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Kinetic H/D Exchange Study of Co(III) Coordination Compounds of Diazines Using NMR Spectroscopy

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The Co(III) diazines complexes having composition $[(NH_3)_5CoPhtz)](ClO_4)_3$ (**1**) (Phtz = phthalazine), $[(NH_3)_5CoPydz)](ClO_4)_3$ (**2**) (Pydz = pyradazine), $[(NH_3)_5Co(3\text{-}Me\text{-}Pydz)](ClO_4)_3$ (**3**) (3-Me-Pydz = 3-methyl pyradazine) and $[(NH_3)_5Co(3\text{-}MePhtz)](ClO_4)_3$ (**4**) (3-MePhtz = 3-methyl phthalazine), $[(NH_3)_5Co(ImH)](ClO_4)_3$ (**5**) (ImH = imidazole), $[(NH_3)_5Co(N\text{-}MeIm)](ClO_4)_3$ (**6**) (N-MeIm = N-methylimidazole) undergo OD^--catalyzed H/D exchange at the *ortho* position of the coordinated site. Rate constants for H/D exchange of these complexes at 25°C or 60°C were obtained in alkaline D_2O solution using NMR spectroscopy. Reaction rate for $[(NH_3)_5CoPhtz)](ClO_4)_3$, $[(NH_3)_5CoPydz)](ClO_4)_3$, $[(NH_3)_5Co(3\text{-}Me\text{-}Pydz)](ClO_4)_3$ and $[(NH_3)_5Co(3\text{-}MePhtz)](ClO_4)_3$ at 25°C are faster compared to $[(NH_3)_5Co(ImH)](ClO_4)_3$, $[(NH_3)_5Co(N\text{-}MeIm)](ClO_4)_3$ (**7**). However $[(NH_3)_5CoImCo(NH_3)_5]Br_5$ complex does not H/D exchange at 60°C even in strong alkaline D_2O solution.

Key Words: Exchange, Complex, Ligand, Diazines.

INTRODUCTION

Studies on the effect of metal ions on the rate of hydrogen exchange at C-2 position in imidazole may be important to the understanding of certain biological processes[1-3]. Storm and coworkers[4] attempted to study exchange in the imidazole ligands of $[(NH_3)_5CoHIm]^{3+}$ and $[(NH_3)_5CoN\text{-}MeIm]^{3+}$ at 40°C and reported that exchange did not occur at any site under either alkaline or acidic conditions. However, Buncel *et al.*[5] have reported that at 60°C in normal water both $[(NH_3)_5Co[2\text{-}^3H]HIm]^{3+}$ and $[(NH_3)_5Co[2\text{-}^3H]\text{-}N\text{-}MeIm]^{3+}$ are detritiated *via* OH^- catalyzed reactions on the 3+ forms of the complex, $k_{OH} = 1.2\ M^{-1}\ s^{-1}$ for the HIm complex and $k_{OH} = 0.15\ M^{-1}\ s^{-1}$ for the N-MeIm complex.

Buncel and coworkers[6] studied the effect of protonation and Cr(III)-coordination on H-2 exchange in imidazole and found that the catalytic effect of a Cr(III) centre exceeded that of protonation at nitrogen by a

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factor of 20. Thus *cis*-$[Cr(en)_2(N\text{-}MeIm)Cl]Cl_2$ is reported to exchanges at C-2 faster than at C-4 and C-5 with a second order rate constant k_{OD} = 6.0 × 10^3 M^{-1} s^{-1} (35°C). It was suggested that isotopic exchange in all three positions of imidazole is largely influenced by the magnitude of the effective nuclear charge. In continuation of our work on isotopic exchange in coordinated diazine ligands[7-10] and also comparison of H/D exchange in different diazine ligands, herein the H/D exchange in 5- and 6-membered diazine ligands coordinated to Co(III) is reported.

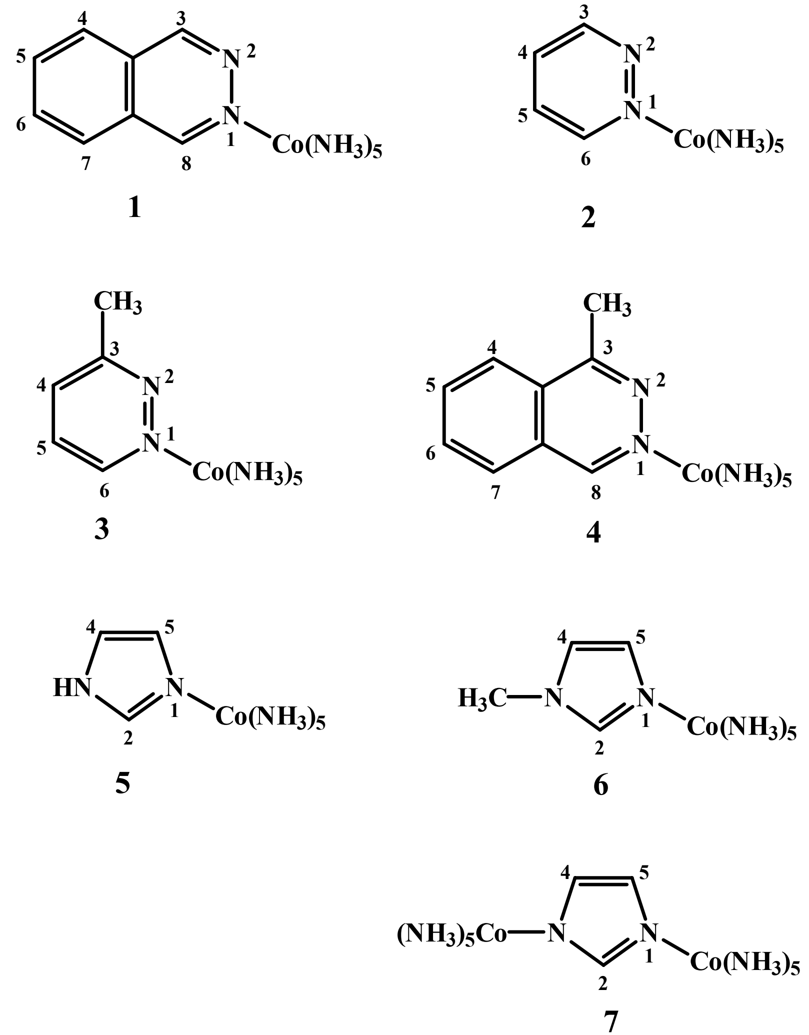
EXPERIMENTAL

All complexes were prepared according to the reported method[11]. ^{1}H NMR spectra at different pD were recorded on Varian Gemini 200 or VXR300 spectrometer using 3-(trimethylsilyl)-2,2,3,3-tetra deuteropropionic acid, sodium salt (TSP) as reference All pD measurements were made using a Radiometer pHM 82 pH meter fitted with a sodium ion insensitive G2040B glass and K4040 calomel electrode. The system was standardized using sodium tetraborate (0.0100 M), disodium hydrogen phosphate (0.0250 M) and potassium dihydrogen phosphate (0.0250 M) buffers. Measurements were carried out using a salt bridge (NH_4NO_3 = 1.6 M, $NaNO_3$ = 0.2 M) to separate the solution from the calomel electrode. pD was calculated using the empirical formula[12] pD = meter reading + 0.40 and $[OD^-]$ from pD using $pK_w(D_2O) = 14.81$,[13] $\gamma = \pm 0.64$ (0.49 M)[14].

For $[(NH_3)_5CoPhtz]^{3+}$ complex, 350 µL of potassium chloride (0.8 M) in D_2O and 350 µL of a fresh solution of complex in D_2O were mixed (I = 0.49 M, KCl) and the pD was brought to the desired value by addition of NaOD. An aliquot of the solution was transferred to an NMR tube and this was placed in the spectrometer. The instrument was quickly shimmed and spectral acquisition started. A PAD program was run for the required time, with spectra being collected at intervals of 5 min to 1 h, depending on reaction velocity. Rates of exchange for $[(NH_3)_5CoPhtz]^{3+}$ were obtained by following the decay of the H-8 signal. Rate constants were obtained from least squares fitting of peak area *vs.* time data. Rate data were fitted to the derived rate laws using MINIM computer program[15].

RESULTS AND DISCUSSION

In all complexes the nitrogen atom coordinated to $(NH_3)_5Co^{3+}$ moiety is called N-1 (**Scheme-I**). Rate constant for five- and six-member ring diazine ligands coordinated to Co(III) is reported at 25°C and 60°C, respectively. Complexes (**1-4**) are decomposed at temperature higher than 25°C and complexes (**5-7**) do not exchange at any C-H position at 25°C.



Scheme-I

Rates of ^{1}H exchange for $[(NH_3)_5CoPhtz]^{3+}$, were obtained by following the decay of H-8 as a function of time. Owing to the slow rates of exchange, measurements were carried out in the high pD region. Fig. 1 gives a series of spectra for the complex at pD 13.30 which shows the slow decay of the signal H-8 at 9.92 ppm.

Peak areas obtained by integration were recorded relative to the area of a non-exchanging signal. The plot of ln (peak area) *vs.* time for the data in Fig. 1 was linear giving $k_{obs} = (3.80 \pm 0.20) \times 10^{-5}\ s^{-1}$. Rates of exchange were also measured at other pDs and these data are collected in Table-1. A plot of k_{obs} *vs.* $[OD^-]$ is shown in Fig. 2. The second-order rate constant for exchange is $(8.0 \pm 0.5) \times 10^{-4}\ M^{-1}\ s^{-1}$.

TABLE-1
RATE DATA FOR EXCHANGE OF H-8 FOR $[(NH_3)_5CoPhtz]^{3+}$ IN D_2O AT DIFFERENT pD's, 25°C, I = 0.49 M

pD	a_{OD^-}/M	$[OD^-]$	k_{obs}/s^{-1}
12.80	9.770×10^{-3}	0.015	1.05×10^{-5}
13.03	0.017×10^{-3}	0.026	2.32×10^{-5}
13.10	0.019×10^{-3}	0.030	2.60×10^{-5}
13.16	0.023×10^{-3}	0.036	3.23×10^{-5}
13.25	0.028×10^{-3}	0.043	3.47×10^{-5}
13.30	0.031×10^{-3}	0.048	3.80×10^{-5}

Fig. 1. ^{1}H NMR spectra of $[(NH^3)^5CoPhtz]^{3+}$ at pD = 13.30 showing decay of the 9.92 ppm signal, with spectra recorded every 1 h, 25°C, I = 0.49 M(KCl)

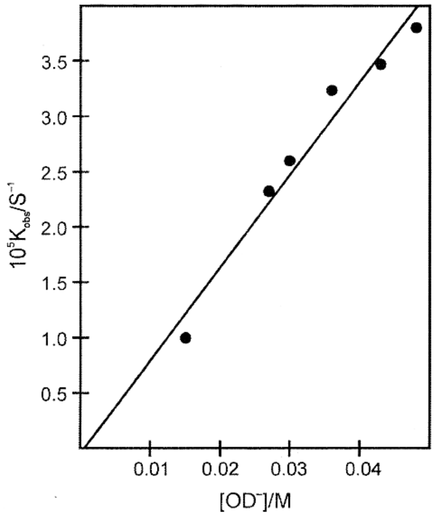


Fig. 2. Plot of k_{obs} *vs.* $[OD^-]$ for H-8 exchange in $[(NH_3)_5CoPhtz]^{3+}$, 25°C, I = 0.49 M

For complexes containing six-member ring diazine ligands the reaction rates for H/D exchange are correlated with ^{1}H NMR chemical shifts, with the fastest exchange being associated with the most electron deficient centre (*i.e.* the lower the field the *ortho* proton signal appears in the NMR spectrum the faster that proton undergoes exchange). The similar pattern is not seen for the ^{1}H NMR chemical shifts of complexes containing five-member ring diazine ligands. For example the rate constant for H-2 of $[(NH_3)_5Co(MeIm]^{3+}$ (**6**), which resonate at higher field (7.90 ppm) compared to that of $[(NH_3)_5Co(HIm]^{3+}$ (**5**), is faster. This attributed to the more stabilized ylide formation for $[(NH_3)_5Co(MeIm]^{3+}$. However the rate constants at 25°C (Table-2) are faster for $[(NH_3)_5CoPhtz]^{3+}$ (**1**), $[(NH_3)_5$ Co(3-MePhtz)$]^{3+}$ (**2**), $[(NH_3)_5CoPydz]^{3+}$ (**3**), $[(NH_3)_5Co(3\text{-}MePydz)]^{3+}$ (**4**) compared to those of $[(NH_3)_5Co(HIm]^{3+}$ (**5**), $[(NH_3)_5Co(MeIm]^{3+}$ (**6**) and $[(NH_3)_5CoIm(NH_3)_5]^{3+}$ (**7**). This trend is in consistent with the electron density of five- and six-member ring. For $[(NH_3)_5CoImCo(NH_3)_5]^{5+}$, containing 5+ charge, an attempt to study H-exchange was carried out in 0.1 M NaOD solution at room temperature. Fig. 3 shows a series of spectra recorded at hourly intervals for 14 h with the peak at 7.71 ppm being the signal due to H-2. Under these conditions H-4 and H-5, like H-2, similarly fail to exchange. Further, there was no evidence for H-2 exchange when this solution was maintained at 60°C for 170 h.

TABLE-2
RATE CONSTANTS FOR H/D IN $[(NH_3)_5Co(diazine)]^{3+}$ AND $[(NH_3)_5CoIm(NH_3)_5]^{5+}$ IONS

Compound	Exchange position	k_{ex} (M^{-1} s^{-1})	^{1}H NMR δ (ppm)
$[(NH_3)_5CoPhtz]^{3+}$ (**1**)	H-8	8×10^{-4}	9.92
$[(NH_3)_5$ Co(3-MePhtz)$]^{3+}$ (**2**)	H-8	5.5×10^{-4a}	9.66
$[(NH_3)_5CoPydz]^{3+}$ (**3**)	H-6	1.0×10^{-4a}	9.37
$[(NH_3)_5Co(3\text{-}MePydz)]^{3+}$ (**4**)	H-6	6.0×10^{-5}	9.15
$[(NH_3)_5Co(HIm]^{3+}$ (**5**)	H-2	0.26^b	8.06
$[(NH_3)_5Co(MeIm]^{3+}$ (**6**)	H-2	2.3^b	7.90
$[(NH_3)_5CoIm(NH_3)_5]^{5+}$ (**7**)	H-2	–	7.71

[a]Calculated from runs at $[OD^-]$ = 0.1 M; [b]Rate constants[7] at 60°C.

It is clear that in Co(III)-complexes, if chemical shift is a measure of electron deficiency[5] at a particular carbon centre, it is not the major factor which governs the rate of H/D exchange. As Table-2 shows the H-2 chemical shift for $[(NH_3)_5Co(MeIm]^{3+}$ (**6**) and $[(ND_3)_5CoImCo(ND_3)_5]^{5+}$ (**7**) is almost the same, but the later does not exchange in alkaline D_2O solution. H/D exchange in ligands coordinated to Co(III) usually takes places by

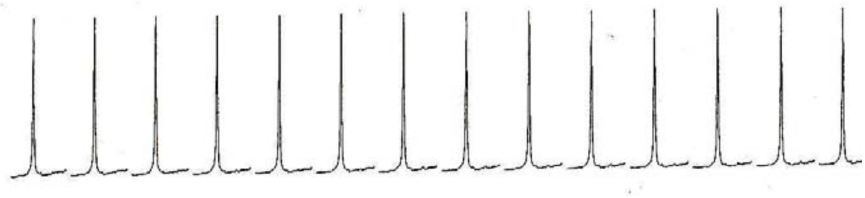


Fig. 3. Partial ^{1}H NMR spectra (7.71 ppm resonance) for $[(ND_3)_5CoImCo(ND_3)_5]^{5+}$ in 0.1 M NaOD at room temperature, interval between spectra 1 h

direct OD^- catalyzed proton abstraction and ylide formation. If H-transfer occurs by this mechanism why do the $[(ND_3)_5CoImCo(ND_3)_5]^{5+}$ undergo H/D exchange so slowly? A likely reason is that two $(NH_3)_5Co^{3+}$ groups provide a combination of steric and H-bonding[9] effects so as to substantially slow addition of OD^-. NOE experiments show that there is a strong NOE between *cis*-NH_3 in the $Co(NH_3)_5$ moiety and the *ortho* proton in the coordinated diazine. This indicates that these two groups are in close proximity and that the steric effect must be operating to some extent. Also, the ammine protons are ideally positioned to H-bond to incoming OD^- and so reduce its ability to act as a nucleophile toward the nearby carbon centre.

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