



**A STUDY ON
METAL ION COMPLEXATION
WITH
A MACROCYCLIC LIGAND**

(A Thermodynamic, Kinetic, and Mechanistic Investigation)

A Thesis Presented for the Degree of
Master of Science
in the University of Adelaide.

by

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ABSTRACT

The values of the acid dissociation constants (K_a) of the ligand, 1, 4, 8, 11-tetrakis(2-hydroxyethyl)-1, 4, 8, 11-tetraazacyclotetradecane (THEC), have been determined at 298.2 (± 0.2) K and ionic strength of 1.50 mol dm⁻³ adjusted with NaNO₃, using the potentiometric titration technique in combination with a pH electrode. The concentration stability constants for the formation of different complex species of Cu²⁺, Ni²⁺, and Co²⁺ with THEC have also been determined under identical conditions using the same technique.

The kinetics of complexation of metal ions, Ni²⁺ and Co²⁺, with THEC have been studied at pH 6.8, 298.2 (± 0.2) K and ionic strength of 1.50 mol dm⁻³ NaNO₃ in aqueous solution under pseudo first-order conditions (more than 10 fold excess concentration of metal ions compared to the concentration of the ligand) using the stopped-flow spectrophotometric technique. The variation of the observed pseudo first-order rate constant $k_{\text{obs.}}$ (s⁻¹) against excess metal ion, $[M^{2+}]_{\text{ex.}}$, is consistent with the following equation,

$$k_{\text{obs.}} = k_d + k_c [M^{2+}]_{\text{ex.}}$$

where k_d (s⁻¹) and k_c (dm³ mol⁻¹ s⁻¹) are the rate constants for decomplexation and complexation respectively.

The kinetics of complexation of Ni²⁺ ion with THEC have also been studied at various pH values, at the same temperature and ionic strength under pseudo first-order conditions, and the variation of $k_{\text{obs.}}$ (s⁻¹) against

hydrogen ion concentration, $[H^+]$ (mol dm^{-3}), is consistent with the following equation:

$$k_{\text{obs.}} = \frac{k'_{(\text{L})} K_{a1} K_{a2} + k'_{(\text{LH}^+)} K_{a2} [H^+] + k'_{(\text{LH}_2^{2+})} [H^+]^2}{K_{a1} K_{a2} + K_{a2} [H^+] + [H^+]^2}$$

where K_{a1} and K_{a2} are the first and second acid dissociation constants for THEC; and $k'_{(\text{L})}$, $k'_{(\text{LH}^+)}$, and $k'_{(\text{LH}_2^{2+})}$ are the first order (s^{-1}) rate constants for the complexation of Ni^{2+} with zero-, mono-, and di-protonated species of THEC respectively. The analyses of the results indicate that the mono-protonated species of the ligand is the only reacting species at pH 6.8, and the values of the second order rate constant, $k_{(\text{LH}^+)}$ ($\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$), for the complexation of Ni^{2+} and Co^{2+} ions with the mono-protonated species of THEC have been evaluated.

The kinetics of acid catalysed decomplexation of the Cu^{2+} -, Ni^{2+} -, and Co^{2+} - complexes of THEC have been studied at various temperatures and at a constant ionic strength of $1.50 \text{ mol dm}^{-3} \text{ NaNO}_3$ in aqueous solution under pseudo first-order conditions (more than 10 fold excess of acid concentration compared to the total concentration complex species) using the same stopped-flow spectrophotometric technique. The variation of the observed rate constant, $k_{\text{obs.}}$ (s^{-1}), against excess acid concentration, $[H^+]_{\text{ex.}}$ (mol dm^{-3}), can be represented by a general relationship of the form:

$$k_{\text{obs.}} = \frac{k_0 + k_1 K_1 [H^+]_{\text{ex.}} + k_2 K_1 K_2 ([H^+]_{\text{ex.}})^2}{1 + K_1 [H^+]_{\text{ex.}} + K_1 K_2 ([H^+]_{\text{ex.}})^2}$$

where k_0 , k_1 and k_2 are the first-order rate constants (s^{-1}) characterising the decomplexation of zero-, mono-, and di- protonated species of metal complexes of THEC ($[M(\text{THECH}_n)]^{(n+2)+}$) respectively, and K_1 and K_2 are the corresponding protonation constants ($\text{dm}^3 \text{mol}^{-1}$).

The activation parameters, ΔH^\ddagger (enthalpy of activation) and ΔS^\ddagger (entropy of activation), for the kinetic parameter, $k_1(s^{-1})$, have been evaluated for all the metal-THEC systems studied.

The mechanistic implications of the observed rate laws have been discussed, and the values of the resolved kinetic parameters have been compared with related macrocyclic systems published in the literature. A mechanism for the complexation of metal ions with the mono-protonated species of the ligand, THECH^+ , has been proposed on the basis of observed rate laws.

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DECLARATION

To the best of my knowledge and belief, this thesis contains no material which has been submitted for any other degree or diploma in any University, nor any material previously published or written by another author except where due reference is made in the text.

Upon being accepted for the award of the degree consent is given for this thesis being made available for photocopying and loan if applicable.

Benu Kumar Dey

This thesis was produced in October 1991, on an Apple-Macintosh computer using MS-Word 4.0, in 8,9,10,12,14,18, and 24 point Times/Symbol font.

Glossary of Abbreviations for Ligands, Solvents etc.

12aneN ₄	1,4,7,10-tetraazacyclododecane
13aneN ₄	1,4,7,10-tetraazacyclotridecane
14aneN ₄	1,4,8,11-tetraazacyclotetradecane
15aneN ₄	1,4,8,12-tetraazacyclopentadecane
16aneN ₄	1,5,9,13-tetraazacyclohexadecane
14aneNSNS	1,8-dithio-4,11-diazacyclotetradecane
14aneNSSN	1,11-dithio-4,8-diazacyclotetradecane
14aneN ₂ S ₂	1,4-dithio-8,11-diazacyclotetradecane
cyclam	1,4,8,11-tetraazacyclotetradecane
cyclen	1,4,7,10-tetraazacyclododecane
DMF	N,N-dimethylformamide
DMSO	dimethylsulphoxide
E	observed potential
E ₀	standard electrode potential
Et ₂ -2,3,2-tet	3,6,10,13-tetraazapentadecane
F	Faraday's constant ($9.6485 \times 10^4 \text{ C mol}^{-1}$)
h	Planck's constant ($6.62618 \times 10^{-34} \text{ J s}$)
K	Kelvin (absolute temperature scale)
K _a	acid dissociation constant ($\text{dm}^3 \text{ mol}^{-1}$)
k _B	Boltzmann's constant ($1.38066 \times 10^{-23} \text{ J K}^{-1}$)

kJ	kilo Joule
K_w	ionisation constant for water ($\text{dm}^3 \text{mol}^{-1}$)
log	logarithm to base 10
ln	logarithm to base e
MBPC	1-(2,2'-bipyridyl-6yl-methyl)-1,4,8,11-tetraazacyclotetradecane
Me	methyl moiety, $-\text{CH}_3$
Me-cyclam	1-methyl-1,4,8,11-tetraazacyclotetradecane
Me_2 -cyclam	1,5-dimethyl-1,5,8,12-tetraazacyclotetradecane
Me_4 -cyclam	1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane
Me_4 trien	1,1,10,10-tetramethyl-1,4,7,10-tetraazadecane
Me_6 trien	1,1,4,7,10,10-hexamethyl-1,4,7,10-tetraazadecane
PIPES	monohydrate sodium salt of [Piperazine-N,N'-bis-(2-ethane-sulphonic acid)]
pH	negative logarithm (to base 10) of hydrogen ion concentration ($-\log_{10}[\text{H}^+]$)
pOH	negative logarithm (to base 10) of hydroxide ion concentration ($-\log_{10}[\text{OH}^-]$)
$\text{p}K_a$	negative logarithm (to base 10) of acid dissociation constant ($-\log_{10}K_a$)
$\text{p}K_w$	negative logarithm (to base 10) of ionisation constant for water ($-\log_{10}K_w$)
R	gas constant ($8.31441 \text{ J K}^{-1} \text{ mol}^{-1}$)

T	absolute temperature (Kelvin)
TCEC	1,4,8,11-tetrakis(2-cyanoethyl)-1,4,8,11-tetraazacyclotetradecane
TETA	1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetraacetate
2,3,2-tet	1,4,8,11-tetraazaundecane
tet-a	meso-5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane
tet-b	racemic-5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane
THEC-12	1,4,7,10-tetrakis(2-hydroxyethyl)-1,4,7,10-tetraazacyclododecane
THEC	1,4,8,11-tetrakis(2-hydroxyethyl)-1,4,8,11-tetraazacyclotetradecane
THECH ⁺	mono-protonated form of THEC
THECH ₂ ²⁺	di-protonated form of THEC
THECH ₃ ³⁺	tri-protonated form of THEC
THECH ₄ ⁴⁺	tetra-protonated form of THEC
THEC-H ⁻	mono-deprotonated form of THEC
THEC-H ₂ ²⁻	di-deprotonated form of THEC
TMC	1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane
trien	1,4,7,10-tetraazadecane