

Chemical Process Analysis: Chemometrics; Instrument Control; Applications in Equilibrium and Kinetic Investigations

A thesis submitted in fulfilment of the requirements for the degree of
Doctor of Philosophy
at the School of Environmental and Life Sciences, Chemistry,
University of Newcastle
by

Sarah E. Norman, B.Sc (Hons.), B.Sc (Chem.) B.Tch

January, 2008

School of Environmental and Life Sciences, Chemistry
University of Newcastle
Callaghan NSW 2308
Australia

Author's Declaration

I hereby certify that the work embodied in this Thesis is the result of original research, the greater part of which was completed subsequent to admission to candidature for the degree. This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being made available for loan and photocopying subject to the provisions of the Copyright Act 1968.

Signature

Sarah Norman

Acknowledgements

There are many people that I am indebted to for making my PhD experience what it has been, but I would like to single out a few who have been the key influences in this project and on this time of my life.

Firstly, my supervisors deserve the biggest thanks: to Associate Professor Marcel Maeder for his constant guidance and support through both Honours and PhD. He has taught me as much about life as about chemistry, his philosophies and insight have been an invaluable contribution to my life and to my learning; and to Professor Geoffrey Lawrance for his encouragement and endless wealth of knowledge and ideas.

I would also like to extend my gratitude to Professor Alan Williams for the unforgettable opportunity to spend three months studying in Geneva, Switzerland in 2006; and a special thanks must also go to Doctor Bobby Neuhold for his friendship, patience and for teaching me the wonders of Matlab.

Particular thanks must also go to all the other postgraduates with whom I have shared the past few years with; particularly Nichola, Jenny, Hubs, Jez, Ewen Ben, and Kate. Also I extend a huge thank you to those in the Chemistry department in Geneva; Alex, Simon, Frank, Thibaut, Oliver, Xavier and Carlos, for welcoming me there so warmly and making my experience unforgettable.

I am also indebted to my family and extended family for their love and support, especially my Mum who encouraged me the whole way, proof read and re-proof read, and who has always been, and continues to be, a huge inspiration.

And lastly, my husband Dave, who is my soul-mate and best friend and who has been on this whole journey with me. I'm looking forward to the next adventure that life takes us on!

‘...the best kind of knowledge to have is that which is learned for its own sake’

Dedication

This thesis is dedicated to my family.

Table of Contents

Author's Declaration.....	iii
Acknowledgements.....	iv
Dedication.....	v
Table of Contents.....	vi
Abstract.....	xiii
List of Abbreviations and Definitions.....	xiv
Chapter 1 Introduction.....	1
1.1 Coordination Chemistry.....	3
1.2 Helices.....	4
1.2.1 Self-assembly.....	5
1.2.2 Chirality.....	7
1.3 Equilibria.....	9
1.3.1 Equilibrium Constants.....	9
1.3.2 Ionic Strength.....	11
1.3.3 Equilibria Terminology.....	14
1.3.4 Unidentate and Polydentate Ligands.....	15
1.3.5 pH Considerations.....	17
1.3.6 Relationship of Thermodynamic and Stoichiometric Constants.....	18
1.3.7 Conventions in Expressions.....	19
1.4 Kinetics.....	21
1.4.1 Reaction Rates.....	21
1.4.2 Order of a Reaction.....	22
<i>First-Order</i>	22
<i>Second-Order</i>	23
<i>Pseudo First-Order</i>	23
1.4.3 Factors Affecting the Rate of a Reaction.....	24
1.4.4 Complexation Kinetics.....	26
1.5 Chemometrics.....	26
1.5.1 Model-Based Data Fitting.....	28
1.5.2 Globalisation.....	30
1.5.3 Computational Techniques.....	32
	vi

1.6 References.....	35
Chapter 2 Programs: Data Acquisition and Analysis.....	43
2.1 Introduction.....	43
2.2 Data Acquisition	44
2.2.1 The Data.....	44
2.2.1.1 Mono-,Bi-, and Multivariate Data.....	45
2.2.2 General Techniques	48
2.2.3 Titration Experimentation	50
2.2.3.1 Overview	50
2.2.3.2 Equilibrium Investigations	52
2.2.3.3 General Experimental Procedure	54
2.2.3.4 Potentiometric Titrations.....	57
2.2.3.5 Spectrophotometric Titrations.....	59
2.2.3.6 Combined Potentiometric and Spectrophotometric Titrations.....	60
2.2.4 Kinetic Experimentation	63
2.2.4.1 Stopped-flow Acquisition - Fast Kinetics	63
2.2.4.2 Spectrophotometric Acquisition - Slow Kinetics.....	64
2.2.5 In-House Developed Software for Instrument Control	65
2.2.5.1 Titration Measurements	67
2.2.5.2 Slow Kinetic Reactions	72
2.3 Non-linear Least Squares Data Analysis	74
2.3.1 Overview.....	74
2.3.2 Globalisation of the Data	76
2.3.3 Model and Parameters.....	78
2.3.3.1 Spectroscopic Technique	80
2.3.3.2 Potentiometric Technique	82
2.3.4 Primary Chemical Models	83
2.3.4.1 Kinetic Analysis, Differential Equations	85
2.3.4.2 Equilibrium Studies, the Law of Mass Action	87
2.3.4.3 Non-Ideal Solutions	88
2.3.5 Fitting the Parameters	90
2.3.5.1 Computing the Calculated Data	90

2.3.5.2 The Residuals and Sum of Squares	91
2.3.6 Linear and Non-linear Parameters	92
2.3.7 Linear Parameters	93
2.3.8 Non-linear Parameters - Least-squares Fitting.....	96
2.3.8.1 Statistics of Output.....	101
2.3.8.2 χ^2 -fitting	102
2.3.8.3 Initial Estimates for Parameters	103
2.3.9 Determining the Correct Model	105
2.3.10 Published Software Packages.....	108
2.3.10.1 Package Details	102
2.3.10.2 Other Aspects of Data Fitting Programs	111
2.4 Our Data Analysis Program Design.....	114
2.4.1 User-Interface	116
2.4.2 Data Manipulation	122
2.4.2.1 Model Construction.....	122
2.4.2.2 Available Parameters	123
2.4.3 Output	124
2.5 Conclusions.....	125
2.5.1 Our Developed Programs.....	130
2.6 References.....	132
Chapter 3 Analysis of Potentiometric and Spectrophotometric Titrations with Polydentate N-donor Ligands.....	137
3.1 Introduction.....	137
3.1.1 Protonation Constants	138
3.1.2 Stability Constants	139
3.1.2.1 Defining Stability Constants	140
3.1.3 Combined Potentiometric and Spectrophotometric Titration Analysis	143
3.2 Solvent Considerations	144
3.2.1 Solvent Properties	144
3.2.2 Water-Alcohol Mixed Solvent Measurements.....	147
3.2.3 Electrode Use in Mixed Solvents.....	148
3.2.4 Ionisation Constants of Mixed Solvents	149

3.3 Experimental	150
3.3.1 Ligand Series	150
3.3.2 Analytical Solution Preparation	151
3.3.3 Titration Technique.....	153
3.4 Detailed Study of Ligand L5 (Pizda)	153
3.4.1 Determining the ‘Best’ Model	154
3.4.1.1 Protonation Model.....	155
3.4.1.2 Stability Model.....	155
3.4.2 Suggested Structures of Copper(II) – Pizda Complexes	166
3.5 Ligand Series Results and Discussion	169
3.5.1 Protonation Constants	169
3.5.1.1 Protonation Data Trends	172
3.5.2 Stability Constants	177
3.5.2.1 Potentiometric Titration Results	177
3.5.2.2 Spectrophotometric Titration Results	181
3.5.2.3 Stability Constant Data Trends	186
3.6 Conclusions	187
3.7 References	189
Chapter 4 Conjoint Chemometric Analysis of Equilibrium and Kinetic Data and Induced Chirality Investigations of a Helicating N-donor Ligand Interacting with Copper(II) and Nickel(II)	193
4.1 Introduction.....	193
4.1.1 Carboxamide-based Ligands	194
4.1.2 Helicate Formation Pathways	197
4.1.3 Induced Circular Dichroism of Racemic Helicates.....	198
4.2 Formation Pathway	198
4.2.1 Kinetic Investigation	198
4.2.1.1 Instrumentation	198
4.2.1.2 Solution Preparation.....	199
4.2.1.3 Data Analysis	201
4.2.2 Equilibrium Investigation	202
4.2.2.1 Instrumentation	202

4.2.2.2 Solution Preparation.....	202
4.2.2.3 Analytical Process.....	203
4.2.3 Conjoint Kinetic and Equilibrium Analysis.....	204
4.2.3.1 Kinetic Analysis.....	204
4.2.3.2 Equilibrium Analysis.....	207
4.2.3.3 Relationship Between Equilibrium and Rate Constants.....	209
4.2.3.4 Reaction Intermediates, $\log K_{\text{kin}} \neq \log K_{\text{eq}}$	214
4.3 Induced Chirality.....	218
4.3.1 Background.....	218
4.3.2 Circular Dichroism.....	219
4.3.3 Induced Circular Dichroism.....	220
4.3.4 PepdaH ₂ Helicity.....	223
4.3.4.1 Factors Affecting ICD Signal.....	224
4.3.5 Equilibrium of Intrinsic Induced Chirality.....	225
4.3.6 Experimental.....	227
4.3.6.1 Interaction with (-)-Tartaric Acid.....	227
4.3.6.2 Interaction with Sodium (+)-Tartrate.....	228
4.3.7 Results and Discussion.....	228
4.3.7.1 (-)-Tartaric Acid ICD Spectra.....	228
4.3.7.2 Sodium (+)-Tartrate ICD Spectra.....	230
4.3.7.3 ICD Analysis.....	232
4.4 Conclusions.....	235
4.5 References.....	238

Chapter 5 Equation Chapter 5 Section 5 Study of Nuclearity and Chirality of Complexes

Formed by a Helicating N-donor Ligand.....	243
5.1 Introduction.....	243
5.1.1 Aims of this Study.....	243
5.1.2 Overview.....	244
5.1.3 Bis(benzimidazole)-based Chelating Ligands.....	245
5.1.3.1 Basic Synthetic Process.....	245
5.1.3.2 Coordination Chemistry.....	246
5.1.3.3 Variations of the Bridging Unit.....	246

5.1.3.4 Substituted Variants	249
5.1.3.5 Applications	250
5.1.4 Stereoselectivity of ML_2 Complexes	251
5.1.4.1 Chirality	251
5.1.4.2 Theory	253
5.1.5 Previous Studies	255
5.2 Experimental	257
5.2.1 Instrumentation	257
5.2.2 Synthesis and Characterisation	257
5.2.3 Coordination Compounds	260
5.2.4 CD Spectra	261
5.2.5 CD Titrations with NaOH and HCl	261
5.2.6 CD Titration Technique for Determining Diastereoselectivity	262
5.2.7 ESMS Investigation of $[M(L-H)]_n$ Compounds	263
5.3 Results and Discussion	263
5.3.1 Preliminary CD and ESMS Investigations of Metal Complexes	263
<i>CD</i>	263
<i>ESMS</i>	266
5.3.2 CD Titrations	267
5.3.3 Determining Diastereoselectivity	272
5.3.4 ESMS Study	280
5.3.4.1 Mixed Ligand Species and Clear Resolution of Nuclearity	282
5.4 Conclusions	287
5.5 References	289
Chapter 6 Combined Glass Electrode Calibration	295
6.1 Introduction	295
6.1.1 The Definition of pH	296
6.1.2 pH Electrode Mechanism	296
6.2 Hydrogen Ion Activity Calibration Methods	298
6.2.1 IUPAC Recommended Methods	298
6.2.2.1 Primary Standard Buffer Solutions	299
6.2.2.2 Secondary Standard Buffer Solutions	302

6.2.2.3 Calibration Using Buffer Solutions.....	303
6.3 Calculating Equilibrium Constants	306
6.4 Hydrogen Ion Concentration Calibration Methods.....	308
6.4.1 Strong Acid / Strong Base Titration Calibration.....	308
6.5 Mixed and Non-aqueous Solvent Measurements.....	310
6.5.1 Standard Buffer Calibration	311
6.5.2 Alternative Calibration Techniques	312
6.5.2.1 Extrapolation.....	312
6.5.2.2 Correction Coefficients	313
6.5.3 Titration Calibration.....	314
6.5.4 Internal Concentration Calibration.....	316
6.5.5 Internal Concentration Computer Programs	318
6.6 Our Global Internal Calibration Program	320
6.6.1 Defining Parameters.....	321
6.7 Activity Approximations	325
6.8 Complex Solution Calibration Applications.....	327
6.8.1 pH Measurements in Beverages.....	328
6.8.1.1 Secondary Calibration.....	329
6.8.1.2 Extended Applications	336
6.8.2 Determination of the Purity of Room-Temperature Ionic Liquids	337
6.8.2.1 Synthetic Process	339
6.8.2.2 Global Analysis Method	340
6.9 Conclusions.....	347
6.10 References.....	350

Abstract

This work presents the development and application of modern data acquisition and analysis techniques for the investigations of equilibrium and kinetic reactions. The analytical technique is known as second order global analysis and a background of this relatively novel approach has been given. The theory behind and characteristics of the computer programs developed analysis as part of this research are described in Chapter Two along with descriptions of the instrumentation and programs developed for the acquisition of both potentiometric and spectrophotometric data.

Applications of the developed programs include a potentiometric and spectrophotometric study of the protonation and stability equilibria of a series of polydentate N-donor ligands, as detailed in Chapter Three. The combination of potentiometric and spectrophotometric analysis has been shown to be a powerful analytical tool.

Spectrophotometric titrations were also combined with fast stop-flow experiments in order to elucidate the complex reaction mechanisms associated with helicing ligands. The helication of the ligand 'PepdaH₂' with copper(II) and nickel(II) is examined in Chapter Four, along with discussions concerning the ability to induce chirality in the helicates from the addition of a chiral counter ion.

Investigations into chirality were further continued in Chapter Five where the stereoselectivity of a benzimidazole-based ligand was investigated with circular dichroism titrations. The synthesis and characterisation of the benzimidazole-based ligands are provided, including a study of the ability of the ligands to form higher order complexes as investigated using electrospray mass spectroscopy.

Chapter Six provides an in-depth discussion concerning the use of combined glass hydrogen selective electrodes for the determination of equilibrium constants, as this was a major focus of this research. Different calibration techniques are discussed and a description of the internal calibration technique developed is provided along with examples of the advantages of performing internal calibration of the electrode.

List of Abbreviations and Definitions

b.p.	Boiling point
Bispidinone	3,7-diazabicyclo[3.3.1]nonan-9-one
CD	Circular Dichroism
DMF	<i>N, N</i> –dimethylformamide
DMSO	Dimethyl sulphoxide
Dp-bispidinone	1,5-diphenyl-3,7-diazabicyclo[3.3.1]nonan-9-one
Dpdb-bispidinone	1,5-diphenyl-3,7-dibenzyl-3,7-diazabicyclo[3.3.1]nonan-9-one
EFA	Evolving Factor Analysis
ESMS	Electrospray Mass Spectroscopy
GA	Genetic Algorithm
¹ H n.m.r.	Proton Nuclear Magnetic Resonance
I	Molar ionic strength ($I = \frac{1}{2} \sum z^2[Z]$) of all species in solution
ICD	Induced Circular Dichroism
IR	Infra-red
K_s	Ionisation constant of a solvent
K_w	Ionisation constant of water
LJP	Liquid Junction Potential
m.p.	Melting point
NBS	National Bureau of Standards
NGL/M	Newton-Gauss-Levenberg/Marquardt
NIST	National Institute of Standards and Technology
NMI	National Metrological Institutes
PepdaH ₂	<i>N,N'</i> -bis[2-(2-pyridyl)methyl]pyridine-2,6-dicarboxamide
Piperazine	1,4-diazacyclohexane
Pizda	1-[(2''-hydroxycyclohexyl)-3'-aminopropyl]-4-[3'-aminopropyl]piperazine
Pot_Anal	Analytical Program for Potentiometric Titration Data
ProKII	Pro-Kineticist II
RLJP	Residual Liquid Junction Potential
Spec_Anal	Analytical Program for Spectrophotometric Titration Data
ssq	Sum of squared residuals

UV	Ultra-violet
x	Bold lower case characters for vectors
X	Bold upper case characters for matrices
<i>x</i>	Italic characters for scalars and chemical species
γ_z	Activity coefficient of a $\pm z$ charged species
[Z]	Molar concentration of species Z
{Z}	Activity of species Z
δ	Standard Deviation
μ	Ionic Strength (M)