The equilibrium constants, rate constants and activation parameters for axial ligation of alkyl(aquo)cobaloximes by N donor ligands in the presence of 0.2 M buffer (to maintain pH) and 1.0 M KCl (to maintain ionic strength) have been determined spectrophotometrically at 442 nm. The rates and activation parameters (ΔH° and ΔS°) for the reactions have been estimated from the effect of concentration of ligand and temperature on the kinetics of these reactions. From the results of experimentally determined rates and activation parameters of cobaloximes, it can be concluded that the reactivity of metal complexes is greatly influenced by the ligand field effect of the co-ordinated groups and the presence of π acceptor ligand, which provides a low energy pathway for electron transfer from a π donor ligand anion leading to rate enhancement. The small negative ΔS° and low ΔH° values suggest the operation of a dissociative interchange (Id) substitution mechanism at the Co(III) center.

The B12 based enzymes are the only ones thus far known whose co-factors contain a metal-carbon bond. Cobaloximes containing a cobalt-carbon σ bond in one of the axial positions and dimethyl glyoximate in the equitorial position are widely used as models for co-enzyme B12. Cobaloximes are capable of reproducing certain chemical properties of the naturally occurring system and are found useful in understanding some basic features of the more complex biologically important rearrangements thereby providing clues into the elusive mechanisms of B12 catalysed enzymatic processes via radical intermediates. The key step in the above rearrangement reactions is considered to be the making and breaking of Co-C bond. These model complexes have shown that the ligand in the trans position to Co-C bond has a strong trans influence on the axial alkyl ligand and the nature of the alkyl group has an influence on the thermodynamic stability of the bond; equilibrium constants, kinetics and mechanism of the substitution reactions. In order to establish the factors affecting the ligand substitution reactions and to establish a suitable mechanism for the Co-C bond breaking, a large amount of work has been done.

Reasonable hypothesis about the nature of the transition state could be formulated utilising the thermal activation parameters (ΔH° and ΔS°). The Co-C bond cleavage is influenced by the basicity of the ligand and steric crowd of the ligand. Hence in the present note we have chosen ligands with varying basicities and sterically crowded 3,5-dimethyl pyrazole. Recently, Van Eldik et al., studied the ligand substitution reactions of trans [(Co(en)2Me(H2O)]2+ with cyanide and imidazole as incoming ligands and also the mechanistic study on the reations of alkyl(aquo)cobaloximes with azole and suggested that an interchange dissociative (Id) substitution mechanism operates where azoles participate in the transition state.

R = ICH2
L = Alanine, alanine methylester, pyrazole or 3,5-dimethylpyrazole

**Experimental**

L-alanine, L-alanine methylester, pyrazole and 3,5-dimethylpyrazole, obtained from Sigma, were used without further purification. KCl, and HPLC grade methanol were obtained from Fluka. Doubly distilled, deionized water was used throughout; to maintain appropriate pH, 0.2M buffers were used in the range 1.0 to 9.0 and were prepared as reported earlier. ICH2Co(DH)2OH2 was prepared using a procedure of Brown et al. All manipulations were performed under minimal illuminations due to photolability of organo cobalt bond. All work with the alkyl (aquocobaloximes was performed in dim light (in dark room) and solutions were covered with
aluminium foil. pH measurements were made with a Digisun digital pH meter equipped with a combined glass electrode. The electrode was standardized at two pH values (4 and 9.2) with standard buffer solutions.

UV and visible spectra were recorded on a Elico BL 198 Bio spectrophotometer, the sample compartment of which is provided with a thermostat and the concentrations of iodomethyl(aquo)cobaloximes (0.0006 M) was fixed at 442 nm.

**Results and discussion**

**Determination of equilibrium constants**

All the \( pK_a \) values of the ligands studied were determined potentiometrically. Apparent equilibrium constants, \( K_{app} \) (Eq.1) for the axial ligation of iodomethyl(aquo)cobaloxime were determined by spectrophotometric measurements at 442 nm (\( \lambda_{	ext{max}} \) of iodomethyl(aquo)cobaloxime). In a 3 ml cuvette, solutions containing cobaloxime, an appropriate buffer (0.2 M) to maintain pH, KCl to maintain unit ionic strength and varying concentrations of ligand were taken in a cell block maintained at 25 ± 0.1°C. Solutions were allowed to temperature equilibrate in the spectrophotometer cell block for at least 15 min. prior to addition of cobaloxime.

\[
K_{app} = \frac{[\text{ICH}_2\text{Co(DH)}_2\text{L}]}{[\text{ICH}_2\text{Co(DH)}_2\text{H}_2\text{O}] [\text{L}]_{\text{free}}} \quad \ldots (1)
\]

Final absorbance readings were taken after equilibrium was established as indicated by the time independence of the readings. UV-visible scan of the complex with alanine, at different concentrations of ligand shows an isosbestic point at 421 nm showing that a single product i.e., \( \text{ICH}_2\text{Co(DH)}_2\text{L} \) is formed.

\( K_{eq} \) was calculated by a linear plot of \( \Delta A \) versus \( \Delta A/[L]_o \). Values of \( K_{app} \) were obtained from the least-squares fit of the plot of \( \Delta A \) versus \( \Delta A/[L]_o \) and the slope is \(-1/K_{app}\). The values for the equilibrium constants for axial ligation with respect to unprotonated ligand were calculated from the relation

\[
K_{eq} = K_{app}/\alpha_{[L]} \quad \ldots (2)
\]

\( \alpha_{[L]} = K_{eq}/(K_{eq} + [H^+]) \)

The values of equilibrium constant \( (K_{app}) \) for the axial ligation of \( \text{ICH}_2\text{Co(DH)}_2\text{H}_2\text{O} \) by various N donor ligands are given in Table 1. The pH dependent binding constants were measured from 1.0 to 6.0 for pyrazole and dimethylpyrazole and for other ligands from 6.0 to 12.0, which demonstrate pH-dependent and pH-independent binding of ligands to \( \text{ICH}_2\text{Co(DH)}_2\text{H}_2\text{O} \). If we observe pH-dependent and pH-independent binding plots (Fig. 1), \( K_{app} \) values increase up to a certain value of pH and after this they are pH-independent. This may be because of the competition of \( \text{H}^+ \) with Co(III) to bind with ligand. Hence, at lower pH most of ligand is protonated and not available for binding with cobalt. At higher pH, ligand available is maximum and binds to Co(III), so the \( K_{app} \) is larger at higher pH. A soft or class b character has been assigned to cobaloximes and is

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\( K_{eq}(M^{-1}) \) 13799.42 5649.80 401.00 338.42

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consistent with its observed greater ligand affinity of cyanide and imidazoles\(^{22-24}\). Similar trends were observed for all the ligands studied. If we compare the equilibrium constants \((K_{eq})\) of various ligands they are in the order \(K_{ALA} > K_{AME} > K_{py} > K_{DMPY}\).

The order of stability depends on ligand basicity and steric hindrance among two series of ligands\(^{16}\), aromatic (PY and DMPY) and aliphatic (ALA and AME). Though DMPY is more basic than pyrazole, it forms less stable complexes than pyrazole due to steric hindrance of the substituents (methyl group) at \(C_3\) and \(C_5\), though \(P\) in \(P(n\text{-but})_3\) is soft\(^{25}\) and more basic than imidazole, it binds weakly due to steric hindrance; this indicates that steric hindrance play a vital role. The decrease in stability with steric hindrance can also be well explained in case of alanine and alanine methyl ester. If we compare the \(pH\) dependent binding plots of alanine and alanine methyl ester, in both the cases \(K_{app}\) increases with increase in \(pH\) and after certain \(pH\) they become \(pH\)-independent; alanine shows \(pH\) dependence up to 9.5 and later becomes \(pH\)-independent, whereas alanine ester binding will be \(pH\)-dependent up to 7.5 and later it becomes \(pH\)-independent.

For each ligand \(L\), the absorbance measurements were carried out at various \(pH\) values, first order rate constants \((k_{obs})\) are determined by monitoring the decrease in absorbance at the same wavelength used for \(K_{app}\) determinations under pseudo-first order condition\(^{15}\) with \(L\), in at least 10 fold excess over cobaloxime concentration (0.0006 \(M\)). First order rate constants \((k_{obs})\) were obtained by least-squares fits of the data to Eq. (3)

\[
\ln [A_t]/[A_0] = k_{obs} \ t \quad \ldots (3)
\]

where \(A_t\) is the absorbance at time \(t\) and \(A_0\) is the final absorbance. At constant temperature, constant \(pH\) and fixed concentration of complex, the plot \(\ln[A_t]/[A_0]\) versus time, for different ligand concentrations, is curved at the initial stage and subsequently linear indicating that the reaction is not a single step process, but a two step consecutive process may be assumed. In order to show that the rates are dependent on \(pH\), rates were determined at different \(pH\) (Table 2), it is observed that the rate is enhanced tremendously near the \(pK_a\) of the ligand (Fig. 2).

The second order rate constants \(k_{on}'\) was determined by plotting \(k_{obs}\) versus the \([ligand]\), the slope of which is \(k_{on}'\). Since this is also \(pH\)-dependent we have calculated \(k_{on}\), \(pH\)-independent second order rate constant (Table 3) using the equation \(k_{on} = k_{on}'/\alpha_{L}\). In order to calculate activation parameters the substitution reaction was studied at varying ligand concentrations, at fixed complex concentration and at a fixed \(pH\). The reaction was studied at 15, 20, 25, 30 and 35°C. The rates showed dependence on ligand concentration as well as on temperature and the results are included in Table 4. Figure 3 shows the temperature dependence of substitution reaction. The
activation parameters for the axial ligation ($\Delta S^*$ and $\Delta H^*$) were calculated from standard Eyring plot and are given in Table 5. Van Eldik et al.\textsuperscript{17} determined the activation parameters ($\Delta S^*$, $\Delta H^*$ and $\Delta V^*$) for the reaction of trans [Co$^{III}$(en)$_2$(Me)H$_2$O]$^{2+}$ with cyanide and imidazole as 49±4 kJ mol$^{-1}$, -38±15 J K$^{-1}$ mol$^{-1}$ and +7.0±0.6 cm$^3$ mol$^{-1}$ and 53±2 kJ mol$^{-1}$, -22±7 J K$^{-1}$ mol$^{-1}$ and +4.7±0.1 cm$^3$ mol$^{-1}$ and concluded that an interchange dissociative, $\text{Id}$ mechanism in which the entering nucleophile could be weakly bound in the transition state was operative. In the present study we have investigated the displacement of the axial H$_2$O molecule in ICH$_2$Co(DH)$_2$OH$_2$ by alanine and found the low activation enthalpy of 71±2 kJ mol$^{-1}$ and low negative activation entropy of -30±2 J K$^{-1}$ mol$^{-1}$ respectively and an isokinetic plot of $\Delta H^*$ versus $\Delta S^*$ support the dissociative nature of the substitution process.

The kinetics of substitution of the axial base in alkylcobaloximes and related cobalt complexes has
been studied under a variety of conditions. In none of the studies was the mechanism established conclusively although in all cases strong evidence was given that the intimate mechanism is dissociative. In most of these studies, the exchanges were performed in water with H$_2$O as the leaving group. There is considerable evidence in the recent literature that this is the case for the alkylcobalt corrin and alkylcobaloximes among B$_{12}$ model chelate system. In view of the evidence presented above for the ligation kinetic studies of others both on alkyl cobalt complexes with other equatorial ligand system and on cobaloxime(III) complexes, an SN mechanism appears to be operative. Nevertheless there is substantial evidence that Co(III) complexes are stabilized enough to exist as penta-coordinate species.

The small dependence of $k_{oa}$ upon ligand basicity within each series of ligands is clearly related to the fact that while the reacting complex is a soft acid, the ligand is hard. The rate constants are better correlated with the relative softness of the ligand among the ligands we have studied. The overall small variation of ligation rates with ligand is probably indicative of an early transition state with rather large ligand to metal.

The incoming ligand and leaving ligand (water) are just loosely bound to cobalt in the transition state. It is difficult to distinguish between a transition state in which both ligands are loosely bound (i.e., Id mechanism), and one in which the leaving ligand has completely dissociated (i.e. SN mechanism).

The stability of pentacoordinate alkyl cobalt complexes and the evidence that both of the dominant soft Co(III) complexes, [Co(CN)$_2$H$_2$O] and [Co(NH)$_2$SO$_4$] undergo ligand substitution reaction as SN mechanism clearly favours this mechanism for ligation reaction of RCo(DH)$_2$OH$_2$. The coordination between the softness of a cobalt(III) complex and the stability of its pentacoordinate species permitting an SN mechanism for ligand substitution and our evidence supporting to the soft character of RCo(DH)$_2$OH$_2$ support the conclusion that the ligation reaction of RCo(DH)$_2$OH$_2$ probably proceed via SN mechanism.

**Conclusions**

The binding of ALA and AME to ICH$_2$Co(DH)$_2$OH$_2$ follow basicity order, whereas PY forms more stable complexes than DMPY due to steric hindrance of the substituent at C$_3$ and C$_5$ of DMPY. It can be concluded from the kinetic and thermodynamic data that an Interchange (Id) substitution mechanism operates during the homolysis of Co-C bond in cobaloximes in which the nucleophile participates in the transition state.

**Table 5 — Activation parameters**

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<th>System</th>
<th>$\Delta H^\ddagger$ (kJmol$^{-1}$)</th>
<th>$\Delta S^\ddagger$ (kJmol$^{-1}$)</th>
<th>Ref.</th>
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**References**