

A Kinetic Studies of Interaction of Ni(II) with d-2,2-(Ethylenediimino)-di-1-butanol

YOGESHWAR SHARMA^{1,*}, HARISH C. MALHOTRA² and GIAN C. SHARMA³

¹Department of Chemistry, Motilal Nehru College, Benito Juarez Marg, University of Delhi South Campus, New Delhi-110 021, India

²Department of Chemistry, University of Delhi, Delhi-110 007, India

³Department of Chemistry, Narmada College of Science & Commerce, Zadeshwar, Bharuch-392 011, India

*Corresponding author: E-mail: yogeshwar_sharma@rediffmail.com; ys.sharma63@gmail.com

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The complexation kinetics between Ni(II) with d-2,2-(ethylenediimino)-di-1-butanol has been investigated at 25, 30, 35 and 40 ± 0.05 °C in the pH range 6.18-7.41 using Aminco Morrow stopped flow spectrophotometer. The ionic strength was maintained at 0.1 M KNO₃. The anionic form of d-2,2-(ethylenediimino)-di-1-butanol is more reactive and the protonated form interacts only to a small extent. Kinetic results indicate that the ligand is not involved in the rate determining step which is, in fact, associated with the release of a water molecule from the shell of the metal ions prior to complexation with the ligand. Enthalpy, entropy of activation, energy of the molecule and heat of formation were also calculated. A mechanism consistent with the kinetic data has been suggested.

Keywords: Kinetics, Complexation, Nickel(II) complex, Activation parameter.

INTRODUCTION

d-2,2-(Ethylenediimino)-di-1-butanol (ethambutol) is a synthetic compound and is used in the treatment of tuberculosis [1]. Its antibacterial spectrum is limited to mycobacteria and only growing cells are affected by inhibiting mycobacterial RNA synthesis. Like EDTA, it is a good chelating agent [2,3]. So it is of interest to examine the effect of d-2,2-(ethylenediimino)-di-1-butanol on our plasma model. To understand these vital processes and steps of metal binding to the ligand, it was thought desirable to carry out a comprehensive kinetic study on the interaction of Ni(II) with d-2,2-(ethylenediimino)-di-1-butanol. Therefore, the kinetics of complexation of metal ions Ni(II) by d-2,2-(ethylenediimino)-di-1-butanol would no doubt give important information regarding the types of interaction of these ions with d-2,2-(ethylenediimino)-di-1-butanol and the clearance of d-2,2-(ethylenediimino)-di-1-butanol in the form of metal-ligand complex through the animal body [4-7]. With the hope that these anomalies might have rational explanation and to understand the biological processes clearly, a comprehensive kinetic study has been undertaken on the reaction of Ni(II) with d-2,2-(ethylenediimino)-di-1-butanol.

EXPERIMENTAL

d-2,2-(Ethylenediimino)-di-1-butanol (Themis Chemicals), bromothymol blue (Loba) and NaClO₄ (Ferak) were used as such. Other chemicals used were of A.R. grade. The pH of

ligand solution and metal ion solution was adjusted to same value using 2,6-lutidine (Merck Schuchardt) and HCl. However, a slight change in pH value (~ 0.05 units) was observed after mixing of two solutions. The final pH was recorded from Radiometer pH meter, pH M26. pH's reported are those of reaction mixtures. The temperature of the system was maintained by immersion type thermostat (German NBE model). The kinetic runs were made on Aminco Morrow stopped flow spectrophotometer under pseudo first order conditions, *i.e.*, [M(II)] >> [d-2,2-(ethylenediimino)-di-1-butanol] (M = Ni) at 620 nm by pH indicator method. This was desirable as very small changes in absorbance values were observed at 620 nm in the absence of the indicator. Under the pH indicator method, nickel nitrate, 10⁻² M, buffer 10⁻² M lutidine and μ = 0.1 M NaClO₄ was mixed with ligand solution containing indicator bromothymol blue ~ 10⁻⁵ M. Blank experiments in which (1) indicator and ligand solutions and (2) indicator and metal ion solutions were mixed showed no absorbance change to interfere with the results. The traces from the oscilloscope gave excellent first order plots, from which second order rate constants (*k*_{obs}) were computed by the relation:

$$k_{\text{obs}} = k'_{\text{obs}}[\text{M(II)}] \quad (1)$$

where *k*'_{obs} is the pseudo first order rate constant.

RESULTS AND DISCUSSION

Ni(II)-d-2,2-(ethylenediimino)-di-1-butanol complexation: The kinetics of complexation of Ni(II)-d-2,2-(ethylene-

diimino)-di-1-butanol was found to be of first order in nickel ion, which was taken in large excess over ligand to ensure pseudo-first order conditions and complete formation of mono complex only [8,9]. As protonated form of the ligand predominates in the pH range 6-7 ($pK_{a2} = 9.49$), the kinetic study of interaction has been made in the pH range 6.13-7.30 at ionic strength 0.1 M KNO_3 and at temperatures 25, 30, 35 and 40 \pm 0.05 $^{\circ}C$, under the condition $[Ni(II)] \gg [d-2,2-(ethylenediimino)-di-1-butanol]$. Oscilloscope traces of voltage versus time were used to determine the values of pseudo-first order rate constants (k'_{obs}) and these were further utilized to evaluate the values of second order rate constants (k_{obs}), using eqn. 1. These rate constants are tabulated in Table-1.

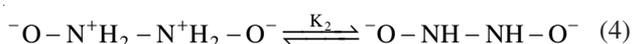
Temp. (\pm 0.05) $^{\circ}C$	pH	k'_{obs}	k_{obs}
25	6.17	6.87	13.4
25	6.38	11.6	22.6
25	6.58	18.0	35.1
25	6.75	24.5	47.8
25	6.90	30.6	59.6
25	7.02	35.1	68.5
25	7.09	37.7	73.4
30	6.13	9.33	18.2
30	6.42	17.9	34.9
30	6.59	24.9	48.6
30	6.75	32.0	62.3
30	6.88	38.4	74.8
30	7.10	42.5	82.9
30	7.30	44.7	87.1
35	6.16	14.2	27.6
35	6.38	23.1	45.0
35	6.55	30.4	59.3
35	6.73	38.7	75.4
35	6.87	43.6	85.1
35	6.98	48.1	93.7
35	7.09	51.3	99.3
40	6.16	17.6	34.3
40	6.46	31.4	61.2
40	6.67	40.3	78.5
40	6.84	47.1	91.9
40	7.00	53.4	104
40	7.09	54.9	107

The rate equation for Ni(II)-d-2,2-(ethylenediimino)-di-1-butanol interaction can be written as:

$$\begin{aligned} \text{Rate} &= -d/dt[Ni(II)] \\ &= -d/dt[d-2,2-(ethylenediimino)-di-1-butanol] \\ &= k_{obs} [d-2,2-(ethylenediimino)-di-1-butanol] \quad (2) \\ &= k'_{obs} [d-2,2-(ethylenediimino)-di-1-butanol] \quad (3) \end{aligned}$$

where $k'_{obs} = k_{obs} [Ni(II)]$

Dissociation equilibria of d-2,2-(ethylenediimino)-di-1-butanol can be represented as:



From eqns. 4, eqn. 3 reduces to

$$\text{Rate} = k'_{obs} \left\{ [{}^-\text{O}-\text{N}^+\text{H}_2-\text{N}^+\text{H}_2-\text{O}^-] + [{}^-\text{O}-\text{NH}-\text{NH}-\text{O}^-] \right\} \quad (4')$$

where ${}^-\text{O}-\text{N}^+\text{H}_2-\text{N}^+\text{H}_2-\text{O}^-$ represent the protonated form and

${}^-\text{O}-\text{NH}-\text{NH}-\text{O}^-$ represents the deprotonated form of the ligand. If it is assumed that these two forms participate in the reaction according to scheme given by Malhotra and Sharma [10-13], then the plots of $k_{obs} \{ [H^+]^2 + K_1[H^+] + K_1K_2 \} / K_1[H^+]$ versus $[H^+]^{-1}$ should be linear. However, these plots at 25, 30, 35 and 40 \pm 0.05 $^{\circ}C$ were found to be non-linear (Fig.1).

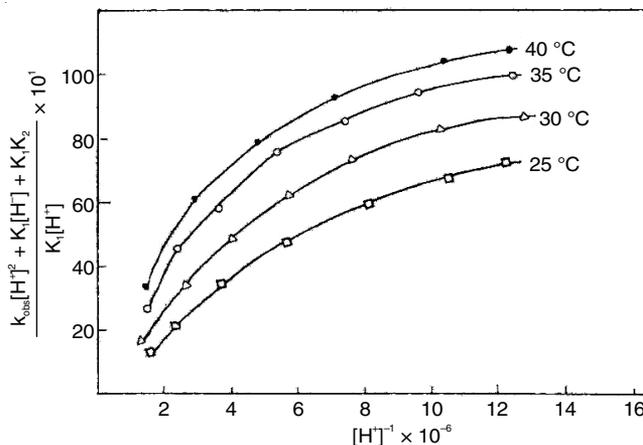
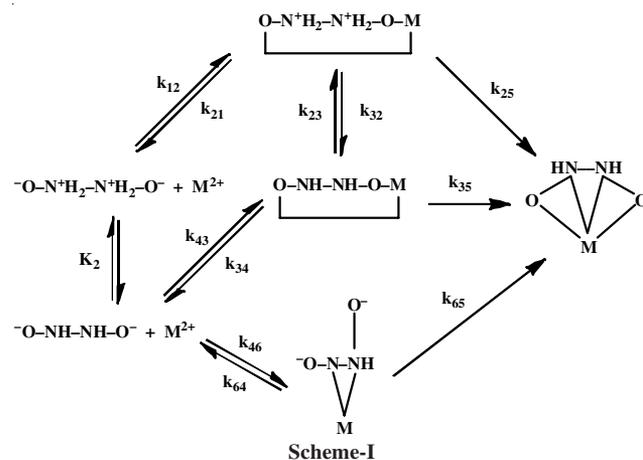


Fig. 1. Variation of $k_{obs} \{ K_2 + [H^+] / [H^+] + K_1K_2 \} / K_1[H^+]$ versus $[H^+]^{-1}$ for Ni(II) - d-2,2-(ethylenediimino)-di-1-butanol interaction at different temperatures

The following **Scheme-I** for complexation of Ni(II) with d-2,2-(ethylenediimino)-di-1-butanol, which could explain non-linearity of the curves was suggested:



The rate of the reaction can be written as:

$$\begin{aligned} \text{Rate} &= k_{25} [O-N^+H_2-N^+H_2-O-Ni] + k_{35} [O-NH-NH-O-Ni] \\ &\quad + k_{65} [O-NH-NH-O^-] \quad (5) \end{aligned}$$

Steady state approximation for species

$$\begin{aligned} [O-NH-NH-O-Ni] \text{ and } [O-NH-NH-O^-] \text{ can be written as} \\ d/dt [O-N^+H_2-N^+H_2-O-Ni] &= k_{12} [Ni(II)] [O-N^+H_2-N^+H_2-O^-] \\ &\quad + k_{32} [H^+]^2 [O-NH-NH-O-Ni] - \\ &\quad (k_{21} + k_{23} + k_{25}) [O-N^+H_2-N^+H_2-O-Ni] = 0 \quad (6) \end{aligned}$$

$$\begin{aligned} \frac{d}{dt} [\text{O-NH-NH-O-Ni}] &= k_{43}[\text{Ni(II)}][\text{O-NH-NH-O}^-] + \\ k_{23}[\text{O-N}^+\text{H}_2\text{-N}^+\text{H}_2\text{-O-Ni}] - k_{32}[\text{O-NH-NH-O-Ni}][\text{H}^+]^2 - \\ k_{34}[\text{O-NH-NH-O-Ni}] - k_{35}[\text{O-NH-NH-O-Ni}] &= 0 \end{aligned} \quad (6')$$

$$\begin{aligned} \frac{d}{dt} [\text{O-NH-NH-O}^-] &= k_{46}[\text{Ni(II)}][\text{O-NH-NH-O}^-] - \\ &\quad \text{Ni} \\ (k_{65} + k_{64})[\text{O-NH-NH-O}^-] &= 0 \end{aligned} \quad (7)$$

Assuming the two proton equilibria to be very fast, *i.e.*

$$\begin{aligned} k_{23}/k_{32} &= \frac{[\text{O-NH-NH-O-Ni}][\text{H}^+]^2}{[\text{O-N}^+\text{H}_2\text{-N}^+\text{H}_2\text{-O-Ni}]} \\ &= 1/K_2 \end{aligned} \quad (8)$$

$$K_2 = \frac{[\text{O-NH-NH-O}^-][\text{H}^+]^2}{[\text{O-N}^+\text{H}_2\text{-N}^+\text{H}_2\text{-O}^-]}$$

Substituting the value of $\frac{[\text{O-N}^+\text{H}_2\text{-N}^+\text{H}_2\text{-O-Ni}]}{[\text{O-NH-NH-O-Ni}]}$ from the above eqn. 8 in eqn. 5, we get

$$\begin{aligned} \text{Rate} &= \{k_{25}k_{32}[\text{H}^+] / (k_{23} + k_{35})\} [\text{O-NH-NH-O-Ni}] + \\ &\quad k_{65}[\text{O-NH-NH-Ni}] \\ &\quad \text{O}^- \end{aligned} \quad (9)$$

Similarly, substituting the value of from eqn. 8 in eqn. 6 and 6', and adding, we get:

$$\begin{aligned} \frac{[\text{O-NH-NH-O-Ni}]}{[\text{O-NH-NH-O}^-]} &= \frac{k_{43}[\text{Ni(II)}][\text{O-NH-NH-O}^-] + \\ &\quad k_{12}[\text{Ni(II)}][\text{O-N}^+\text{H}_2\text{-N}^+\text{H}_2\text{-O-Ni}]}{k_{43} + k_{35} - (k_{21} + k_{45}) K'_2[\text{H}^+]} \end{aligned} \quad (10)$$

Eqn. 7 is rearranged to get:

$$\begin{aligned} [\text{O-NH-NH-O}^-] &= \frac{k_{46}[\text{Ni(II)}][\text{O-NH-NH-O}^-]}{(k_{65} + k_{64})} \\ &\quad \text{Ni} \end{aligned} \quad (11)$$

Substituting (eqns. 10 and 11) in eqn. 9, we obtain:

$$\begin{aligned} \text{Rate} &= \frac{\{k_{25}k_{32}[\text{H}^+]/k_{23} + k_{35}\} k_{12}[\text{Ni(II)}][\text{O-N}^+\text{H}_2\text{-N}^+\text{H}_2\text{-O-Ni}] + k_{43}[\text{Ni(II)}][\text{O-NH-NH-O}^-]}{k_{43} + k_{35} - (k_{21} + k_{25}) K'_2[\text{H}^+]} \\ &= \frac{k_{65}k_{46}[\text{Ni(II)}][\text{O-NH-NH-O}^-]}{(k_{46} + k_{65})} \end{aligned} \quad (12)$$

The value of $[\text{O-NH-NH-O}^-]$ from eqn. 89 is substituted in eqn. 12 to give eqn. 13:

$$\begin{aligned} \text{Rate} &= \{k_{25}k_{32}[\text{H}^+]/k_{23} + k_{35}\} \times \frac{(k_{12} + k_{43}K_2 / [\text{H}^+])}{k_{43} + k_{35} - (k_{21} + k_{25})K'_2[\text{H}^+]} \\ &\quad + \frac{k_{65}k_{46}K_2[\text{Ni(II)}][\text{O-N}^+\text{H}_2\text{-N}^+\text{H}_2\text{-O-Ni}]}{(k_{46} + k_{65})[\text{H}^+]} \end{aligned} \quad (13)$$

Now combining eqn. 4' and 8, we get:

$$\text{Rate} = \frac{k_{\text{obs}}(K_2 + [\text{H}^+])[\text{Ni(II)}][\text{O-N}^+\text{H}_2\text{-N}^+\text{H}_2\text{-O-Ni}]}{[\text{H}^+]} \quad (14)$$

From eqns. 13 and 14, we get:

$$\begin{aligned} k_{\text{obs}} \frac{(K_2 + [\text{H}^+])}{[\text{H}^+]} &= \frac{k_{65}k_{46}K_2}{k_{46} + k_{65}[\text{H}^+]} + \{k_{45}K'_2[\text{H}^+] + k_{35}\} \times \\ &\quad \left\{ \frac{k_{12} + k_{43}K_2 / [\text{H}^+]}{k_{34} + k_{35} - (k_{21} + k_{45})K'_2[\text{H}^+]} \right\} \end{aligned} \quad (15)$$

If the reaction goes to completion we can very well assume that $k_{35} \gg k_{34}$ and $k_{65} \gg k_{64}$. Eqn. 15, therefore, reduces to:

$$\begin{aligned} k_{\text{obs}} \frac{(K_2 + [\text{H}^+])}{[\text{H}^+]} &= \{k_{45}K'_2[\text{H}^+] + k_{35}\} \times \\ &\quad \left\{ \frac{k_{12} + k_{43}K_2 / [\text{H}^+]}{k_{35} - (k_{21} + k_{45})K'_2[\text{H}^+]} \right\} + k_{46}K_2 / [\text{H}^+] \end{aligned} \quad (16)$$

Rearrangement of eqn. 16, yields eqn. 17:

$$k_{\text{obs}} \frac{(K_2 + [\text{H}^+])}{[\text{H}^+]} = \left\{ \frac{k_{12} + (k_{43} + k_{46})K_2 / [\text{H}^+]}{k_{35} - (k_{21} + k_{45})K'_2[\text{H}^+]} - 1 \right\} + \frac{[\text{H}^+]}{K_2 + [\text{H}^+]} \quad (17)$$

Eqn. 17 is of the form:

$$k_{\text{obs}} = \frac{X + Y / [\text{H}^+]}{Z / [\text{H}^+] - 1} \times \frac{[\text{H}^+]}{K_2 + [\text{H}^+]} \quad (18)$$

where $X = k_{12}$, $Y = (k_{43} + k_{46}) K_2$, $Z = k_{35}/(k_{21} + k_{45})K'_2$.

To evaluate the values of X, Y, and Z, a non-linear regression analysis along with least square analysis was carried out. The values of X, Y and Z at 25, 30, 35 and 40 °C are given in Table-2. Using the values of X, Y and Z from Table-2, the values of $(k_{12} + k_{46})$ and $[k_{35}/(k_{21} + k_{45})] K'_2$ were obtained. These values are given in Table-3.

TABLE-2
VALUES OF X, Y AND Z FOR THE COMPLEXATION OF Ni(II) WITH d-2,2-(ETHYLENEDIIMINO)-di-1-BUTANOL

Temp. (± 0.05) °C	X × 10 ⁵ (s ⁻¹)	Y × 10 ⁻¹ (M ⁻¹ s ⁻¹)	Z × 10 ⁻⁷ (M ⁻¹)
25	4.03 ± 0.3	4.36 ± 2.6	2.38 ± 12
30	5.62 ± 0.6	5.33 ± 3.6	2.58 ± 12
35	10.2 ± 0.7	9.76 ± 4.0	3.46 ± 15
40	14.5 ± 0.9	13.0 ± 4.5	4.27 ± 16

TABLE-3
VALUES OF k_{12} , $(k_{43} + k_{46})$ AND $k_{35} / (k_{21} + k_{45}) K'_2$ FOR THE COMPLEXATION OF Ni(II) WITH d-2,2-(ETHYLENEDIIMINO)-di-1-BUTANOL

Temp. (± 0.05) °C	$(k_{43} + k_{46}) \times 10^{-3}$ (M ⁻¹ s ⁻¹)	$K_{12} \times 10^{-5}$ (M ⁻¹ s ⁻¹)	$k_{35}/(k_{21} + k_{45})K'_2 \times 10^{-7}$ (M ⁻¹ s ⁻¹)
25	1.09	4.03	2.38
30	1.33	5.62	2.58
35	2.45	10.2	3.46
40	3.26	14.5	4.27

In the absence of **Scheme-I**, it was difficult to predict that the rate constants corresponding to which of the two steps (k_{43} or k_{46}) is larger. From **Scheme-I**, it is evident that k_{43} is larger than k_{46} , due to strong electrostatic attraction between negatively charged oxygen and positively charged nickel ions.

Values of energies of activation corresponding to specific rate constants k_{12} and $(k_{43} + k_{46})$ were calculated from linear plot of $\log k$ versus $1/T$ and those of entropies and enthalpies of activation corresponding to k_{12} and $(k_{43} + k_{46})$ were calculated from linear plot of $\log k/T$ versus $1/T$ (Figs. 2 and 3). These values are given in Table-4.

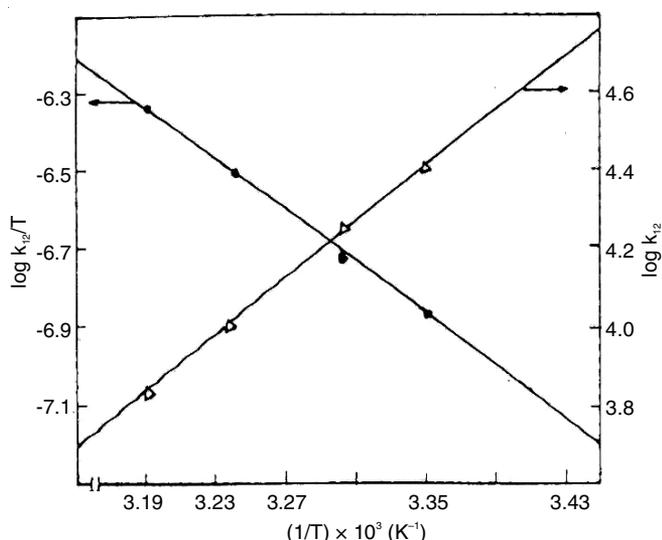


Fig. 2. Plots of $\log k_{12}$ and $\log k_{12}/T$ versus $(1/T)$ for the interaction of Ni(II)-d-2,2-(ethylenediimino)-di-1-butanol

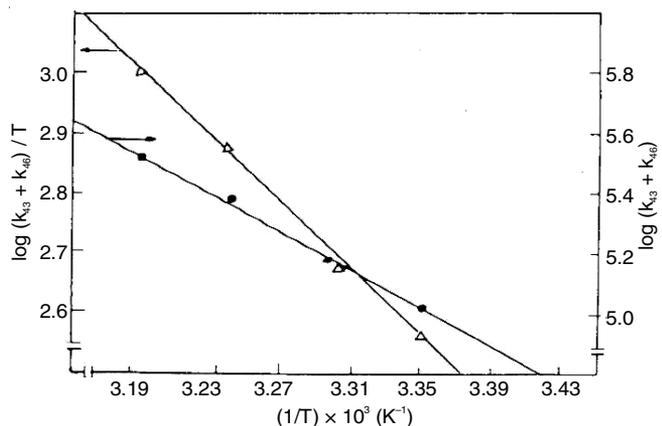


Fig. 3. Plots of $\log (k_{43} + k_{46})$ and $\log (k_{43} + k_{46}) / T$ versus $(1/T)$ for the interaction of Ni(II)-d-2,2-(ethylenediimino)-di-1-butanol

TABLE-4 VALUES OF ACTIVATION PARAMETERS CORRESPONDING TO $(k_{43} + k_{46})$ AND k_{12} FOR THE COMPLEXATION OF Ni(II) WITH d-2,2-(ETHYLENEDIIMINO)-di-1-BUTANOL		
	$(k_{43} + k_{46})$	k_{12}
ΔH^\ddagger (kJ mol ⁻¹)	53.1 ± 3.5	63.6 ± 3.9
ΔE^\ddagger (kJ mol ⁻¹)	59.0 ± 3.8	73.6 ± 4.5
ΔS^\ddagger (J K ⁻¹ mol ⁻¹)	-99.0 ± 4.6	146.0 ± 6.9

Mechanism: Based on **Scheme-I**, following mechanism for the complexation of Ni(II) with d-2,2-(ethylenediimino)-di-1-butanol has been suggested (**Scheme-II**).

The zwitterionic form undergoes complexation with Ni(II) via k_{12} . Low value of k_{12} ($4.03 \times 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$ at 25 °C) shows that zwitterionic form is highly unreactive. The deprotonated form reacts with Ni(II) in two ways (i) Ring formation via nitrogen and (ii) Ring formation via oxygen. It is evident from

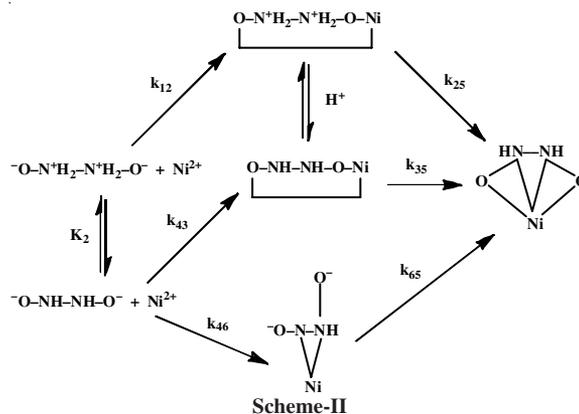


Table-3 that deprotonated form will react more rapidly with Ni(II) as compared to the zwitterionic form. Due to strong electrostatic interaction between the positive charge of Ni(II) and negative charge on the oxygen of d-2,2-(ethylenediimino)-di-1-butanol, it is inferred that k_{43} is greater than k_{46} . The value of activation parameters corresponding to $(k_{43} + k_{46})$ further confirm that the deprotonated form is more reactive than the zwitterionic form of the ligand. This mechanism is further confirmed by the values of energy of activation and entropy of activation. The positive value of entropy of activation corresponding to k_{12} step suggests that the reaction is occurring

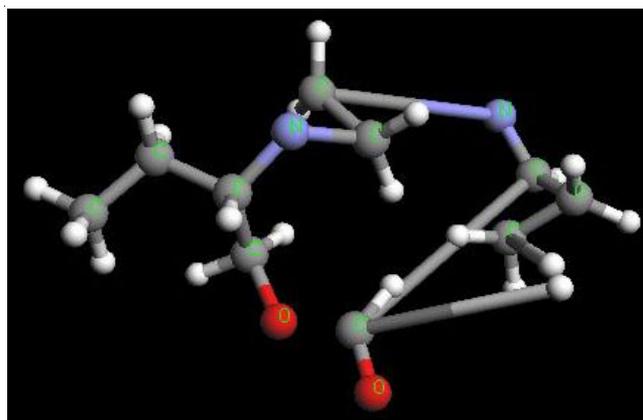


Fig. 4. Deprotonated form of d-2,2-(ethylenediimino)-di-1-butanol; Final geom energy = -55357.0379 kcal/mol; Heat of formation = 31.7745 kcal/mol

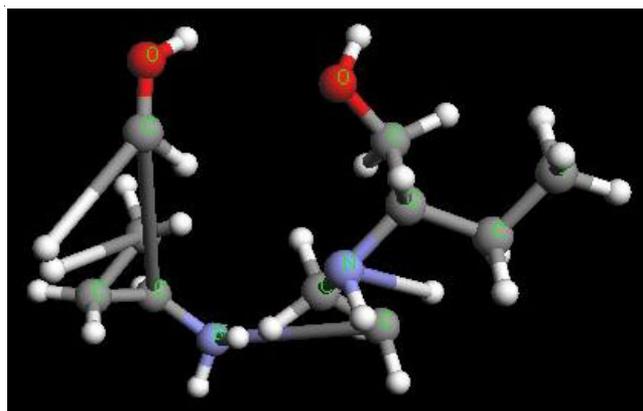


Fig. 5. Protonated form of d-2,2-(ethylenediimino)-di-1-butanol; Final geom energy = -57558.0705 kcal/mol; Heat of formation = -47.8176 kcal/mol

between ions having similar type of charges. The high negative value of entropy of activation is suggestive of associative mechanism being observed. This mechanism is further confirmed from the molecular modelling method in which the energy as well as the heat of formation of the zwitterionic form and protonated form has been calculated [14-18]. Values of the energies as well as heat of formation were calculated after optimizing the geometry of the molecules. These values are given in Figs. 4 and 5. It has been found that the zwitterionic form is more reactive than the protonated form.

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