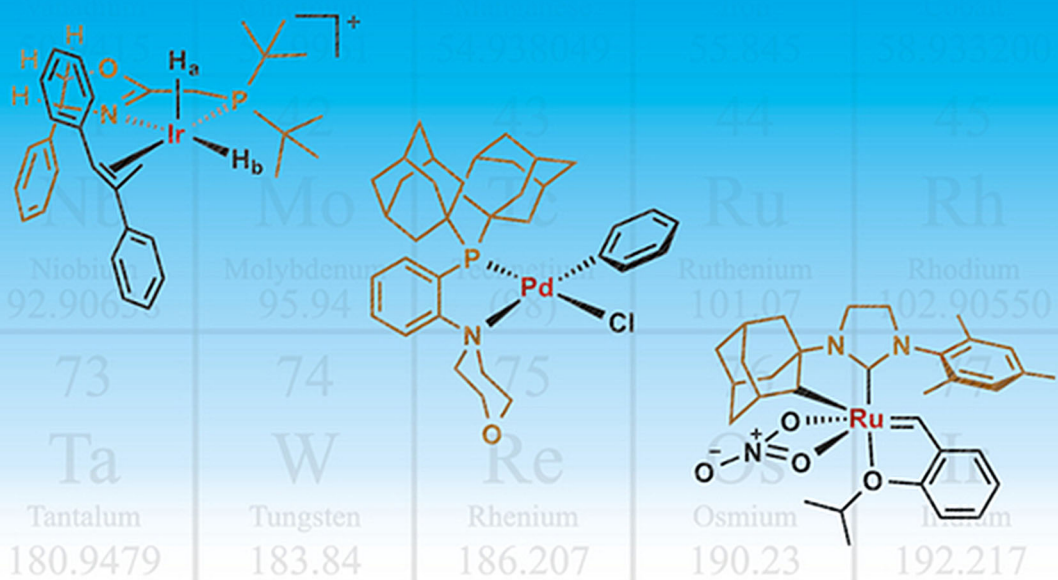


# Ligand Design in Metal Chemistry

## Reactivity and Catalysis

EDITED BY MARK STRADIOTTO • RYLAN J. LUNDGREN



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# **Ligand Design in Metal Chemistry**



# **Ligand Design in Metal Chemistry**

**Reactivity and Catalysis**

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**WILEY**

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# Contents

<i>List of Contributors</i>	xii
<i>Foreword by Stephen L. Buchwald</i>	xiv
<i>Foreword by David Milstein</i>	xvi
<i>Preface</i>	xvii
<b>1 Key Concepts in Ligand Design: An Introduction</b>	<b>1</b>
<i>Rylan J. Lundgren and Mark Stradiotto</i>	
1.1 Introduction	1
1.2 Covalent bond classification and elementary bonding concepts	2
1.3 Reactive versus ancillary ligands	4
1.4 Strong- and weak-field ligands	4
1.5 <i>Trans</i> effect	6
1.6 Tolman electronic parameter	6
1.7 Pearson acid base concept	8
1.8 Multidenticity, ligand bite angle, and hemilability	8
1.9 Quantifying ligand steric properties	10
1.10 Cooperative and redox non-innocent ligands	12
1.11 Conclusion	12
References	13
<b>2 Catalyst Structure and <i>Cis–Trans</i> Selectivity in Ruthenium-based Olefin Metathesis</b>	<b>15</b>
<i>Brendan L. Quigley and Robert H. Grubbs</i>	
2.1 Introduction	15
2.2 Metathesis reactions and mechanism	17
2.2.1 <i>Types of metathesis reactions</i>	17
2.2.2 <i>Mechanism of Ru-catalyzed olefin metathesis</i>	19
2.2.3 <i>Metallacycle geometry</i>	19
2.2.4 <i>Influencing syn–anti preference of metallacycles</i>	22
2.3 Catalyst structure and <i>E/Z</i> selectivity	24
2.3.1 <i>Trends in key catalysts</i>	24
2.3.2 <i>Catalysts with unsymmetrical NHCs</i>	26
2.3.3 <i>Catalysts with alternative NHC ligands</i>	29
2.3.4 <i>Variation of the anionic ligands</i>	31

2.4	Z-selective Ru-based metathesis catalysts	33
2.4.1	Thiophenolate-based Z-selective catalysts	33
2.4.2	Dithiolate-based Z-selective catalysts	34
2.5	Cyclometallated Z-selective metathesis catalysts	36
2.5.1	Initial discovery	36
2.5.2	Model for selectivity	37
2.5.3	Variation of the anionic ligand	38
2.5.4	Variation of the aryl group	40
2.5.5	Variation of the cyclometallated NHC substituent	41
2.5.6	Reactivity of cyclometallated Z-selective catalysts	42
2.6	Conclusions and future outlook	42
	References	43
<b>3</b>	<b>Ligands for Iridium-catalyzed Asymmetric Hydrogenation of Challenging Substrates</b>	<b>46</b>
	<i>Marc-André Müller and Andreas Pfaltz</i>	
3.1	Asymmetric hydrogenation	46
3.2	Iridium catalysts based on heterobidentate ligands	49
3.3	Mechanistic studies and derivation of a model for the enantioselective step	57
3.4	Conclusion	63
	References	64
<b>4</b>	<b>Spiro Ligands for Asymmetric Catalysis</b>	<b>66</b>
	<i>Shou-Fei Zhu and Qi-Lin Zhou</i>	
4.1	Development of chiral spiro ligands	66
4.2	Asymmetric hydrogenation	73
4.2.1	Rh-catalyzed hydrogenation of enamides	73
4.2.2	Rh- or Ir-catalyzed hydrogenation of enamines	73
4.2.3	Ir-catalyzed hydrogenation of $\alpha,\beta$ -unsaturated carboxylic acids	75
4.2.4	Ir-catalyzed hydrogenation of olefins directed by the carboxy group	78
4.2.5	Ir-catalyzed hydrogenation of conjugate ketones	79
4.2.6	Ir-catalyzed hydrogenation of ketones	80
4.2.7	Ru-catalyzed hydrogenation of racemic 2-substituted aldehydes via dynamic kinetic resolution	81
4.2.8	Ru-catalyzed hydrogenation of racemic 2-substituted ketones via DKR	82
4.2.9	Ir-catalyzed hydrogenation of imines	84
4.3	Carbon–carbon bond-forming reactions	85
4.3.1	Ni-catalyzed hydrovinylation of olefins	85
4.3.2	Rh-catalyzed hydroacylation	85
4.3.3	Rh-catalyzed arylation of carbonyl compounds and imines	86
4.3.4	Pd-catalyzed umpolung allylation reactions of aldehydes, ketones, and imines	87



4.3.5	<i>Ni-catalyzed three-component coupling reaction</i>	87
4.3.6	<i>Au-catalyzed Mannich reactions of azlactones</i>	89
4.3.7	<i>Rh-catalyzed hydrosilylation/cyclization reaction</i>	89
4.3.8	<i>Au-catalyzed [2 + 2] cycloaddition</i>	90
4.3.9	<i>Au-catalyzed cyclopropanation</i>	91
4.3.10	<i>Pd-catalyzed Heck reactions</i>	91
4.4	<b>Carbon–heteroatom bond-forming reactions</b>	91
4.4.1	<i>Cu-catalyzed N–H bond insertion reactions</i>	91
4.4.2	<i>Cu-, Fe-, or Pd-catalyzed O–H insertion reactions</i>	93
4.4.3	<i>Cu-catalyzed S–H, Si–H and B–H insertion reactions</i>	95
4.4.4	<i>Pd-catalyzed allylic amination</i>	95
4.4.5	<i>Pd-catalyzed allylic cyclization reactions with allenes</i>	97
4.4.6	<i>Pd-catalyzed alkene carboamination reactions</i>	98
4.5	<b>Conclusion</b>	98
	<b>References</b>	98
<b>5</b>	<b>Application of Sterically Demanding Phosphine Ligands in Palladium-Catalyzed Cross-Coupling leading to C(sp<sup>2</sup>)–E Bond Formation (E = NH<sub>2</sub>, OH, and F)</b>	<b>104</b>
	<i>Mark Stradiotto and Rylan J. Lundgren</i>	
5.1	<b>Introduction</b>	104
5.1.1	<i>General mechanistic overview and ancillary ligand design considerations</i>	105
5.1.2	<i>Reactivity challenges</i>	107
5.2	<b>Palladium-catalyzed selective monoarylation of ammonia</b>	108
5.2.1	<i>Initial development</i>	109
5.2.2	<i>Applications in heterocycle synthesis</i>	110
5.2.3	<i>Application of Buchwald palladacycles and imidazole-derived monophosphines</i>	112
5.2.4	<i>Heterobidentate <math>\kappa^2</math>-P,N ligands: chemoselectivity and room temperature reactions</i>	115
5.2.5	<i>Summary</i>	117
5.3	<b>Palladium-catalyzed selective hydroxylation of (hetero)aryl halides</b>	117
5.3.1	<i>Initial development</i>	118
5.3.2	<i>Application of alternative ligand classes</i>	120
5.3.3	<i>Summary</i>	122
5.4	<b>Palladium-catalyzed nucleophilic fluorination of (hetero)aryl (pseudo)halides</b>	123
5.4.1	<i>Development of palladium-catalyzed C(sp<sup>2</sup>)–F coupling employing (hetero)aryl triflates</i>	124
5.4.2	<i>Discovery of biaryl monophosphine ancillary ligand modification</i>	125
5.4.3	<i>Extending reactivity to (hetero)aryl bromides and iodides</i>	127
5.4.4	<i>Summary</i>	128
5.5	<b>Conclusions and outlook</b>	129
	<b>Acknowledgments</b>	130
	<b>References</b>	131

<b>6 Pd-N-Heterocyclic Carbene Complexes in Cross-Coupling Applications</b>	<b>134</b>
<i>Jennifer Lyn Farmer, Matthew Pompeo, and Michael G. Organ</i>	
6.1 Introduction	134
6.2 <i>N</i> -heterocyclic carbenes as ligands for catalysis	135
6.3 The relationship between <i>N</i> -heterocyclic carbene structure and reactivity	136
6.3.1 <i>Steric parameters of NHC ligands</i>	136
6.3.2 <i>Electronic parameters of NHC ligands</i>	138
6.3.3 <i>Tuning the electronic properties of NHC ligands</i>	139
6.4 Cross-coupling reactions leading to C—C bonds that proceed through transmetalation	140
6.5 Kumada–Tamao–Corriu	141
6.6 Suzuki–Miyaura	148
6.6.1 <i>The formation of tetra-ortho-substituted (hetero)biaryl compounds</i>	149
6.6.2 <i>Enantioselective Suzuki–Miyaura coupling</i>	153
6.6.3 <i>Formation of <math>sp^3</math>—<math>sp^3</math> or <math>sp^2</math>—<math>sp^3</math> bonds</i>	156
6.6.4 <i>The formation of (poly)heteroaryl compounds</i>	158
6.7 Negishi coupling	163
6.7.1 <i>Mechanistic studies: investigating the role of additives and the nature of the active transmetalating species</i>	166
6.7.2 <i>Selective cross-coupling of secondary organozinc reagents</i>	168
6.8 Conclusion	170
References	171
<b>7 Redox Non-innocent Ligands: Reactivity and Catalysis</b>	<b>176</b>
<i>Bas de Bruin, Pauline Gualco, and Nanda D. Paul</i>	
7.1 Introduction	176
7.2 Strategy I. Redox non-innocent ligands used to modify the Lewis acid–base properties of the metal	179
7.3 Strategy II. Redox non-innocent ligands as electron reservoirs	181
7.4 Strategy III. Cooperative ligand-centered reactivity based on redox active ligands	192
7.5 Strategy IV. Cooperative substrate-centered radical-type reactivity based on redox non-innocent substrates	195
7.6 Conclusion	200
References	201
<b>8 Ligands for Iron-based Homogeneous Catalysts for the Asymmetric Hydrogenation of Ketones and Imines</b>	<b>205</b>
<i>Demyan E. Prokopchuk, Samantha A. M. Smith, and Robert H. Morris</i>	
8.1 Introduction: from ligands for ruthenium to ligands for iron	205
8.1.1 <i>Ligand design elements in precious metal homogeneous catalysts for asymmetric direct hydrogenation and asymmetric transfer hydrogenation</i>	205

8.1.2	<i>Effective ligands for iron-catalyzed ketone and imine reduction</i>	212
8.1.3	<i>Ligand design elements for iron catalysts</i>	213
8.2	First generation iron catalysts with symmetrical [6.5.6]-P-N-N-P ligands	216
8.2.1	<i>Synthetic routes to ADH and ATH iron catalysts</i>	217
8.2.2	<i>Catalyst properties and mechanism of reaction</i>	218
8.3	Second generation iron catalysts with symmetrical [5.5.5]-P-N-N-P ligands	220
8.3.1	<i>Synthesis of second generation ATH catalysts</i>	220
8.3.2	<i>Asymmetric transfer hydrogenation catalytic properties and mechanism</i>	222
8.3.3	<i>Substrate scope</i>	226
8.4	Third generation iron catalysts with unsymmetrical [5.5.5]-P-NH-N-P' ligands	227
8.4.1	<i>Synthesis of bis(tridentate)iron complexes and P-NH-NH<sub>2</sub> ligands</i>	227
8.4.2	<i>Template-assisted synthesis of iron P-NH-N-P' complexes</i>	228
8.4.3	<i>Selected catalytic properties</i>	229
8.4.4	<i>Mechanism</i>	230
8.5	Conclusions	231
	Acknowledgments	232
	References	232
<b>9</b>	<b>Ambiphilic Ligands: Unusual Coordination and Reactivity Arising from Lewis Acid Moieties</b>	<b>237</b>
	<i>Ghenwa Bouhadir and Didier Bourissou</i>	
9.1	Introduction	237
9.2	Design and structure of ambiphilic ligands	238
9.3	Coordination of ambiphilic ligands	242
9.3.1	<i>Complexes featuring a pendant Lewis acid</i>	242
9.3.2	<i>Bridging coordination involving M → Lewis acid interactions</i>	243
9.3.3	<i>Bridging coordination of M—X bonds</i>	248
9.3.4	<i>Ionization of M—X bonds</i>	250
9.4	Reactivity of metallic complexes deriving from ambiphilic ligands	251
9.4.1	<i>Lewis acid enhancement effect in Si—Si and C—C coupling reactions</i>	251
9.4.2	<i>Hydrogenation, hydrogen transfer and hydrosilylation reactions assisted by boranes</i>	255
9.4.3	<i>Activation/functionalization of N<sub>2</sub> and CO</i>	262
9.5	Conclusions and outlook	264
	References	266

<b>10</b>	<b>Ligand Design in Enantioselective Ring-opening Polymerization of Lactide</b>	<b>270</b>
	<i>Kimberly M. Osten, Dinesh C. Aluthge, and Parisa Mehrkhodavandi</i>	
10.1	Introduction	270
10.1.1	<i>Tacticity in PLA</i>	271
10.1.2	<i>Metal catalysts for the ROP of lactide</i>	272
10.1.3	<i>Ligand design in the enantioselective polymerization of racemic lactide</i>	274
10.2	Indium and zinc complexes bearing chiral diaminophenolate ligands	292
10.2.1	<i>Zinc catalysts supported by chiral diaminophenolate ligands</i>	292
10.2.2	<i>The first indium catalyst for lactide polymerization</i>	294
10.2.3	<i>Polymerization of cyclic esters with first generation catalyst</i>	295
10.2.4	<i>Ligand modifications</i>	296
10.3	Dinuclear indium complexes bearing chiral salen-type ligands	297
10.3.1	<i>Chiral indium salen complexes</i>	297
10.3.2	<i>Polymerization studies</i>	297
10.4	Conclusions and future directions	301
	References	302
<b>11</b>	<b>Modern Applications of Trispyrazolylborate Ligands in Coinage Metal Catalysis</b>	<b>308</b>
	<i>Ana Caballero, M. Mar Díaz-Requejo, Manuel R. Fructos, Juan Urbano, and Pedro J. Pérez</i>	
11.1	Introduction	308
11.2	Trispyrazolylborate ligands: main features	310
11.3	Catalytic systems based on $Tp^*ML$ complexes ( $M = Cu, Ag$ )	311
11.3.1	<i>Carbene addition reactions</i>	312
11.3.2	<i>Carbene insertion reactions</i>	314
11.3.3	<i>Nitrene addition reactions</i>	319
11.3.4	<i>Nitrene insertion reactions</i>	321
11.3.5	<i>Oxo transfer reactions</i>	322
11.3.6	<i>Atom transfer radical reactions</i>	324
11.4	Conclusions	326
	Acknowledgments	326
	References	327
<b>12</b>	<b>Ligand Design in Modern Lanthanide Chemistry</b>	<b>330</b>
	<i>David P. Mills and Stephen T. Liddle</i>	
12.1	Introduction and scope of the review	330
12.2	C-donor ligands	333
12.2.1	<i>Silylalkyls</i>	333
12.2.2	<i>Terphenyls</i>	335
12.2.3	<i>Substituted cyclopentadienyls</i>	336
12.2.4	<i>Constrained geometry cyclopentadienyls</i>	338
12.2.5	<i>Benzene complexes</i>	340

12.2.6	Zerovalent arenes	342
12.2.7	Tethered N-heterocyclic carbenes	343
12.3	N-donor ligands	344
12.3.1	Hexamethyldisilazide	344
12.3.2	Substituted trispyrazolylborates	347
12.3.3	Silyl-substituted triamidoamine, $[N(CH_2CH_2NSiMe_2Bu^t)_3]^{3-}$	348
12.3.4	NacNac, $\{N(Dipp)C(Me)CHC(Me)N(Dipp)\}^-$	349
12.4	P-donor ligands	349
12.4.1	Phospholides	349
12.5	Multiple bonds	350
12.5.1	$Ln=CR_2$	350
12.5.2	$Ln=NR$	354
12.5.3	$Ln=O$	355
12.6	Conclusions	356
	Notes	357
	References	357
<b>13</b>	<b>Tight Bite Angle N,O-Chelates, Amidates, Ureates and Beyond</b>	<b>364</b>
	<i>Scott A. Ryken, Philippa R. Payne, and Laurel L. Schafer</i>	
13.1	Introduction	364
13.1.1	N,O-Proligands	366
13.1.2	Preparing metal complexes	367
13.2	Applications in reactivity and catalysis	377
13.2.1	Polymerizations	377
13.2.2	Hydrofunctionalization	385
13.3	Conclusions	400
	References	401
	<i>Index</i>	406

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# Foreword

Ligands have the ability to dramatically affect the way that metal complexes react.

In the context of this book, their ability to enhance the reactivity and/or selectivity in the transformation of small molecules is at the heart of the matter. In recent years there has been a growing emphasis on developing an understanding of how structural features of ligands play out in the catalytic transformations in which they are employed. In our work at MIT (described in part by Stradiotto and Lundgren in Chapter 5), we have found that the use of very bulky (steric), electron-rich (electronic) ligands can be particularly effective in palladium-catalyzed carbon–heteroatom bond-forming reactions. We have systematically examined how the change in ligand structure impacts the observed catalytic activity. In addition to the obvious effects of size and the arrangement of substituents, issues such as how coordination number affects the stability and reactivity of the catalytically active intermediates must be taken into account. Most of the basic strategies that we have relied upon were built on the fundamental research conducted by legions of chemists over the years. It is this continued, combined effort, that ultimately leads to successful outcomes.

This book describes the efforts of organic, inorganic and organometallic chemists to apply old principles and develop new ones in an incredible set of contexts. Those with experience in the field realize that good ligands for metals in one area of the periodic table often cannot be used when moving to the right or left. This has led to the need to find different creative solutions to, for example, develop catalysts for hydroamination reactions using group 4 metals rather than for the use of group 8 metals for asymmetric hydrogenation. The many exciting chapters in this book lay out how this has been achieved. Included are some of the most important and topical areas of research in organometallic chemistry. From the perspective of organic synthesis, olefin metathesis, asymmetric hydrogenation and palladium-catalyzed reactions have become some of the most widely used transformations in both the fine chemical industry and academia. The use of metals other than palladium, rhodium, iridium and ruthenium is of growing interest and chapters describing the use of iron catalysts for asymmetric hydrogenation and coinage metals for a variety of reactions are illustrative of this. The chemistry of early transition metal and lanthanide complexes which possess intriguing reactivity and with very different ligands than, for example, with palladium or rhodium



is nicely described in two chapters. Finally, two chapters describe “less conventional” types of ligands: non-innocent ligands and ambiphilic ligands. The first of these describes a situation where the ligand may change structure or have some sort of secondary function (e.g., recognition). The second reflects ligands that combine donor and acceptor capabilities.

Overall, this book provides a broad overview of both many areas in which ligands hold sway and the means by which they accomplish this. I am certain it will serve as a great resource for students and practitioners in the field alike.

Stephen L. Buchwald  
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# Foreword

These are great times for catalysis research. It is widely recognized that catalysis is of key importance in addressing the central societal needs of sustainability, including sustainable chemical synthesis, energy, and the environment. Aided by the current knowledge base in the field, and by advanced computational methods, much progress has already been made in catalytic design aimed at these goals.

The Editors of this book, Professors Mark Stradiotto and Rylan Lundgren, are to be commended for assembling an impressive book of excellent chapters, covering key aspects of the important and timely field of ligand design, which is of course essential to the development of selective and efficient reactions catalyzed by transition metal complexes.

Historically, the development of the fundamentals of ligand design has been largely driven by industrial needs. For example, some of the basic concepts, such as the Tolman ligand cone angle, and the Tolman electronic parameter, described by the Editors in the first chapter of this book, were postulated by Chad Tolman at DuPont Central Research in conjunction with the development of the industrially very important nickel-catalyzed process of butadiene hydrocyanation to adiponitrile *en route* to nylon 6,6, pioneered by Bill Drinkard. The success of this ligand design approach has led to further long-term intensive research on organometallic ligand design, as I had the privilege to personally experience in both industry and academia.

Several useful new families of ligands have evolved in the last few decades. Among those, NHC-type and pincer-type ligands have become quite popular and influential in organometallic chemistry and homogeneous catalysis. A particularly fascinating aspect for me is the ability of pincer-type complexes to effectively function by metal–ligand cooperation, in which both the ligand and the metal are involved in bond breaking and making. This has resulted in recent developments of various environmentally benign synthetic reactions, as well as findings relevant to sustainable energy.

I believe that the reported key concepts of ligand design and the catalytic reactions based on them, covered in this book by leading groups in this field, will capture the imagination of practitioners and students in this exciting field, and will likely lead to further exciting developments in catalysis.

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# Preface

Synthetic inorganic/organometallic chemistry represents a burgeoning field of study, in which the discovery of fundamentally new bonding motifs and stoichiometric reactivity can in turn underpin the practical development of catalytic substrate transformations on bench-top and industrial scales. The design and application of ancillary ligands to modify the reactivity properties of metal complexes has figured and continues to figure directly in enabling such advances. A number of important ancillary ligand design strategies have emerged that have served to advance the state-of-the-art across a range of reaction classes.

In recognizing the difficulty associated with comprehensively documenting all aspects of ancillary ligand design within a single, accessible monograph, we opted instead to assemble a diverse collection of cutting-edge chapters from international leaders in synthetic inorganic/organometallic chemistry and homogeneous catalysis that highlight the breadth and depth of modern ancillary ligand design. In some cases, we have directed the reader to allied texts that may be informative.

We envision that this book will be of particular interest to academic and industry practitioners working in the field of ancillary ligand design. Furthermore, given the significant impact of ancillary ligand design in transition metal catalysis, this text is also likely to be informative to scientists in the fields of synthetic organic chemistry, medicinal chemistry, polymer science, materials chemistry, and beyond. The relatively short “readable” chapters, each featuring a brief historical account followed by more advanced aspects of modern ancillary ligand design, renders this text well-suited to students in advanced undergraduate and graduate chemistry programs, as well as related short courses.

The book is organized into thirteen chapters, with Chapter 1 providing a brief overview of some of the key concepts and terminology that are employed within the ensuing chapters. Chapter 2 covers aspects of ancillary ligand design related to selectivity in ruthenium-catalyzed olefin metathesis. Chapter 3 describes the design of ancillary ligands for use in the iridium-catalyzed asymmetric hydrogenation of challenging unsaturated substrates, while Chapter 4 details the development of chiral spirocyclic ligands for such applications and beyond. Chapters 5 and 6 describe the development of sterically demanding phosphine and *N*-heterocyclic carbene ancillary ligands,

respectively, for use in addressing challenges in palladium-catalyzed cross-coupling chemistry. Redox non-innocent ancillary ligands are the focus of Chapter 7, while Chapters 8 and 9 deal with divergent facets of metal–ligand cooperative reactivity. Ancillary ligand design related to the enantioselective ring-opening polymerization of lactide is the focus of Chapter 10, while the application of trispyrazolylborate ancillary ligands in advancing coinage-metal chemistry is presented in Chapter 11. Chapter 12 details ancillary ligand strategies employed in lanthanide chemistry. Finally, Chapter 13 is focused on the development of tight bite angle *N,O*-chelates and their application in supporting catalytically active early metal complexes.

Our goal is that the collective insights provided by these diverse chapters will serve to educate experts and novice readers alike, so as to inspire future advances in the field.

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*Halifax, Nova Scotia, Canada, and Edmonton, Alberta, Canada*

# 1

## Key Concepts in Ligand Design: An Introduction

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### 1.1 Introduction

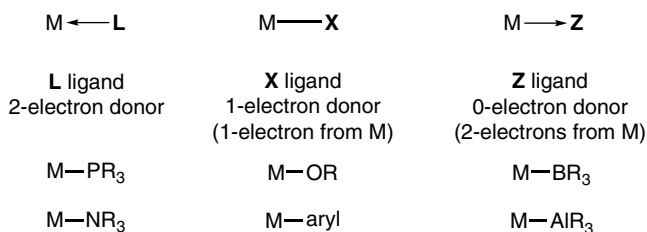
Organic or main-group molecules and ions that bind to metal centers to generate coordination complexes are referred to as ligands. Metal–ligand bonding interactions that arise upon coordination of a ligand to a metal serve both to modulate the electronic properties of the metal, and to influence the steric environment of the metal coordination sphere, thereby allowing for some control over the structure and reactivity of metal complexes. Thus, the fields of transition metal and organometallic chemistry, as well as homogeneous metal catalysis, have been greatly enriched by the design and study of new ligand motifs. An understanding of how ligands influence the structural and reactivity properties of metal species has allowed for the discovery of new and improved metal-catalyzed reactions that are exploited widely in the synthesis of a broad spectrum of molecules (e.g., pharmaceuticals) and materials (e.g., polymers). Moreover, such an understanding has enabled chemists to isolate and interrogate reactive intermediates of relevance to important biological or industrial processes, and to uncover fundamentally new modes of bonding between metal centers and

organic or main-group compounds. This chapter is meant to serve as a brief overview of what the authors believe are some of the important basic concepts when considering how ligands can alter the behavior of soluble metal complexes with respect to chemical reactivity and catalysis. General overviews of ligand structure, bonding, and nomenclature can be found in most introductory inorganic or organometallic textbooks, as can historical aspects of the importance of ligands in the development of these fields. We direct the reader to such resources for a more thorough treatment of the subject.<sup>[1]</sup>

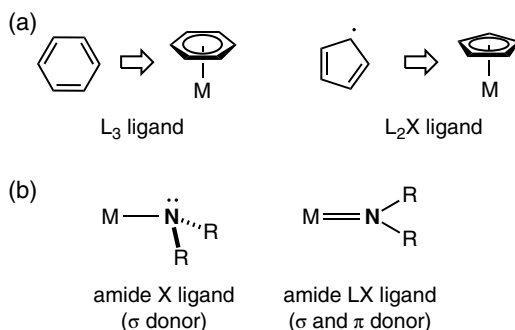
## 1.2 Covalent bond classification and elementary bonding concepts

In most simple cases, ligands act as Lewis bases, donating electron density to Lewis acidic metal centers. A prevailing method to classify the number and type of interactions between a metal and ligand, the Covalent Bond Classification, has been formulated by Green and Parkin (Figure 1).<sup>[2]</sup> Using this formalism, neutral two electron donor fragments are described as L-type ligands. The metal–ligand bond can be considered a dative interaction, whereby the valence of the metal is not changed upon ligand coordination. For simplicity, formal atom charges on the donor (ligand) and acceptor (metal) atom are invariably not depicted in chemical structures featuring such L-type interactions. Examples of L-type ligands include many classical Lewis bases, such as amines and phosphines. Single electron donors (or alternatively described, anionic two electron donors), such as halides, alkoxides, or carbon-based aryl or alkyl groups, are described as X-type ligands. The metal–ligand bond can be considered a covalent bond whereby one electron comes from both the metal and the ligand, raising the valence of the metal by one upon ligand coordination. Certain molecules can bind to metals in a fashion such that they accept, rather than donate, two electrons and are classified as Z-type ligands. This type of dative interaction formally increases the valence state of the metal by two. The most common Z-type ligands feature B or Al acceptor atoms.

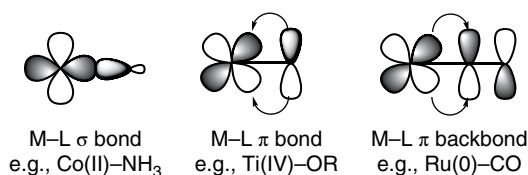
Ligands can bind to metals via one or more points of attachment, and/or can engage simultaneously in multiple bonding interactions with a metal center, via combinations



**Figure 1** Classification and examples of L, X, and Z ligands according to the Covalent Bond Classification method



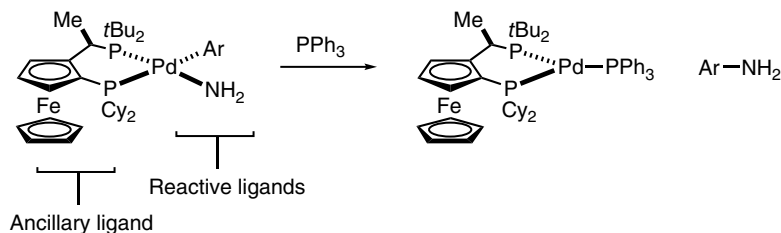
**Figure 2** (a) Examples of ligands which bind to metals via multiple L- or LX-type interactions. (b) Examples of metal–amide single (X) and double (LX) bonding



**Figure 3** Simplified schematic of metal–ligand  $\sigma$  and  $\pi$  bonding, as well as  $\pi$  backbonding

of L-, X- and Z-type interactions. The type and strength of the metal–ligand bonding involved will depend on the metal and oxidation state, among other factors. Prototypical examples of such bonding scenarios include arene–metal structures, where the three double bonds of the aromatic act as electron pair donors (an L<sub>3</sub>-type ligand), as well as the cyclopentadienyl group, an L<sub>2</sub>X-type ligand (Figure 2a). Simultaneous LX-type bonding can also arise to generate formal M=L double bonds, as is prevalent in many amide and alkoxide complexes (Figure 2b). The classification of these ligands as X-type or LX-type ligands is usually evidenced by the crystallographically determined bond angles about the donor atom, in addition to the observed M–L interatomic distance.

From an elementary molecular orbital perspective, filled ligand orbitals, such as lone pairs, donate to metals to form metal–ligand  $\sigma$  bonds while generating an accompanying empty metal–ligand  $\sigma^*$  orbital. Ligands can also donate electron density from orbitals of  $\pi$  symmetry. In instances where the metal has empty  $d\pi$  orbitals, for example  $d^0$  metals such as Ti<sup>4+</sup>, the bond between the metal and the  $\pi$ -donor ligand can be particularly strong. Ligands possessing empty p orbitals or  $\pi^*$  orbitals can act as  $\pi$  acids, accepting electron density from filled metal d orbitals of appropriate energy and symmetry (Figure 3). This type of  $\pi$  backbonding renders the metal center more electrophilic and strengthens the metal–ligand interaction. The combination of  $\sigma$ - and  $\pi$ -bonding interactions will dictate the overall M–L bond strength, as well as the reactivity properties of the M–L fragment.



**Figure 4** An example of a metal complex with ancillary and reactive ligands

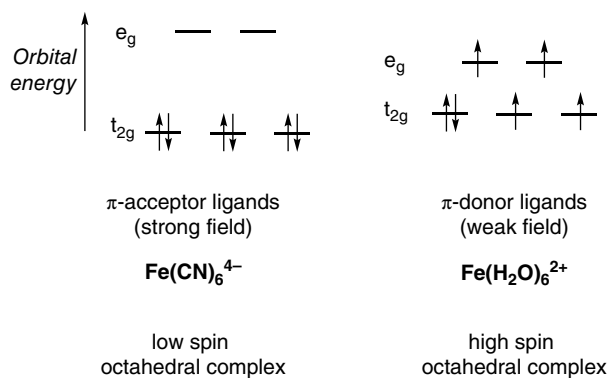
### 1.3 Reactive versus ancillary ligands

When considering the behavior of ligands coordinated to a metal center, two general classifications arise. Reactive ligands, when bound to a metal, undergo chemical change, which can include irreversible chemical transformations or dissociation from the metal. Prototypical examples of reactive ligands include hydride, aryl or alkyl groups. Ancillary ligands are defined as supporting ligands that can modulate the reactivity of a metal center, but do not themselves undergo irreversible transformations (Figure 4). The contents of this book deal generally with ancillary ligand design aimed at modulating the behavior of reactive ligands in reaction chemistry and catalysis. Undesired ancillary ligand reactivity, such as oxidation or cyclometallation, is a common cause of metal complex decomposition or deactivation during catalysis. It should be noted that depending on the reaction setting, a coordinated ligand could behave in a reactive or ancillary manner; CO and olefins serve as examples of such ligands. Non-innocent and cooperative ligands,<sup>[3]</sup> discussed in more detail below, operate between these definitions.

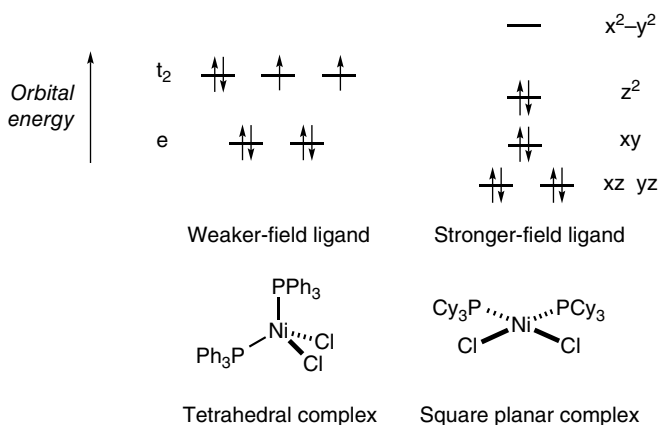
### 1.4 Strong- and weak-field ligands

Ligands have a large influence over the electronic configuration (or spin state), as well as the geometry, of transition metal complexes. Moreover, the ability of ligands to act as  $\pi$  donors or  $\pi$  acceptors can alter the relative energies of the d orbitals on the ligated metal center. Ligands that are  $\pi$ -accepting, such as CO, CN<sup>-</sup> or imine-type donors such as bipyridines, cause a large splitting in the energies of the d orbitals in a ligand field. For example, in ideal octahedral complexes the large energy difference between  $t_{2g}$  orbitals ( $d_{xz}$ ,  $d_{yz}$ ,  $d_{xy}$ ) and  $e_g$  orbitals ( $d_{x^2-y^2}$ ,  $d_{z^2}$ ) causes metals of certain d-electron counts to adopt low-spin configurations, as in  $\text{Fe}(\text{CN})_6^{4-}$ . Conversely,  $\pi$ -donating ligands, such as halides or alkoxides reduce the energy difference of the  $t_{2g}$  and  $e_g$  orbitals and promote high-spin configurations as in  $\text{Fe}(\text{H}_2\text{O})_6^{2+}$  (Figure 5).<sup>[1c]</sup> Similar trends occur for metals in other coordination geometries, such as tetrahedral or trigonal bipyramidal structures. The ability of ligands to act as donors or acceptors to induce changes in d-orbital energies (especially for octahedral complexes) can be easily assessed by use of spectroscopic methods, thus giving rise to the





**Figure 5** Influence of weak-field and strong-field ligands on the spin state of two prototypical octahedral  $d^6$  metal complexes



**Figure 6** Coordination geometry controlled by ligand field strength in four-coordinate  $\text{Ni}(\text{II})$  complexes

spectrochemical series, which ranks ligand  $\pi$ -bonding strength indirectly by measuring the octahedral  $e_g/t_{2g}$  energy gap.

Ligand field strength can also affect the geometry of transition metal complexes. An illustrative example is that of four coordinate  $d^8$  complexes. Binding to weak-field ligands promotes the formation of tetrahedral complexes, for example  $\text{NiCl}_4^{2-}$  or  $\text{NiCl}_2(\text{PPh}_3)_2$ , whereas strong-field ligands promote the formation of square planar complexes, such as  $\text{Ni}(\text{CN})_4^{2-}$  or  $\text{NiCl}_2(\text{PCy}_3)_2$  (Figure 6). A similar phenomenon is observed with  $d^6$   $\text{Fe}(\text{II})$  complexes, where strong field phosphine ligands can promote square planar geometries over the typically observed tetrahedral arrangement.<sup>[4]</sup> While strong-field or weak-field ligands generally influence coordination geometry to much lesser extent with second- or third-row transition metals [most  $\text{Rh}(\text{I})$ ,  $\text{Ir}(\text{I})$ ,  $\text{Pd}(\text{II})$ , and  $\text{Pt}(\text{II})$  complexes are square planar], they can influence the relative

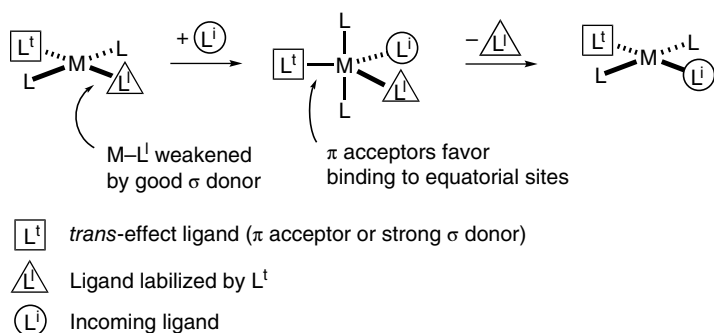
d-orbital energies, thus altering the ordering of the metal-based molecular orbitals within derived coordination complexes.<sup>[5]</sup>

## 1.5 *Trans* effect

Ligand coordination can influence a metal ion so as to alter the kinetics of ligand substitution and the bond strengths of the donor groups located at the *cis* or *trans* positions. This topic has been described in detail elsewhere.<sup>[1b]</sup> The kinetic *trans* effect observed for square planar d<sup>8</sup> complexes is illustrative. In these cases, ligands that are good  $\pi$  acceptors or strong  $\sigma$  donors can increase the rate of associative ligand substitution at the *trans* position by several orders of magnitude. Upon the formation of the trigonal bipyramidal structure by incoming ligand association, strong  $\pi$ -acceptor ligands (such as olefins) bind favourably to the more  $\pi$ -basic equatorial sites and labilize the other equatorial positions (Figure 7). By contrast, strong  $\sigma$  donors, for example silyl or alkyl groups, weaken the *trans* M–L bonds in square planar species by overlapping with the same metal orbitals as those involved in bonding with the *trans* L group.

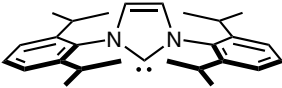
## 1.6 Tolman electronic parameter

The ability to measure and predict ligand donor (or acceptor) strength is an important tool in ligand design. Lone-pair basicity can be determined by pK<sub>a</sub> measurements of the corresponding conjugate acid, but as most metals are softer Lewis acids than a proton, these values can be misleading. The overall donor strength of a ligand when bonding with soft transition metals can be determined more accurately by measuring carbonyl stretching frequencies of ligated M(CO)<sub>n</sub> species, as originally described by Tolman's study of Ni(CO)<sub>3</sub>L species (Tolman electronic parameter, TEP).<sup>[6]</sup> In such complexes a reduction in the carbonyl stretching frequency wavenumber correlates to a metal center being made more electron rich via ligand (L) donation. Select TEP values for representative phosphine and carbene ligands are provided in Figure 8. More

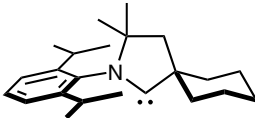


**Figure 7** Overview of the *trans* effect for square planar complexes

Ligand	TEP (cm <sup>-1</sup> )	
P(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub>	2091	<div style="display: flex; align-items: center; justify-content: center;"> <div style="flex: 1; border-left: 1px solid black; margin: 0 10px;"></div> <div style="writing-mode: vertical-rl; transform: rotate(180deg);">Increasing donor strength</div> </div>
P(OPh) <sub>3</sub>	2085	
P(OBu) <sub>3</sub>	2077	
PPh <sub>3</sub>	2069	
P(NMe <sub>2</sub> ) <sub>3</sub>	2062	
PEt <sub>3</sub>	2062	
P( <i>i</i> Pr) <sub>3</sub>	2059	
P( <i>t</i> Bu) <sub>3</sub>	2056	
IPr	2024	
CAAC	2020	



IPr

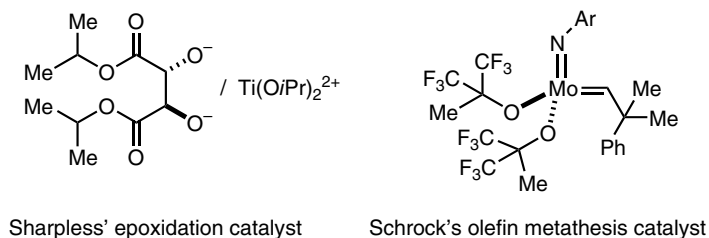


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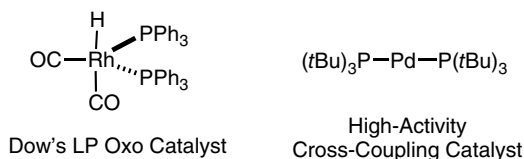
**Figure 8** Selected TEP values for phosphines and carbenes

comprehensive data on a vast range of ligands are available in the literature, including values that have been obtained through computational analysis with other metals.<sup>[6,7]</sup> Given the toxicity of Ni(CO)<sub>4</sub>, it is more common to benchmark ligand donicity experimentally with carbonyl stretching frequencies of Ir(CO)<sub>2</sub>CIL complexes, which Crabtree has correlated to the TEP.<sup>[8]</sup>

From the large collection of TEP data on ligand donor ability, a few generalizations can be made with regard to ligand structure and metal bonding. Trialkylphosphines are stronger donors than aryl phosphines. The donicity of aryl phosphines can be modulated by the introduction of P-*aryl*-group substituents, thus allowing for some control over the electron-richness of the ligated metal. Many *N*-heterocyclic carbenes are very strong donors, even stronger than bulky trialkylphosphines. Nitrogen-based ligands are generally poorer  $\sigma$  donors, especially when binding to low oxidation state late transition metals. Pyridines, imines, and related *N*-heterocyclic donors (such as oxazolines) are good  $\pi$ -acceptor ligands and can be used to enhance metal electrophilicity. These *N*-ligand frameworks have most commonly been exploited with success in combination with first-row transition metals (e.g., Fe, Ni, and Cu) or metals in relatively high oxidation states (e.g., Pt<sup>4+</sup>). In all cases, the donor ability and nature of the metal–ligand interaction will depend highly on the transition metal, oxidation state, and other connected ligands.



**Figure 9** Representative early/mid transition metal catalysts featuring hard metal/ligand interactions



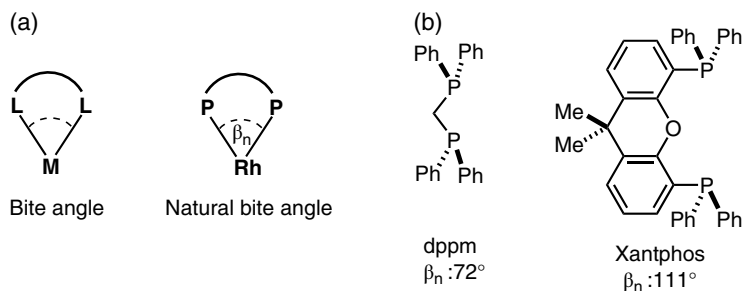
**Figure 10** Representative late transition metal catalysts featuring soft metal/ligand interactions

## 1.7 Pearson acid base concept

Consideration of hard and soft Lewis acid/base properties (Pearson acid base concept) can provide an intuitive concept to estimate metal–ligand bond strength on the basis of electrostatics and orbital overlap.<sup>[9]</sup> Hard transition metals, such as high oxidation state complexes of the Group 3, 4, or 5 metals, as well as lanthanides, form strong bonds to hard Lewis basic ligands such as those featuring N- and O-donor atoms. Particularly noteworthy examples of catalysts demonstrating this trend include Sharpless' Ti catalysts for epoxidation<sup>[10]</sup> and Schrock's catalysts for olefin metathesis<sup>[11]</sup> (Figure 9). Conversely, larger and more polarizable transition metals in relatively low oxidation states bind strongly to softer donors, such as phosphines and carbenes. This helps explain the domination of these ligand classes for platinum-group metal catalyzed reactions such as Rh-catalyzed hydroformylation<sup>[12]</sup> and Pd-catalyzed cross-coupling (Figure 10).<sup>[13]</sup>

## 1.8 Multidenticity, ligand bite angle, and hemilability

Species that bind by more than one point of attachment to a metal center are described as chelating or polydentate ligands. The increased favorability of polydentate ligand binding to a given metal, compared with that of similar monodentate ligands, is referred to as the chelate effect. Chelating ligands are ubiquitous in transition metal bond activation and catalysis, as they can provide increased stability and a higher degree of control over the coordination environment of a metal compared with analogous monodentate ligands.

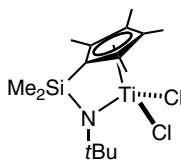


**Figure 11** Bite angle and natural bite angle of bidentate ligands, with representative examples of small (dpmm) and large (Xantphos) bite angle bisphosphine ligands

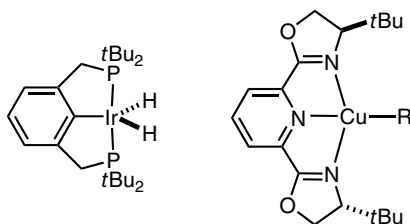
Bite angle is a parameter that is used to describe the angle between two donor atoms and the metal (i.e., the L–M–L angle; Figure 11a). Geometric constraints imposed by the backbone of chelating ligands can restrict how close the donor groups can be to a metal; as such, chelating ligands can bind with bite angles that are much larger or smaller than the geometrical ideal, thereby influencing the ground state or transition state of metal complexes undergoing a chemical reaction. The term natural bite angle ( $\beta_n$ ) is used to describe the preferred chelation angle determined by the ligand backbone constraints, and is obtained using molecular mechanics calculations employing a standard Rh–P bond length of 231.5 pm, rather than being determined experimentally.<sup>[14]</sup> For example, bis(diphenylphosphino)methane (dpmm) binds to five-coordinate Rh(I) with a  $\beta_n$  of  $72^\circ$ , whereas the wide bite angle bisphosphine Xantphos binds at an angle of  $111^\circ$ . Both observed structures represent a major deviation from the ideal bond angle of  $90^\circ$  between axial and equatorial positions in trigonal pyramidal structures, or *cis* positions in square planar structures (Figure 11b). A noteworthy example of the impact ligand bite angle has on metal-centered reactivity is seen in Rh-catalyzed hydroformylation reactions, in which increasing the ligand bite angle provides favorable reactivity.<sup>[14,15]</sup> The flexibility range of chelating ligands, defined as the range of bite angles adoptable within 3 kcal/mol of strain energy, is a useful term to judge the degree of allowable distortion chelating ligands can undergo upon metal binding. The widespread utility of Xantphos-type ligands in homogeneous catalyst highlights the importance of bite angle tuning in ligand design.

Conceptually similar “constrained geometry” catalysts feature distorted cyclopentadienyl/ $\sigma$ -donor ligands and have found widespread use in early transition metal catalysis, most notably polymerization.<sup>[16]</sup> In these cases, the bite angle of the cyclopentadienyl (Cp)–metal–amido is compressed by  $\sim 25\text{--}30^\circ$  compared to unstrained metallocenes (Figure 12).<sup>[17]</sup>

A particularly important class of chelating ligands called pincers feature three adjacent, often coplanar, donors. Pincer complexes tend to display high stability due to their tight binding and rigid structure. Metal complexes supported by pincer ligands have been demonstrated to exhibit a wide range of reactivity in bond activation and catalysis.<sup>[17,18]</sup> A commonly employed pincer ligand motif features two phosphorus



**Figure 12** Constrained geometry catalyst precursor featuring Cp–metal–amido bond angle compression



**Figure 13** Structure of an Ir-PCP pincer complex and of a Cu-PyBox complex

L donors flanking a central cyclometallated aryl carbon group (i.e., an X donor), referred to as a PCP pincer (Figure 13), although an extremely broad range of pincer ligands with B, C, N, O, Si and P donor groups have been reported. Planar, tridentate ligands have also found widespread utility in metal-mediated asymmetric catalysis. For example, pyridine-centered bisoxazolines, termed PyBox ligands, have found utility in many Cu-, Ni-, and Ru-catalyzed reactions thanks to their tight chelation and tunable  $C_2$  symmetry.<sup>[19]</sup> The utility of pincer complexes has been reviewed extensively and we direct the reader to a recent monograph.<sup>[20]</sup>

Flexible polydentate ligands featuring a combination of strong and weak donor groups (often a mix of hard and soft donors) can often undergo facile coordination/decoordination events in the presence of reactants or under catalytic conditions. This dynamic property is called hemilability. The design of hemilabile ligands offers the opportunity to employ relatively stable coordinatively saturated complexes, which in turn provide access to highly reactive low-coordinate metal species in the presence of substrate molecules. The remarkable effects of ligand hemilability can be found in both foundational and modern organometallic chemistry and catalysis. For example, Shaw demonstrated that a phosphine ligand containing a hemilabile methoxy group dramatically enhanced the rates of oxidation addition to Ir(I) complexes (Figure 14).<sup>[21]</sup>

## 1.9 Quantifying ligand steric properties

The space a ligand occupies around the metal center, or steric bulk, is an extremely important parameter for modulating the reactivity and stability of complexes. Ligand sterics are most often modified by changing the substituent groups of the donor atom.