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Introduction

At irregular intervals, it is announced that organic synthesis is dead, that it is a completed science, that all possible molecules can be made by the application of existing methodology, and that there are no new reactions or methods to discover – everything worth doing has been done. And yet new molecular structures come up to challenge the imagination, most often from nature, and new challenges arise from the demands of society and industry, usually to be more selective, to be more efficient and to be more green. The tremendous progress that has been made in the last few decades, including the hectic period since the first edition of this work appeared, is more than ample to prove the prophecies of doom to be wrong. The art and science of organic synthesis continues to make progress as the new challenges are met. While much of the limelight has been taken up by the expansion of the once small and neglected field of asymmetric organocatalysis, huge progress has also been made in the use of transition metals. The academic and practical significance of this area can be seen by a glance at the list of Nobel prizes for chemistry (even if not all of the laureates had intended to contribute to organic synthesis): Sabatier, shared with Grignard (1912), Ziegler¹ and Natta² (1963), Wilkinson³ and Fischer⁴ (1973), Sharpless,⁵ Noyori⁶ and Knowles⁷ (2001), Grubbs, Schrock⁸ and Chauvin⁹ (2005) and, most recently, Heck, Negishi¹⁰ and Suzuki¹¹ (2010).

Advances in the area have not been uniform. With the challenge of greenness, atom economy and sustainability, the most progress has been made in the area of catalysis.¹² Progress in the use of stoichiometric transition-metal reagents and with transition-metal complex intermediates has lagged, while progress in catalysis has surged ahead. Four areas of transition-metal chemistry have been at the forefront of recent progress. One is the tremendous advances and applications made in the area of alkene metathesis chemistry and its spin-off fields. What was once a mainstay of the petrochemical industry, but a curiosity to synthetic organic chemistry has become a standard method for carbon–carbon bond formation. New metathesis catalysts continue to open up new possibilities. The second, not unrelated, area is the development of new ligands. At one time, except for asymmetric catalysis, triphenylphosphine was the option as a ligand, with a small number of variants available. Driven by the demand for greater efficiency and wider substrate scope, a myriad of complex ligands is now available. While their initial impact was upon coupling reactions, their influence is spreading to other areas. The emergence of the *N*-heterocyclic carbene ligands has provided a second stimulus in this area and opened up further opportunities. In addition to more ligands, a greater number of the transition metals are finding applications in organic synthesis. While palladium probably remains the most widely used metal, its “market share” has shrunk, with the increasing use other metals. Most notable is the glittering rise of gold and gold catalysis. The final area had been present in the literature for decades but only took off recently.

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This is the area of C–H activation, based upon the realization that C–H bonds are not passive spectators, but, with the ability of transition metals to insert into them under mild conditions, are potent functional groups.

This is an area of science that is very much alive and moving forwards. Transition-metal chemistry is not only used for academic purposes, but also in the fine chemicals industry. The reader will find references to these real-life applications in the appropriate chapters.

1.1 The Basics

Why? What is special about the transition metals and the chemistry that we can do using them? What makes metals such as palladium, iron and nickel different from metals such as sodium, magnesium and lithium? The answer lies in the availability of d-orbitals, filled or empty, that have energy suitable for interaction with a wide variety of functional groups of organic compounds. In an important example, transition metals can interact with alkenes. In ordinary organic chemistry, simple alkenes are relatively unreactive, being ignored by almost all bases and nucleophiles, requiring a reactive radical or a strong electrophile or oxidizing agent, such as bromine, ozone or osmium tetroxide (watch out – osmium is a transition metal!). But they coordinate to transition metals and their reactivity changes. An important molecule that has almost no “ordinary” organic chemistry is CO. It is ignored by metal ions such as Na^+ and Mg^{2+} , but forms complexes with almost all transition metals and is ubiquitous in transition-metal chemistry. The reactions of CO, catalysed by transition metals, has made it a fundamental C_1 building block for both complex molecules and bulk chemicals.

Organometallic chemistry begins with the work of Frankland in the 1840s who made the first organozinc compounds. Grignard’s work with organomagnesium compounds rapidly became part of the standard repertoire of organic chemists, and remains there today. The pathway for transition metals was not so smooth and took much longer. Indeed, it followed two tracks. One track was in industry, where the understandable objective is a profitable process even if there is no understanding of what is happening in the mechanistic “black box”. This track produced alkene metathesis and hydroformylation. The other track was in academia, restrained by the need to understand. Alongside the isolation of then unexplainable complexes, such as an ethylene complex of platinum by Danish apothecary Zeise,¹³ one of the starting points is with Ludwig Mond in the late nineteenth century.¹⁴ He serendipitously discovered $\text{Ni}(\text{CO})_4$ – an amazing compound in that it is a gas under normal conditions, yet is made from so-solid metallic nickel. In terms of using transition metals for synthetic chemistry, a great advance was by Sabatier at the end of the nineteenth century who showed that finely divided metals such as nickel, palladium or platinum could catalyse the hydrogenation of alkenes. This discovery rapidly led to the manufacture of margarine, for instance. A real turning point was with the determination of the structure of ferrocene by Wilkinson – many decades after Mond. This gave chemists a stable organometallic compound to study and understand. Aided by advances in instrumentation, it was in this period that chemists were able to study organotransition-metal complexes thoroughly and understand the ground rules of their reactivity.

Thus, the use of transition metals enables the organic chemist to do reactions that are difficult or, more often, impossible otherwise, opening up new synthetic pathways and selectivities. Transition-metal organometallics do this through a different set of rules. To understand what is done and what can be done, it is important to be familiar with these rules.

1.2 The Basic Structural Types

While some of the structures found look similar to those formed by s-block and p-block metals, many do not. Many organometallic complexes are classified by the number of contiguous atoms, usually carbon atoms, but

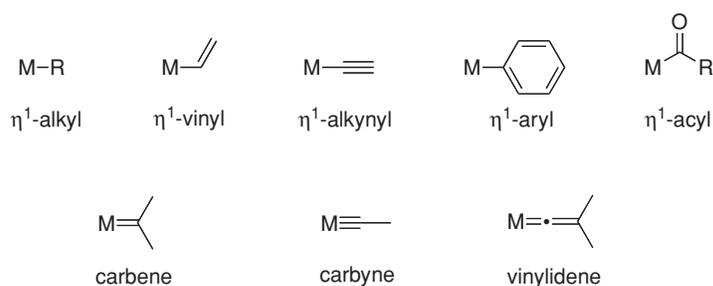


Figure 1.1 η^1 -Complexes.



Figure 1.2 η^2 -Alkene complex.

not always, bound to the metal. This number is known as the hapticity or hapto number. As this is symbolized as a superscript with the Greek letter “eta”, η , it is sometimes called the eta number.

η^1 -Complexes contain a metal–carbon single bond (Figure 1.1). The organic group may be alkyl, vinyl, alkynyl, aryl or acyl. With the exception of the acyl complexes, there are analogous compounds of more familiar metals, such as magnesium and zinc. It is also possible to have complexes with metal–carbon double and triple bonds; these are known as carbenes and carbynes. Cumulenes are also known, such as in vinylidene complexes.

η^2 -Complexes do not have analogues amongst the main group metals. They are formed by the interaction of the metal with the π -orbitals of alkenes and alkynes (Figure 1.2). They may also be drawn as their metallacyclopropane resonance structures, although this representation is less frequently used. The first such complex, isolated in the early nineteenth century, is the platinum–ethylene complex known as Zeise’s salt (Figure 1.3).¹⁵

The reason for the ability of transition metals to bind to alkenes (and alkynes) lies in the fact that electrons can be donated in both directions, resulting in a synergistic effect (Figure 1.4). The π^* -orbital of the alkene can accept electrons from filled d-orbitals on the metal, while the filled π -orbital of the alkene can donate back to empty metal orbitals. This is known as the Chatt–Dewar–Duncanson model.¹⁶

η^3 -Allyl complexes, also known as π -allyl complexes, have three atoms bonded to the metal (Figure 1.5). They are frequently in equilibrium with the corresponding η^1 -allyl complex.

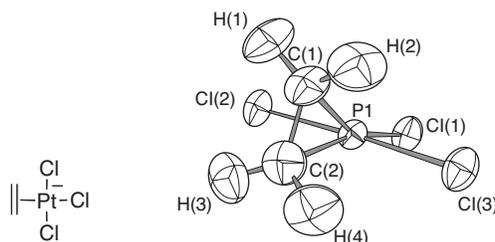


Figure 1.3 Zeise’s salt. Reprinted with permission from Love, R. A.; Koetzle, T. F. et al. *Inorg. Chem.* **1975**, *14*, 2653. © 1975 American Chemical Society.

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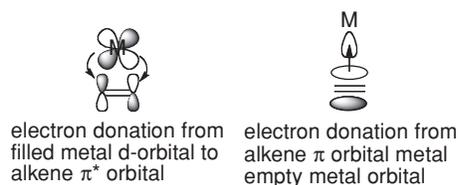
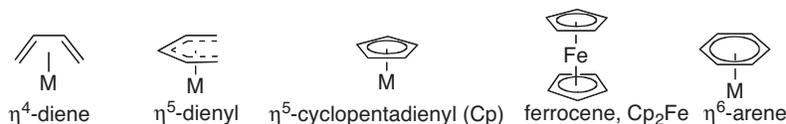


Figure 1.4 The Chatt–Dewar–Duncanson model.

Figure 1.5 The η^3 – η^1 equilibrium in allyl complexes.Figure 1.6 η^4 , η^5 and η^6 -complexes.

η^4 -diene, η^5 -dienyl and η^6 -arene complexes have four, five or six atoms bonded to the metal (Figure 1.6). The chemistry of these complexes is explored in Chapter 10. Amongst the η^5 -dienyl complexes, the best known is the η^5 -cyclopentadienyl ligand. Such is its ubiquity, that it has its own symbol: Cp. The best known of the cyclopentadienyl compounds is ferrocene (Cp_2Fe) with two Cp rings, the original sandwich compound. The permethyl derivative, pentamethylcyclopentadienyl, is known as Cp^* . The most important class of η^6 -complexes by far is the η^6 -arene complexes in which a metal is coordinated to the face of a benzene derivative through the π -system. η^7 -Complexes are unusual in synthesis: an example may be found in Chapter 11. In all of these complexes, the carbon atoms are coplanar, with the metal occupying one face.

A ligand of special importance is carbon monoxide. The reactivity of CO is a key difference between transition-metal chemistry and classical organic chemistry. Several of the transition metals, such as Mond's nickel, can even form complexes with only CO. The HOMO of CO is its σ^* -orbital, concentrated on the carbon atom, hence CO is most commonly bonded to the metal via its carbon atom. Backbonding then occurs with electron donation from metal d-orbitals into the LUMO of carbon monoxide which is the π^* -orbital (Figure 1.7). This is the case for the simple metal carbonyls including $\text{Ni}(\text{CO})_4$, $\text{Fe}(\text{CO})_5$ and $\text{Cr}(\text{CO})_6$.

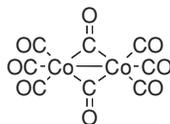
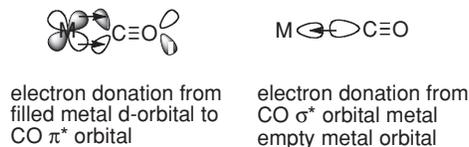


Figure 1.7 Carbonyl complexes.

Carbon monoxide may also be a bridging ligand between two metal atoms. Some of the CO ligands in the complexes $\text{Fe}_2(\text{CO})_9$, $\text{Co}_2(\text{CO})_8$ and $\text{Fe}_3(\text{CO})_{12}$ can behave in this way.

Heteroatoms may also be ligands. These include oxygen, nitrogen, sulfur and halogen atoms. Some of these, such as oxygen, may form double bonds to the metal, as in OsO_4 . A variety of nitrogen species may complex to the metal including the rather special case of the nitrosyl ligand, NO^+ , which can replace CO.

1.2.1 Phosphines

The most widely employed heteroatom ligands are the phosphines. Although they are largely spectators and do not participate directly in bond formation (and when they do, the result is often highly undesirable), they are not innocent bystanders. The size and electronic nature of the three groups attached to phosphorus have a profound effect on the course of the reaction and may make the difference between success and failure. An example is with the Grubbs catalyst (Chapter 8). The bis(triphenylphosphine) complex is of little use. The bis(tricyclohexylphosphine) complex is Nobel-prize winning.

Triphenylphosphine **1.1** has always been the most commonly used ligand, due to cost, availability, ease of handling and habit. While triphenylphosphine **1.1** remains commonly used, it no longer has its old ubiquity. An entire field of research, which might be termed “ligand engineering”, has grown up, centred on the design of new ligands with tailor-made electronic and steric properties (Figure 1.8). In a great many of the early applications of transition metals to organic synthesis, triphenylphosphine was used almost exclusively. An early exception is the use of a modified version, tri-*o*-tolylphosphine **1.2**, in Heck reactions.¹⁷ This was done to suppress quaternization of the phosphine by adding steric hindrance, though its success may actually be due to formation of Herrmann’s catalyst *in situ*.¹⁸ Addition of one or more sulfonate groups to the phenyl rings gives water-soluble analogues, such as **1.3**. Triphenylphosphine has also been modified by changing the donor atom. Both triphenylarsine **1.4** and triphenylstibine **1.5** have been employed. Changing the phenyl groups to furyl groups giving the more electron-rich tri-(2-furyl)phosphine **1.6** can also be beneficial. Alternatively, adding fluorine atoms gives an electron-poor ligand in tris(pentafluorophenyl)phosphine **1.7**. One or more of

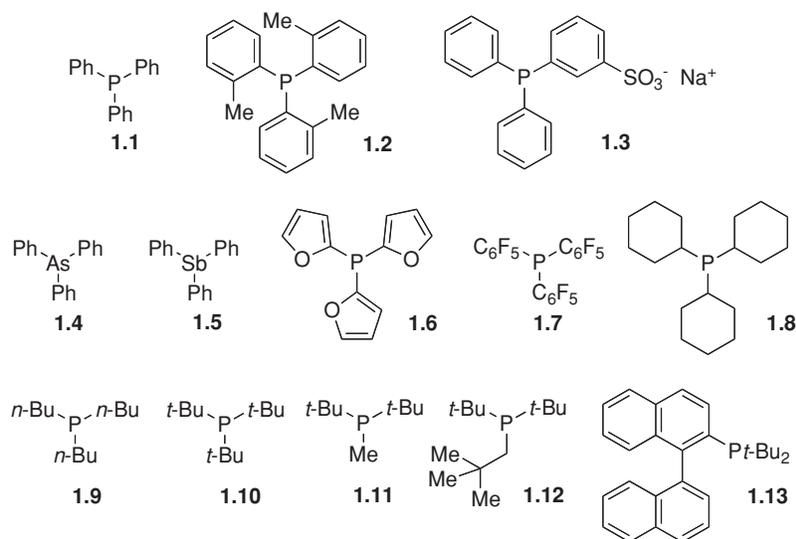


Figure 1.8 Phosphine ligands.

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the aryl groups attached to phosphorus may be changed to alkyl groups. Tri(cyclohexyl)phosphine **1.8** has found considerable application from being both more electron rich and more bulky than its aromatic analogue, triphenylphosphine. The related tricyclopentylphosphine is also known. Acyclic alkyl groups have also been used. Tri-*n*-butylphosphine **1.9** is readily available and used in organic procedures, such as Staudinger reactions and Wittig reactions, but is relatively uncommon as a ligand. In contrast, tri-*t*-butylphosphine **1.10**, has proved to be valuable. Its bulk promotes ligand dissociation and, hence, catalytic reactivity. As you can have too much of a good thing, the less-hindered di(*t*-butyl)methylphosphine **1.11** is also available. The neopentyl group and binaphthyl groups has also been used to replace one of the *t*-butyl groups. The binaphthyl modification **1.13** is known as Trixiephos. A disadvantage of using alkyl phosphines is their air sensitivity. All phosphines can be oxidized to the corresponding phosphine oxides, but this tendency is more pronounced with alkyl phosphines. A solution is to store and handle them as a salt, such as the tetrafluoroborate salt.¹⁹ If a small amount of a base is added to the reaction mixture, and many reaction mixtures already contain a base, then the phosphine is liberated *in situ*.

The focus of development of more sophisticated ligands has mainly been concerned with replacing one of the groups on phosphorus with a biphenyl group (Figure 1.9). Johnphos **1.14** and its dicyclohexyl analogue **1.15** contain the unadorned biphenyl moiety. Addition of *ortho*-substituents to the second phenyl group changes the steric and electronic properties, as in Sphos **1.16** and the closely related Ruphos **1.17**, both with alkoxy substituents. Mephos **1.18** and Xphos **1.19** have different alkyl substituents. Davephos **1.20** and its *t*-butyl analogue **1.21** possess a potentially chelating amino group. More highly substituted ligands, such as Brettphos **1.22** and Jackiephos **1.23**, have also been developed. Qphos **1.24**, with a highly substituted ferrocene moiety, can also be considered in this class of ligands.

The popularity of the biphenyl moiety in many ligands is not a mere result of adding bulk. The second aryl ring, twisted at an angle to its partner, may affect the metal directly by coordination, as in the cationic gold complex (Figure 1.10).²⁰ The X-ray structure (anionic counter ion not shown) clearly shows the proximity of the second ring to the metal atom.

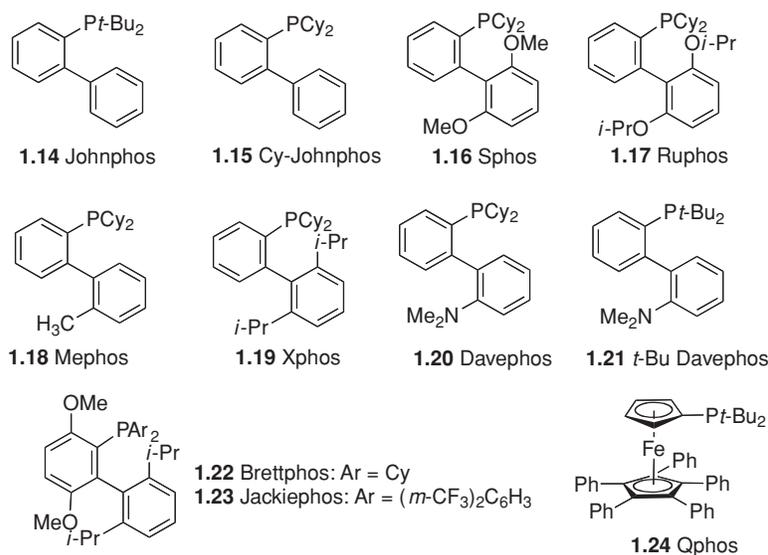


Figure 1.9 Phosphine ligands with a biphenyl motif.

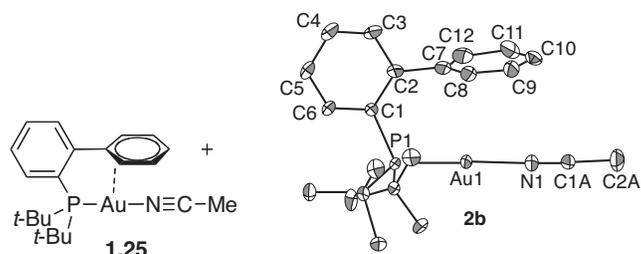


Figure 1.10 A gold(I) biphenylphosphine complex. Reprinted with permission from Herrero-Gómez, E.; Nieto-Oberhuber, C. et al. *Angew. Chem., Int. Ed.* **2006**, 45, 5455. © 2006 Wiley-VCH Verlag GmbH & Co. KGaA.

Bidentate phosphines have been used for many years (Figure 1.11). They provide the complex with greater stability because, for complete ligand dissociation, two metal–phosphine bonds must be broken, rather than one. Simple bidentate ligands consist of two diphenylphosphino units linked by an alkyl chain or group (**1.26–1.30**). More complex ligands use more elaborate linkers. Bis(diphenylphosphino)ferrocene, with a ferrocenyl linker, has proved to be a useful ligand. Most other linkers are based upon aromatic motifs. BINAP **1.33**, most often employed as a chiral ligand for asymmetric catalysis, has sometimes been used. Xantphos **1.34** and DPEphos **1.35** form a special subset of bidentate ligands. In square planar complexes, such as complexes with palladium(II), due to the geometrical demands of the linker, the two phosphines are capable of being *trans*.²¹ The other bidentate ligands tend to be *cis*.

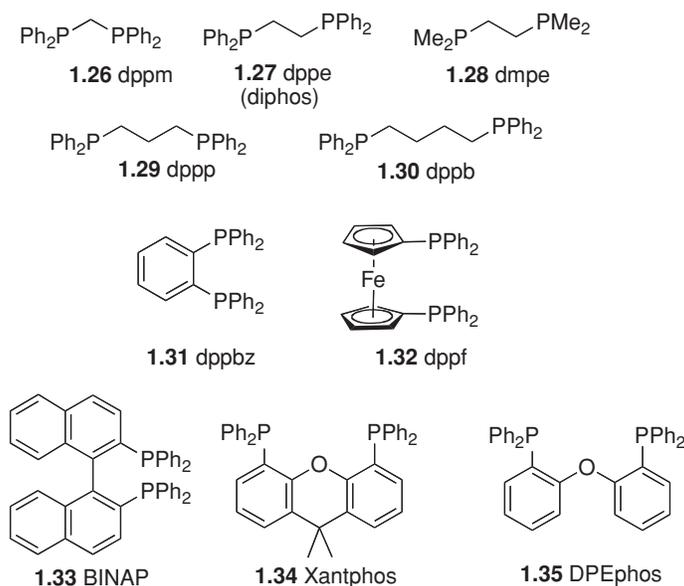


Figure 1.11 Bidentate phosphines.

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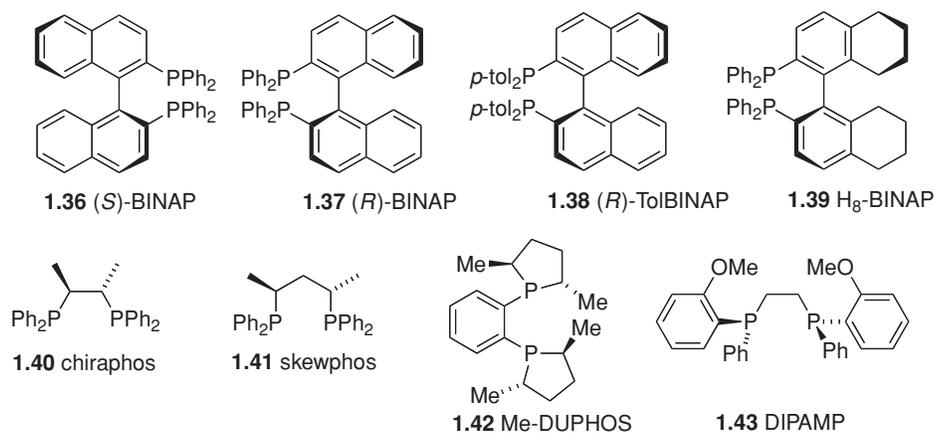


Figure 1.12 Chiral phosphine ligands.

The list given above is just a small selection of the ligands reported, and a tiny selection of the ligands that are possible.

The use of chiral phosphines has been the principle way to achieve asymmetric reactions in organometallic chemistry. A small selection of the huge number of chiral phosphines reported so far is presented in Figure 1.12. While chiral monodentate species have been used, most of the ligands are bidentate. Their designs can be divided into three groups. One group has the chirality present in the chain that links the two phosphorus atoms. Many of these are axially chiral. The two enantiomers of BINAP, **1.36/1.37**, are the first in this group, and many derivatives and modifications of BINAP have been reported. Others, such as chiraphos **1.40** and skewphos **1.41** have stereogenic carbon atoms in the chain. A second group, represented here by Me-DUPHOS **1.42** has the chirality in the phosphorus substituents, rather than the chain. A third and rarer group exploits the chirality of the phosphorus atom. DIPAMP **1.43**, the first effective ligand for asymmetric hydrogenation, is in this group. Applications of asymmetric catalysis are included in several chapters. For a deeper discussion, the reader is referred to more specialized textbooks.²²

1.2.2 Phosphites

Phosphites are closely related to phosphines, but have P–O bonds in place of P–C bonds (Figure 1.13). While they have been found to be useful ligands in certain reactions (see Section 4.4 and Sections 11.1.1 and 11.2.2), they have not been subject to the same widespread use or development as phosphines.

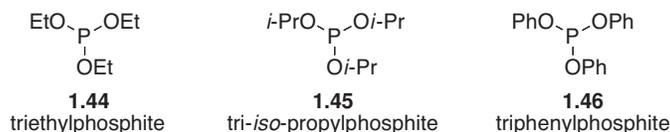
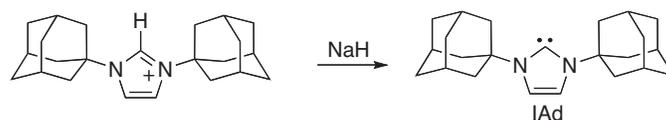


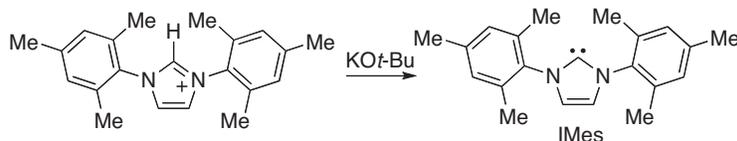
Figure 1.13 Phosphites.

1.2.3 *N*-Heterocyclic Carbenes

Carbene complexes have been known since the 1960s. Their chemistry revolves around the reactions of the carbene moiety (Chapter 8). The isolation of the first stable carbene by Arduengo,²³ and the realization that such carbenes could function as useful ligands for transition metals, in a similar way to phosphines, opened up a new chapter in organometallic chemistry.^{24,25} Arduengo's first stable carbenes were formed by the deprotonation of imidazolium salts (Schemes 1.1 and 1.2). The carbene carbon is built into a stabilizing nitrogen heterocycle. The *N*-substituents provide steric stabilization that is not, however, essential.²⁶ They are, therefore, referred to as *N*-heterocyclic carbenes or NHCs. The many NHC ligands that have followed have largely been variations on Arduengo's original (Figure 1.14). The *N*-mesityl, rather than *N*-adamantyl, has been commonly used, although families of *N*-alkyl carbenes have been produced. The double bond in the *N*-heterocycle may be absent, as in the Grubbs second-generation catalyst (Chapter 8). The heterocycle may also be varied, as in TPT **1.50**. Numerous more complex carbenes, including chelating bis-carbenes, have also been synthesized.



Scheme 1.1



Scheme 1.2

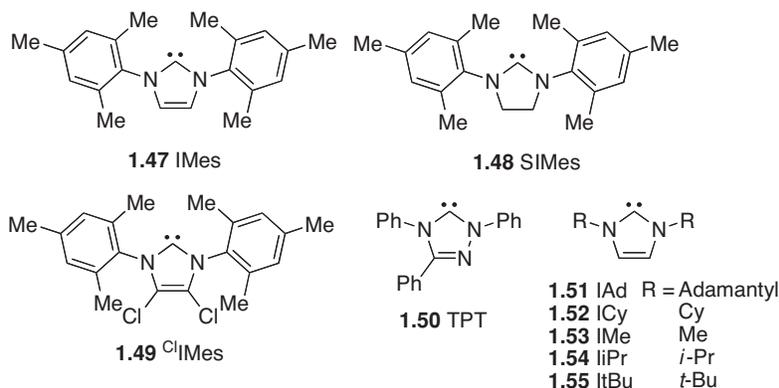
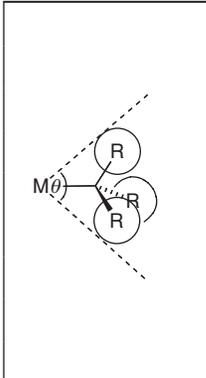


Figure 1.14 *N*-heterocyclic carbene (NHC) ligands.

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Table 1.1 Cone angles

	Ligand	Cone angle, θ
	PH ₃	87°
	P(OEt) ₃	109°
	PPhMe ₂	122°
	<i>Pn</i> -Bu ₃	132°
	PPh ₃	145°
	PCy ₃	170°
	<i>Pt</i> -Bu ₃	182°
	P(mesityl) ₃	212°

1.2.4 Other Ligands

Many other species have been employed as ligands, including amines and nitrogen heterocycles, sulfides and sulfoxides, halides, alkoxides and nitriles. Dienes, such as 1,5-cyclooctadiene, are commonly used as ligands.

1.2.5 Quantifying Ligand Effects

The two principle effects of the ligand are electronic and steric.²⁷ The concept of cone angle is used to describe the size of a ligand (Table 1.1). It is the angle of a cone that has its point at the metal and just contains the phosphine ligand. As this angle will vary depending on the metal–ligand bond length, the standard is taken as the nickel tricarbonyl derivative, (OC)₃NiL.

Is cone angle still adequate to describe the increasingly complex phosphine ligands, and the new NHC ligands that are far from cone shaped? New quantifiers are being proposed.²⁸

1.2.6 Heterogeneous Catalysis

The vast majority of the transition-metal catalysed reactions in this book use transition-metal species that are soluble in the reaction medium. These are often well-defined and characterized complexes. It does not have to be this way. Sources of transition metals that are insoluble in the reaction medium, especially heterogeneous sources of palladium, can be very effective. Palladium on inert supports, such as carbon, has been employed for many decades for hydrogenation reactions. They can also be employed for carbon–carbon bond-forming reactions.²⁹ Other heterogeneous sources, such as perovskites, which are better known as components of car exhaust systems, have also been used. Catalysts of this type may act as sources of palladium, releasing palladium as complexes or nanoparticles into the reaction medium, then reclaiming it.³⁰ Often, these systems leave less residual metal contamination in the final product and, therefore, are particularly useful industrially.

1.3 Just How Many Ligands Can Fit around a Metal Atom?

This is a fairly easy question to answer. If we think about elements such as carbon, nitrogen and oxygen, we know that their valency can be explained by the importance of filling the outer valence

shell with eight electrons and obtaining an inert-gas configuration. As they have to fill up an s orbital and three p orbitals, this means acquiring eight electrons, including the electrons that they already possess.

Transition metals have to fill an s orbital, three p orbitals and five d orbitals. This requires eighteen electrons. This is the eighteen-electron rule. These electrons must either belong to the metal atom already or must be supplied by the ligand. We must also adjust for the charge.

There are two methods for adding up electrons, both are based on counting the electrons contributed to the complex from the metal and the ligands. The methods have been referred to as the “covalent” and “ionic” methods as they differ in the notional origin of the electrons.³¹ It has to be clearly understood that this is the *notional* origin, not the actual origin. A hydride ligand is assigned as bringing 1 or 2 electrons to the complex respectively, whether its actual origin was from LiAlH_4 , H_2 or HCl . The same answer is obtained whichever method is used. The important thing is to not get the two methods mixed up! Examples of both methods are given in Figures 1.15–1.18.

1.3.1 Method 1: Covalent

Electrons from the metal: This is equal to its group number. Just count from the far left-hand column (group 1) of the periodic table (Table 1.2).

Electrons from the ligands: this depends, naturally on the ligands. For hydrocarbon ligands, the number is equal to the haptic number. Single-bonded ligands (hydride, halide etc) count as 1 (although a bridging halide counts as 2 – a lone-pair donor), while carbenes and carbynes count as 2 and 3, respectively. Lone-pair donors, such as phosphines and CO, count as 2.

Charge: electrons have a negative charge. A positive charge on your complex means a missing electron, so subtract one. A negative charge means an extra electron, so add one.

1.3.2 Method 2: Ionic

Electrons from the metal: first, the oxidation state of the metal must be assigned. Oxidation state is a formalism, but a useful formalism. The assignment can be done by the notional stripping off of ligands to reveal a notional metal ion. Ligands that are donors of pairs of electrons, or multiple pairs of electrons are removed with their pair(s) of electrons and do not effect the charge of the metal. Examples include alkenes, dienes and arenes (all of which have an *even* haptic number), CO, phosphines and carbenes. Ligands with a sigma bond are stripped off as anions even if this makes no chemical sense. Examples are alkyl, allyl, dienyl and even acyl ligands (all of which have an *odd* haptic number), hydride, halide and carbynes. The number of electrons contributed by the metal is then its group number (count from the far left-hand column (group 1) of the periodic table) minus the oxidation state. This is also the number of d electrons, d^x . This number is useful for comparing metals with different oxidation states across groups of the periodic table.

Table 1.2 Transition metals and numbers of electrons

3	4	5	6	7	8	9	10	11
Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu
Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag
La	Hf	Ta	W	Re	Os	Ir	Pt	Au

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Electrons from the ligands: The number of electrons supplied by a ligand is related to how the ligand was notionally stripped off above. Hydrocarbon ligands with even hapto numbers were stripped off as neutral molecules, so the number of electrons donated is equal to their hapto number. Hydrocarbon ligands with odd hapto numbers were stripped off as anions, so the number of electrons donated is equal to their hapto number plus one. Thus, an allyl group is a donor of four electrons. Lone-pair donors donate two electrons; sigma-bonded ligands stripped off as anions also donate two electrons.

Charge: The assignment of the oxidation state has already taken the charge into account, so there is no further adjustment.

1.3.3 Examples

The rule is often broken. d^8 -Complexes of metals towards the right-hand side of the d-block often form stable square-planar complexes, such as $(\text{Ph}_3\text{P})_2\text{PdCl}_2$. Bulky ligands may prevent a complex reaching 18 electrons: palladium forms an eighteen-electron complex with triphenylphosphine to give the popular catalyst $(\text{Ph}_3\text{P})_4\text{Pd}$, but only a fourteen-electron complex with the bulkier tri(*t*-butyl)phosphine, $(t\text{-Bu}_3\text{P})_2\text{Pd}$. Complexes with fewer than 18 electrons are not impossible; it is just that they tend to be less stable. What is important to remember is that stable complexes are unreactive. To get them to participate in chemistry, it is usually first necessary to get them away from their stable state (meaning, in most cases, 18 electrons) by forcing them to dissociate a ligand.

Example 1: $\text{Cp}(\text{Ph}_3\text{P})\text{CoMe}_2$			
Oxidation state = +3			
Method 1		Method 2	
Ligands: Cp =	5	Ligands: $\text{Cp}^- =$	6
Ph ₃ P =	2	Ph ₃ P =	2
Me = 2 x 1 =	2	Me ⁻ = 2 x 2 =	4
Metal: Co =	9	Metal: Co(+3) =	6
Charge = 0	0		
Total =	18	Total =	18

Figure 1.15

Example 2:			
Oxidation state = +1			
Method 1		Method 2	
Ligands: 4 x CO = 4 x 2 =	8	Ligands: 4 x CO = 4 x 2 =	8
ketone lone pair =	2	ketone lone pair =	2
η^1 -aryl =	1	η^1 -aryl =	2
Metal: Mn =	7	Metal: Mn(+1) =	6
Charge =	0		
Total =	18	Total =	18

Figure 1.16

Example 3: $(C_6H_6)(C_4H_6)(C_3H_5)Mo^+PF_6^-$			
Oxidation state = +2			
Method 1		Method 2	
Ligands: $\eta^6-C_6H_6 =$	6	Ligands: $\eta^6-C_6H_6 =$	6
$\eta^4-C_4H_6 =$	4	$\eta^4-C_4H_6 =$	4
η^3 -allyl =	3	η^3 -allyl =	4
Metal: Mo =	6	Metal: Mo(+2) =	4
Charge = +1	<u>-1</u>		
Total =	18	Total =	18

Figure 1.17

Example 4: $NaCo(CO)_4$			
$Co(CO)_4^- \rightleftharpoons Co^- + 4 CO$			
Oxidation state = -1			
Method 1		Method 2	
Ligands: $4 \times CO = 4 \times 2 =$	8	Ligands: $4 \times CO = 4 \times 2 =$	8
Metal: Co =	9	Metal: Co(-1) =	10
Charge = -1	<u>+1</u>		
Total =	18	Total =	18

Figure 1.18

1.4 Mechanism and the Basic Reaction Steps

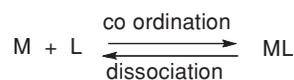
To adapt the well-known phrase of Lord Rutherford, organic chemistry without mechanism is just stamp collecting. Mechanisms have been proposed for all of the major reactions catalysed or mediated by transition metals and used in organic synthesis. In many cases, the proposed mechanisms are supported by sound and thorough studies. In other cases, this is not so. The reader should approach any published mechanism (including those in this book) with caution. Unless the mechanism is backed up by the proper experiments such as kinetics and isotopic labeling, it should be regarded as speculative and fully open to reinterpretation. Nevertheless, thinking about mechanisms is one of the most valuable activities and an excellent source of new ideas.

Mechanisms for reactions catalysed or mediated by transition metals are multistep. While the overall result can be complex and bewildering, the individual steps are taken from a quite small and relatively simple list. Some of these are common to “classical” organic chemistry; others are specific to the transition metals. While the basic reactions such as nucleophilic and electrophilic attack do operate, the presence of transition metals means that another set of basic reaction steps also operate. Combinations of these steps give us the overall reactions that we use.

1.4.1 Coordination and Dissociation

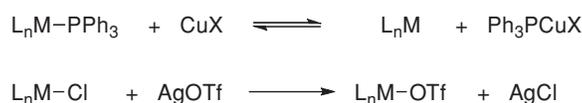
The most fundamental step is the simple coordination and dissociation of ligands (Scheme 1.3). This is important because a stable complex cannot coordinate the substrate, but must first dissociate a ligand. Although some ligands are sufficiently labile to dissociate under mild conditions, in other cases it is necessary to use heat or light to achieve this. Often, reaction conditions are dictated by this initial dissociation.

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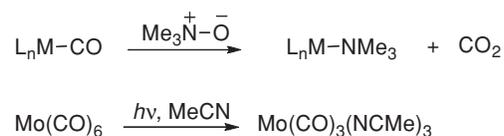
Scheme 1.3

The equilibrium between the coordinated and dissociated species may be driven towards the dissociated side, to generate the more reactive complex, by the addition of a second metal ion (Scheme 1.4). The purpose of the second ion is to absorb the dissociated ligand, thus driving the equilibrium according to le Chatelier's principle. In the case of phosphine ligands, this can be done using copper(I) salts (see Section 2.5.7). In the case of chloride ligands, this can be done, effectively irreversibly, but the addition of silver(I) salts (see Section 6.2 and Section 11.3.1). In this latter situation, what is achieved is the exchange of the chloride for a more labile anionic ligand, often triflate, but also perchlorate, tetrafluoroborate and hexafluoroantimonate.



Scheme 1.4

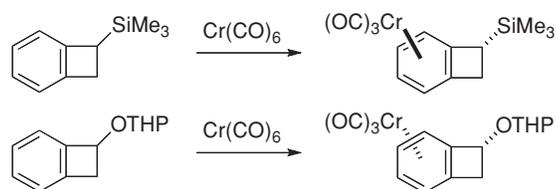
Dissociation may also be made easier by replacing a strongly bound ligand with a weakly bound ligand in a separate step (Scheme 1.5). This can be achieved by destruction of a ligand. This is often done by oxidation of a CO ligand to CO₂ using an amine oxide. The vacant site is then taken up by the more labile amine ligand. Another strategy is to substitute a less-labile ligand for a more-labile ligand in a separate step, so that the substrate avoids the more brutal conditions required for dissociation.



Scheme 1.5

Exchange of ligands may also be employed to modify the reactivity of a complex. Substitution of CO by NO⁺ will make a complex much more electrophilic (see Scheme 10.19). Substitution of CO by PPh₃ will achieve the opposite.

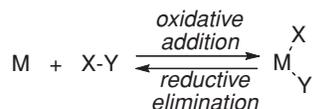
Complexation can also raise stereochemical issues. When a π-system is involved, the metal may attach to either face (Scheme 1.6). Selectivity is often observed, and can be exploited. The selectivity may be due to steric effects or neighbouring group effects.³²



Scheme 1.6

1.4.2 Oxidative Addition and Reductive Elimination

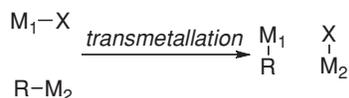
Oxidative addition is the most important method for the formation of a metal–carbon single bond, although it is not limited to just this. In oxidative addition, a transition-metal fragment, which must have less than eighteen electrons, inserts into the X–Y bond, and the oxidation state of the metal increases by 2 (Scheme 1.7). Usually X is an organic group and Y is a leaving group, such as a halide. There are, however, many other possibilities, including the simple one where both X and Y are hydrogen. The reverse process is reductive elimination in which the metal fragment is expelled by formation of an X–Y bond, and the oxidation state of the metal drops by 2.



Scheme 1.7

1.4.3 Transmetallation

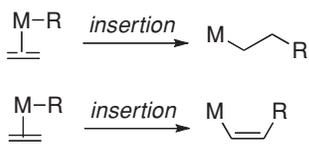
Oxidative addition is often followed by transmetallation in which an organic group on a second metal, usually a main group metal, is transferred in exchange for a group such as a halide (Scheme 1.8). This is another important method for formation of a transition metal–carbon bond. There is no change in oxidation state.



Scheme 1.8

1.4.4 Alkene and Alkyne Insertion

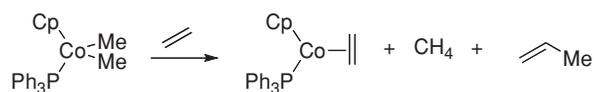
A fundamental process for coordinated alkenes and alkynes is insertion (also called migratory insertion), usually into a metal–carbon or metal–hydrogen bond (Scheme 1.9). This is a stereospecifically *syn* process, so insertion of alkynes results in *cis*-vinyl complexes. There is no change of oxidation state.



Scheme 1.9

The insertion of ethylene into a carbon–cobalt bond was carefully studied as part of work on the mechanism of Ziegler–Natta polymerization (Scheme 1.10).³³

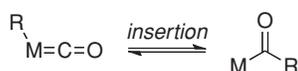
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Scheme 1.10

1.4.5 CO insertion

Similarly, CO insertion (or migratory insertion) is the fundamental transformation of the CO ligand. It is a reversible process and an equilibrium will exist between the η^1 -alkyl and η^1 -acyl complexes (Scheme 1.11). This insertion is not observed for the formation of formyl ligands ($R = H$), owing to the low thermodynamic stability of the formyl group.

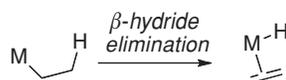


Scheme 1.11

1.4.6 β -Hydride Elimination

For alkyl transition-metal complexes, β -hydride elimination is a significant process and many alkyl organometallics are unstable because of this facile transformation. It is the reverse of an alkene-insertion process (Scheme 1.12). As with insertion, there is no change in oxidation state. While the initial product is a η^2 -complex, it is frequently followed by dissociation to give the free alkene. Stereochemically, it is also a *syn* process and, thus, quite unlike the familiar E2 reaction in classical organic chemistry.

If there is no β -hydrogen available, then β -hydride elimination is (almost) impossible. η^1 -Acyl, aryl and vinyl complexes do not undergo this reaction. The reaction is impossible for alkyl complexes possessing no β -hydrogens at all, such as neopentyl derivatives (Figure 1.19). β -Hydrogens may also be unavailable for geometrical reasons. In the norbornyl complex, H_a is unavailable as the rigidity of the bicyclic structure prevents a *syn* relationship with the metal. H_b is unavailable, as elimination would produce a structure in breach of Bredt's rule. The same is true if the metal is at the bridgehead position of a norbornane structure, as in the stable tetranorbornyl derivative of cobalt (Figure 1.20).³⁴ Complexes that are unable to undergo β -hydride elimination for these reasons are sometimes referred to as β -blocked.



Scheme 1.12

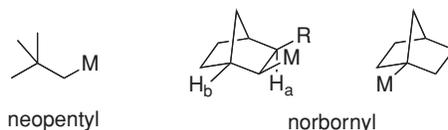


Figure 1.19 β -Blocked complexes. Reprinted with permission from Byrne, E. K.; Theopold, K. H. J. Am. Chem. Soc. **1989**, 111, 3887. © 1989 American Chemical Society.

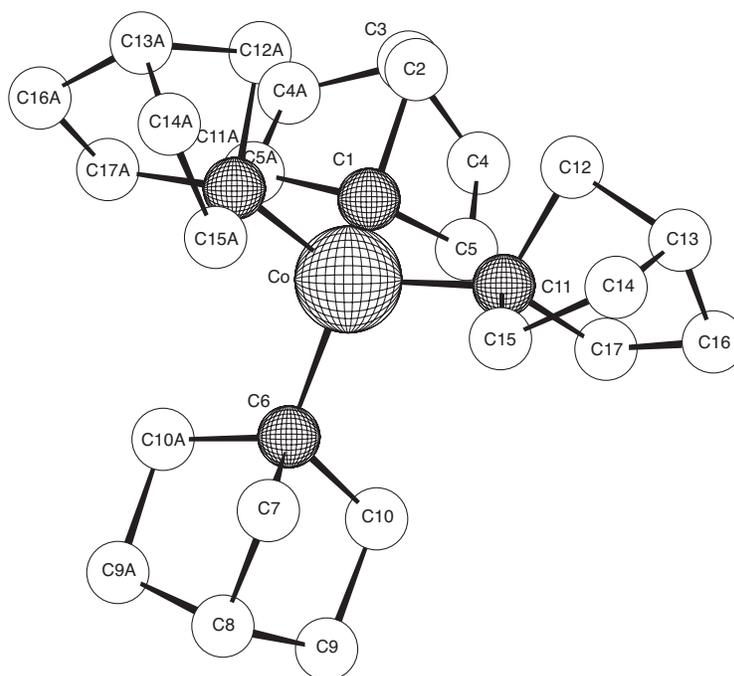
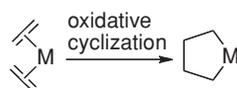


Figure 1.20 A norbornyl cobalt complex. Reprinted with permission from Byrne, E. K.; Theopold, K. H. J. Am. Chem. Soc. **1989**, 111, 3887. Copyright 1989 American Chemical Society.

1.4.7 Oxidative Cyclization

Oxidative cyclization (or oxidative coupling) is also a key reaction of alkene complexes, giving rise to metallacycles (Scheme 1.13). The oxidation state of the metal increases by 2.



Scheme 1.13

1.5 Catalysis

A catalyst is a substance that, when present in a reaction, increases the rate without itself being consumed.³⁵ However, the catalyst cannot change the ΔG or ΔH of the reaction, or the position of an equilibrium; the change of rate is due to lowering of the activation energy. Most of the reactions catalysed by transition metals cannot occur in the absence of the catalyst. Transition-metal catalysts therefore increase the rate from zero, by opening up new molecular pathways. This is unlike many catalysts in classical organic chemistry. For instance, the formation of esters by the reaction of a carboxylic acid and an alcohol does proceed, albeit at a snail's pace, even in the absence of a strong acid. The phenomenon of catalysis was discovered (amongst others) by Döbereiner, a Chemist in the German city of Jena, in 1823.³⁶ He found that when a jet of hydrogen

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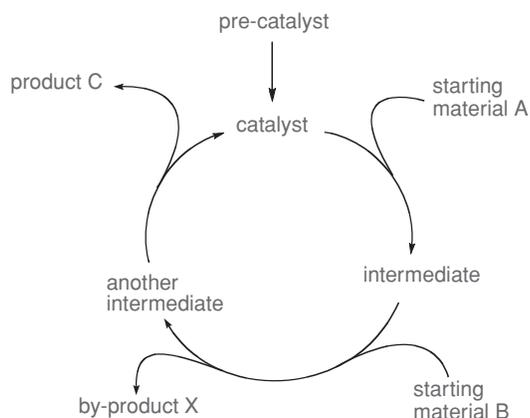


Figure 1.21 A catalytic cycle.

gas (generated by the reaction between zinc and sulfuric acid) played upon a piece of platinum foil in air, the gas immediately ignited even though no flame was present. This discovery not only provided the world's first lighter, but also introduced the concept of catalysis, a term coined by the great Swedish chemist, Berzelius.³⁷

Catalysis has become increasingly important. Many organometallic processes – though not all – are catalytic. Catalysis reduces waste and reduces cost. Ideally, the loading of the catalyst should be as low as possible. Many reactions employed in academic labs are run at 5 mol%. It seems likely that these could work at much lower loadings. While low catalyst loading is obviously desirable, it must be remembered that there is nothing in the definition of a catalyst about the loading. Thus, a material used in excess can still be a catalyst. Whatever the loading, the test as to whether something is acting as a catalyst is to draw the mechanism as a catalytic cycle (Figure 1.21). If the cycle brings the species back to where it started, then the reaction is catalytic.

The term catalyst is widely used. It is often applied to molecules that are not the catalyst, but a precursor for the catalyst. These should be termed “pre-catalysts”. This is particularly the case in industrial processes. A combination of metal salts, reagents, ligands and supports are combined in a reactor. Somehow, they combine *in situ* to generate the catalyst. Due to this combination process, some reactions may have an induction period.

The activity of the catalyst is an important issue. While the reactivity can be judged empirically by looking at the reaction conditions, temperature, concentration, pressure if a gas is involved, for catalysts, the loading is an important factor. In academic laboratories, it is common practice to employ 5 or 10 mol% as a standard loading. In academic research, cost of chemicals and waste disposal is often less of an issue, and the cost of a catalyst is of lesser importance when the investigator is fifteen steps into a thirty-step sequence! An additional factor is that many academic reactions are run on milligrammes of substrate, and measuring anything less than 5 mol% of catalyst is very difficult. The situation is quite different in industry. Catalyst loading must be reduced to reduce the cost of the process, to reduce the cost of waste disposal and to minimize the amount of residual metal that may contaminate the final product. In this age, it is time for all academic labs to address the issue of catalyst loading to train students to think in this way for green and cost-effective chemistry.

So how do we measure the activity of the catalyst? This is usually discussed as the turnover number (TON), a concept adapted from enzymology. For mechanistic studies in organometallic chemistry, the turnover number is the number of times the catalyst can go around the catalytic cycle before becoming deactivated.³⁸

In practice, for organic synthesis, the limit is often when the substrate is consumed, even if the catalyst is still active. Hence, for practical purposes, TON quoted will be calculated based upon the number of moles of product formed divided by the number of moles of catalyst employed, so a reaction proceeding in 80% chemical yield with 5 mol% of a catalyst will have a turnover number of $80/5 = 16$.³⁹ TOF is the turnover number per unit time.

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