is formed in step-1 and removed in backward direction in step-1 and in forward direction in step-2.

We find that rate of formation of $\tau n_2$ = rate of removal of $\tau n_2$ (use of steady state condition).

$$k_1[S] = k_2[In_1] + k_3[In_1][Br_2] \qquad \text{.....(7)}$$
$$k_1[S] = In_1\left[k_3 + k_3[Br_2]\right]$$

$$In_1 = \frac{k_1[S]}{k_2 + k_3[Br_2]} \qquad \text{.....(8)}$$

Substituting the Valueitif $\tau n_1$ in cqn. (6) we get

$$\frac{dx}{dt} = \frac{k_3[Br_2]\,k_1[S]}{k_2 + k_3[Br_2]} \qquad \text{.....(9)}$$

Dividing the numerator and denominator by $k_2$ we get

$$\frac{dx}{dt} = \frac{\frac{k_2 + k_3}{k_2}[Br_2][S]}{\frac{k_3[Br_2]}{k_2}}$$

as $\frac{k_3[Br_2]}{k_2}$ <<< 1

**REFERENCES**

1. Hutchinson 1, Chua Mei-szc, Browne Hele & Trapani V. J Med Chem, 44(9), 2001, 1446.
2. Sccrborough R M, Laibclmann A M & Clizbe L. A. Bio Org Med Chem Lett, 11(14), 2001, 1805.
3. Nadkami A B, Kamat V & Khadse G B. Indian J Hetero Chem. 9(4), 2000, 309.
4. Late Pathrikar G Y, Bondgc S P. Burungale A S. Bhingolikar V E. Ingle R D & Mane R A, Indian J Chan, 41 A, 2002, 2518.
5. Varma R S, Kumar D and Leiscn P J, J Chem Soc Perkin Trans 1, 1998, 4093.
6. Costa S P, Ferreira J A, Oliveira Campos A. J Chem Research (S).1997. 314.
7. Zaware B H, Mane R A & Ingle D B. Indian Chem Soc. 77,2000,214 & references cited therein.
8. Vogel A I, Text Book of Practical Organic Chemistry. 5th Ed, published by Longman Group UK,1994.
9. Kirk R E and Othmer D F, Encyclopaedia of Chemical Technology, 7,1951, 443.
10. Chaudhari S R, Ph.D. Thesis, Dr B.A.M.U. Aurangabad 1975.

Review Of Research
Vol. 3 | Issue. 9 | June. 2014
Impact Factor : 2.1002 (UIF)
ISSN:-2249-894X
Available online at www.ror.isrj.net

**Table III. -** Rate constants for the reaction of benzohydroxamic acid and acetic anhydride using acetonitrile / dioxane in absence and in presence of catalyst, pyridine / triethyl amine at 303 K.

k $dm^3$ $mol^{-1}$ $s^{-1}$
[HA = 0.0025 mol $dm^{-3}$] [AA = 0.0025 jr.ol $dm^{-3}$]
[Base 10.0025]

| Catalyst | BHA | | p-Me BHA | | p–OMe BHA | | p-C1 BHA | | Ph.Ac. HA | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Acetonitrile | Dioxane | Acetonitrile | Dioxane | Acetonitiil e Dioxane | Dioxane | Acetonitrile | Dioxane | Acetonitrile | Dioxare |
| Without catalyst | 0.090 | - | 0.066 | - | 0.514 | - | 0.039 | - | 0.054 | |
| | ±0.001 | | ± 0.001 | | ± 0.001 | | ± 0.002 | | ± 0.001 | - |
| Pyridine | 0.190 | 0.392 | 0.140 | 0.299 | 0.121 | 0.264 | 0.098 | 0.218 | 0.12-1 | - |
| | ± 0.002 | ± 0.002 | ± 0.003 | ±0.001 | ±0.001 | ± 0.004 | ± 0.002 | ± 0.001 | ± 0.02 | - |
| Triethyl amine | 0.501 | 1.340 | 0.391 | 0.987 | 0.304 | 0.712 | 0.243 | 0.533 | 0.337 | - |
| | ± 0.005 | ±0.02 | ± 0.006 | ± 0.01 | ± 0.007 | ± 0.01 | ± 0.003 | ± 0.004 | ±0.001 | - |

**Table II --** Rate constants for reaction of hydroxamic acids with acetic anhydride in acetonitrile / dioxane medium at 303 K using pyridine [Hydroxamic acid = 0.0025 Mol $dm^{-3}$] kdnr $mol^{-1}$ $s^{-1}$ at [acetic anhydride] mol $drn^{-3}$

| Acids | 0.0025 | | 0.00225 | | 0.002 | | 0.00175 | | 0.0015 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Acetonitrile | Dioxane | Acetonitrile | Dioxane | Acetonitrile | Dioxane | Acetonitrile | Dioxane | Acetonitrile | Dioxa r e |
| Berizohydroxamic | 0.190 | 0.392 | 0.188 | 0.382 | 0.186 | 0.375 | 0.181 | 0.371 | 0.176 | 0.358 |
| acid | ± 0.002 | ± 0.002 | ± 0.004 | ± 0.002 | ± 0.002 | ± 0.001 | . ± 0.001 | ± 0.002 | ± 0.003 | ±0.001 |
| p-Me BHA | 0.140 | 0.299 | . 0.139 | 0.292 | 0.138 | 0.286 | 0.138 | 0.279 | 0.132 | 0.282 |
| | " 0.003 | ± 0.001 | ± 0.001 | ± 0.001 | ± 0.001 | ± 0.001 | ± 0.001 | ± 0.001 | ± 0.001 | ± 0.002 |
| p-OMe BHA | 0.120 | 0.264 | 0.121 | 0.260 | 0.116 | 0.253 | 0.114 | 0.260 | 0.116 | 0.250 |
| | ± 0.001 | ± 0.004 | ± 0.002 | ± 0.001 | ± 0.001 | ± 0.003 | ± 0.002 | ± 0.001 | ± 0.001 | ±0.001 |
| PM BHA | 0.093 | 0.218 | 0.100 | 0.20 | 0.095 | 0.120 | 0.093 | 0.196 | 0.090 | 0.192 |
| | ±0.002 | ±0.001 | ± 0.002 | ± 0.001 | ± 0.003 | ±0.001 | ± 0.001 | ± 0.002 | ± 0.002 | ±0.002 |
| Ph Ac HA | 0.124 | - | 0.123 | - | 0.121 | - | 0.118 | - | 0.113 | - |
| | ±0.002 | | ± 0.001 | | ± 0.001 | | ± 0.001 | | ± 0.002 | |

**Table IV -** Rate constants at different temperatures and activation parameters for the reaction ofhydroxamic acids with acetic anhydride using acetonitril dioxane medium in presence of pyridine.

[Hydroxamic acids = 0.0025 M] [Acetic anhydride - 0.0025 M]

| | 303 K | | 308K | | 313 K | | 318 K | | 323 K | | Δ H* kJ $mol^{-1}$ | | ΔS* J $mol^{-1}$ $K^{-1}$ | | ΔG* kJ $mol^{-1}$ | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adds | Acei.o. | Diox. | Aceto. | Diox. | Acelo. | Diox. | Aceto. | Diox. | Aceto. | Diox. | Aceto. | Diox. | Acelo. | Diox. | Acelo. | Diox. |
| BHA | 0.190 | 0.392 | 0.25-1 | 0.624 | 0.363 | 1.02 | 0.502 | 1.601 | 0.704 | - | 50.56 | 71.68 | -87.46 | -78.36 | 76.79 | 74.12 |
| | ± 0.002 | ± 0.002 | ± 0.00-1 | ± 0.005 | ± 0.002 | ± 0.001 | ± 0.002 | + 0.02 | = 0.001 | - | | | | | | |
| p-MeBHA | 0.140 | 0.299 | 0.192 | 0.421 | 0.246 | 0.607 | 0.304 | 0.902 | 0.412 | - | 39.40 | 55.01 | -122.88 | -65.23 | 77.86 | 75.27 |
| | 0.003 | ± 0.001 | + 0.001 | ± 0.003 | ± 0.003 | ± 0.005 | ± 0.001 | ± 0.003 | = 0.001 | | | | | | | |
| p-OMeBHA | 0.120 | 0.264 | 0.142 | 0.362 | 0.172 | 0.501 | 0.215 | 0.680 | 0.254 | | 27.98 | 47.47 | -162.09 | -91.05 | 78.71 | 75.75 |
| | ± 0.001 | ± 0.C04 | ± 0.003 | ± 0.002 | ± 0.002 | ± 0.001 | ± 0.002 | ± 0.002 | = 0.004 | | | | | | | |
| p-ClBHA | 0.098 | 0.218 | 0.124 | 0.309 | 0.146 | 0.362 | 0.173 | 0.437 | ' 0.203 | | 25.29 | 33.29 | -172.03 | -139.10 | 80.00 | 76.48 |
| | ± 0.002 | ± 0.001 | ± 0.003 | ± 0.003 | ± 0.004 | ± 0.001 | ± 0.002 | ± 0.004 | = 0.005 | - | | | | | | |
| Ph. Ac. HA | 0.124 | - | 0.152 | - | 0.134 | - | 0.223 | - | 0.293 | - | 30.82 - | | -152.32 | - | 78.50 | - |
| | ±0.002 | | ±0.004 | | ±0.003 | | ±0.004 | | =0.004 | | | | | | | |