Metal Complexes of Acyclic and Macrocyclic Multifunctional Ligands

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Abstract

This thesis describes the design, synthesis and study of metal derivatives of new acyclic and macrocyclic ligands containing pyridine and amide groups.

Chapter 1 provides an overview of metal-carboxamide and pyridinamide chemistry including a number of important pincer compounds, macrocyclic involvement in formation of metal-templated rotaxanes and catenanes, oxidation catalysts, anion receptors and bimetallic complexes.

Chapter 2 discusses new palladium(II) complexes of an acyclic ligand bearing pendant 2-pyridyl-6-methyl arms, *N,N′*-bis(6-methyl-2-pyridinyl)-2,6-pyridinedicarboxamide (H_2L_{Me}). H_2L_{Me} formed a dimer $[Pd(L_{Me})]_2$ when treated with palladium(II) salts and non-ligating bases, but in the presence of DBU the palladium-DBU adduct, $Pd(L_{Me})(DBU)$, was formed. Reaction of $Pd(L_{Me})(DBU)$ with methyl iodide resulted in the displacement of the DBU ligand and the concomitant formation of cationic monomeric complex, $[PdI(L_{Me}\{Me\}_2)]I$ and dimeric *N*-methylpyridinium complex, $[Pd(L_{Me}\{Me\})]_2I_2$. A series of ligands, *N,N′*-bis(*x*-tolyl)-2,6-pyridinedicarboxamide (*x* = 2, 3, 4) ($H_2L_{x\text{tol}}$), bearing *ortho*-, *meta*- and *para*-tolyl groups, was prepared and these were coordinated to palladium(II) in their deprotonated form so that the effect of the pendant pyridine rings and steric environment around the metal on the reactivity of metal derivatives could be investigated. Stable palladium(II) derivatives of the deprotonated $H_2L_{x\text{tol}}$ ligands, $Pd(L_{x\text{tol}})(E)$ (E = DBU, *n*-butylamine, *p*-tolylisocyanide) were prepared. The *p*-tolylisocyanide adducts reacted with pyrrolidine or *p*-toluidine to afford the stable bis(amino)carbene complexes, $Pd(L_{x\text{tol}})(=C(NH\text{-}p\text{-tolyl})(pyrl))$ and $Pd(L_{x\text{tol}})(=C(NH\text{-}p\text{-tolyl})_2)$, respectively. The coordinated DBU ligands in $Pd(L_{x\text{tol}})(DBU)$ and $Pd(L_{Me})(DBU)$ were displaced by *n*-butylamine to afford the corresponding *n*-butylamine adducts, and their relative rates of exchange were determined by ^1H NMR spectroscopy.

Chapter 3 discusses palladium(II) complexes of dicationic *N*-methylpyridinium ligands prepared by treating H_2L_{Me} or the series of ligands, *N,N′*-bis(*x*-pyridinyl)-2,6-pyridinedicarboxamide (*x* = 2, 3, 4) ($H_2L_{x\text{py}}$) that contain pendant 2-, 3-, or 4-pyridyl groups, with methyl triflate to form $[H_2L_{Me}\{Me\}_2][OTf]_2$ or $[H_2L_{x\text{py}}\{Me\}_2][OTf]_2$,

respectively. These ligands were coordinated in their deprotonated forms to palladium(II) to give [PdCl(L_{x}py{Me}$_2$)]OTf. The chloro ligands in these metallated complexes were displaced on treatment with silver triflate in acetonitrile or water to afford the corresponding solvent adducts. The coordinated solvent molecules in [Pd(L_{Me}{Me}$_2$)(NCCH$_3$)][OTf]$_2$ and [Pd(L_{opy}{Me}$_2$)(OH$_2$)][OTf]$_2$ could in turn be displaced by *p*-tolylisocyanide to form isocyanide adducts, [Pd(L_{Me}{Me}$_2$)(CN-*p*-tolyl)][OTf]$_2$ and [Pd(L_{opy}{Me}$_2$)(CN-*p*-tolyl)][OTf]$_2$. Dicationic bis(amino)carbene complexes [Pd(L_{Me}{Me}$_2$)(=C(NH-*p*-tolyl)$_2$)][OTf]$_2$ and [Pd(L_{opy}{Me}$_2$)(=C(NH-*p*-tolyl)$_2$)][OTf]$_2$ were prepared by treating the corresponding isocyanide precursors with *p*-toluidine. A ^{1}H NMR spectroscopic study was performed to compare the relative rates of reaction of *p*-toluidine with the neutral tolyl isocyanide complexes Pd(L_{x}tol)(CN-*p*-tolyl) and the dicationic isocyanide complexes [Pd(L_{Me}{Me}$_2$)(CN-*p*-tolyl)][OTf]$_2$ and [Pd(L_{opy}{Me}$_2$)(CN-*p*-tolyl)][OTf]$_2$ to determine the influence of the steric and electronic environments on the reactivity of the isocyanide ligand. On deprotonation of the amide groups in [H$_2L_{Me}${Me}$_2$][OTf]$_2$ and [H$_2L_{opy}${Me}$_2$][OTf]$_2$ the neutral free bis(imine) compounds L_{Me}{Me}$_2$ and L_{opy}{Me}$_2$ could be isolated.

Chapter 4 discusses extended acyclic ligands H$_4L_{pdnA}$ and H$_4L_{SpyA}$ (H$_4L_{xA}$) that were derived from the precursor *N,N′*-bis(6-acrylamido-2-pyridinyl)pyridine-2,6-dicarboxamide (H$_4L_{acrA}$) through Michael addition of pyrrolidine or 2-mercaptopyridine, respectively, to the acrylyl groups. The double-helical dimers [M(H$_2L_{xA}$)]$_2$ were formed when these ligands were treated with palladium(II) or mercury(II) acetate, and in the presence of DBU the adducts Pd(H$_2L_{xA}$)(DBU) were formed. In the absence of added base, palladium(II) acetate coordinated between the tail amine groups of the ligand H$_4L_{pdnA}$ which bears terminal pyrrolidyl groups.

Chapter 5 discusses complexes of macrocycles formed from double Michael-type addition of the amines *n*-butylamine, 2-(aminomethyl)pyridine, 2-(aminoethyl)pyridine, *N,N*-dimethylethylenediamine and *N,N′*-bis(2-pyridylmethyl)ethylenediamine to the pendant acrylyl groups of H$_4L_{acrA}$. The macrocycle synthesised from addition of *n*-butylamine, H$_4L_{nBu}$, reacted with palladium(II) acetate and DBU to form a complex in which palladium was coordinated in the macrocycle headgroup and an aminolactam resulting from hydrolysis of DBU was coordinated on the fourth site of the metal, Pd(H$_2L_{nBu}$)(NH$_2$Lac[7]). A palladium derivative of H$_4L_{nBu}$ with a labile water ligand, Pd(H$_2L_{nBu}$)(OH$_2$), was prepared and used for subsequent syntheses of n-butylamine,

DBU and *p*-tolylisocyanide adducts. When treated with *p*-toluidine, the isocyanide ligand of the macrocyclic *p*-tolylisocyanide adduct was displaced to form a *p*-toluidine adduct. Modified macrocycles with other amine donors incorporated into the tail were prepared in order to provide an additional site for metal complexation. The macrocycle with an additional *N,N*-dimethylamino group, H_4L_{dmen}, reacted with metal salts to form complexes where metallation had taken place at the tail amide groups and the tail amine group interacted with the metal.

For my parents Graeme and Robyn and my wife Anna –

This thesis is as much a product of your work as it is of mine.

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Finally,

"To him who is able to keep you from falling and to present you before his glorious presence without fault and with great joy – to the only God our Saviour be glory, majesty, power and authority, through Jesus Christ our Lord, before all ages, now and forevermore! Amen." – Jude 1 v 24-25 (NIV)

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List of Equations

List of Abbreviations

1D = One dimensional

2D = Two dimensional

AR = Analytical reagent

bipy = 2,2′-Bipyridyl

BPEDA = *N,N′*-Bis(2-pyridylmethyl)ethylenediamine

BTDP = (2-Benzoylimino)-1,4,6-trimethyl-1,2-dihydropyridine

br = Broad

Calc = Calculated

CCDB = Cambridge Crystallographic Database

CCDC = Cambridge Crystallographic Data Centre

COD = 1,5-Cyclooctadiene

COSY = Homonuclear correlation spectroscopy

Cp = Cyclopentadiene

d = Doublet

DBN = 1,5-Diazabicyclo[4.3.0]non-5-ene

DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene

DEPT 135 = Distortionless Enhancement by Polarization Transfer, 135° pulse angle

DIPA = Diisopropanolamine

DMSO = Dimethylsulfoxide

DPPM = bis(diphenylphosphino)methane

DPPP = 1,3-bis(diphenylphosphino)propane

Edited-HSQC = Heteronuclear Single Quantum Coherence, CH_2 peaks inverted

EI = Electron Impact

FAB = Fast Atom Bombardment

gem = Geminal

H_2EDTA^{2-} = Ethylenediaminetetraacetic acid, disodium salt

HMBC = Heteronuclear Multiple Bond Correlation

HSQC = Heteronuclear Single Quantum Coherence

LUMO = Lowest Unoccupied Molecular Orbital

m = Multiplet (NMR) / Medium (infrared)

NDB = Norbornadiene

$NH_2Lac[5]$ = *N*-(3-Aminopropyl)-γ-butyrolactam

$NH_2Lac[7]$ = *N*-(3-Aminopropyl)-ε-caprolactam

NHC = *N*-heterocyclic carbene

NMR = Nuclear Magnetic Resonance

N_{obs} = Number of observations

ORTEP = Oak Ridge Thermal Ellipsoid Plot

q = Quaternary

RCM = Ring Closing Metathesis

s = Singlet

SCE = Saturated calomel electrode

SD = Standard deviation

t = Triplet

TFA = Trifluoroacetate anion

THF = Tetrahydrofuran

TLC = Thin-layer chromatography

TMS = Tetramethylsilane

TOCSY = Total Correlation Spectroscopy

VT NMR = Variable Temperature Nuclear Magnetic Resonance