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***N*-Heterocyclic Carbenes as Ligands for High-Oxidation-State Metal Complexes and Oxidation Catalysis**

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Abstract *N*-Heterocyclic carbenes (NHCs) possess properties that are ideally suited for their use as ligands in transition-metal oxidation chemistry and catalysis. Their strong sigma-donating ability stabilizes metals in high oxidation states, and their high M–L bond dissociation energies reduce their tendency to dissociate and undergo oxidative decomposition of the free carbene. In this chapter, we summarize these unique properties and survey the use of NHCs as ligands to stabilize high-valent transition-metal chemistry and their role in metal-catalyzed oxidation reactions. Catalytic applications of NHC-metal complexes include alcohol oxidation and alkene and alkane functionalization.

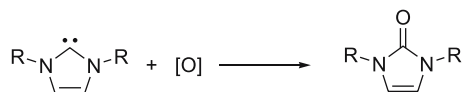
Keywords *N*-Heterocyclic Carbenes · Oxidation · Catalysis · Dioxygen

Abbreviations

COD	1,5-cyclooctadiene
Cp*	Pentamethylcyclopentadienyl
IAd	1,3-diadamantyl-2,3-dihydro-1 <i>H</i> -imidazol-2-ylidene
I ^{<i>t</i>} Bu	1,3-di- <i>tert</i> -butyl-2,3-dihydro-1 <i>H</i> -imidazol-2-ylidene
IBu	1,3-dibutyl-2,3-dihydro-1 <i>H</i> -imidazol-2-ylidene
ICy	1,3-dicyclohexyl-2,3-dihydro-1 <i>H</i> -imidazol-2-ylidene
IMe	1,3-dimethylimidazolin-3-ylidene
IMes	1,3-bis(2,4,6-trimethylphenyl)-2,3-dihydro-1 <i>H</i> -imidazol-2-ylidene
I ^{<i>i</i>} Pr	1,3-bis(2,6-diisopropylphenyl)-2,3-dihydro-1 <i>H</i> -imidazol-2-ylidene
IPh	1,3-Diphenyl-2,3-dihydro-1 <i>H</i> -imidazole
ITmt	1,3-bis-(2,6,2'',6''-tetramethyl-[1,1';3'.1''] terphenyl-5'-yl)-2,3-dihydro-1 <i>H</i> -imidazol-2-ylidene
ITol	1,3-Di- <i>p</i> -tolyl-2,3-dihydro-1 <i>H</i> -imidazole
^{<i>Me</i>} IPr	1,3-diisopropyl-4,5-dimethyl-2,3-dihydro-1 <i>H</i> -imidazol-2-ylidene
NHC	<i>N</i> -Heterocyclic Carbene
OPiv	2,2-dimethylpropionate (pivalate)
^{<i>Ph</i>} IPr	1,3-Diisopropyl-4,5-diphenyl-2,3-dihydro-1 <i>H</i> -imidazole
SI ^{<i>t</i>} Bu	1,3-di- <i>tert</i> -butyl-4,5-dihydroimidazol-2-ylidene
SIMes	1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene
SI ^{<i>i</i>} Pr	1,3-bis(2,6-diisopropylphenyl)-4,5-dihydroimidazol-2-ylidene
TIMY	1,3,4,5-tetramethyl-2,3-dihydro-1 <i>H</i> -imidazol-2-ylidene
Triazol	4,5-dihydro-1 <i>H</i> -1,2,4-triazol-5-ylidene
Tp'	Hydridotris(3- <i>tert</i> -butyl-5-methylpyrazolyl)borate

1**Introduction**

N-Heterocyclic carbenes (NHCs) continue to emerge as effective ligands in transition-metal chemistry and homogeneous catalysis. Since the isolation of the first stable free carbene in 1991 [1], interest in these compounds as ligands for transition-metal complexes has grown dramatically [2–7]. This interest can be attributed, in part, to both their similarities to and differences from ubiquitous phosphine ligands. Phosphines are seldom used as ancillary ligands in oxidation chemistry because of their intrinsic oxidative instability. Free NHCs are also susceptible to oxidative decomposition (e.g., Eq. 1), but when coordinated to a metal center, NHCs are remarkably robust and hold significant promise for use in oxidation chemistry. NHCs possess key properties that enhance their potential utility: their strong

**Equation 1**

σ -donating ability stabilizes metals in high oxidation states and their high M–L bond dissociation energies render them less susceptible to oxidative decomposition. A discussion of these properties, a survey of the applications of NHCs to the stabilization of high-oxidation-state metal complexes, and the use of NHC's as ancillary ligands in metal-catalyzed oxidation reactions are provided below.

2

Overview of NHC Ligand Properties

Thorough analysis of the chemical properties of NHCs as ligands is provided elsewhere in this volume. The following brief survey highlights those properties of NHCs that make them well suited for application to oxidation chemistry.

2.1

Electronic Properties

Several systematic experimental and computational studies have compared the sigma-donating abilities of NHCs and tertiary phosphines for a variety of transition-metal complexes [8–17]. As illustrative examples, analyses of the nickel-carbonyl complex **1** and iridium carbonyl complex **2** (Fig. 1) re-

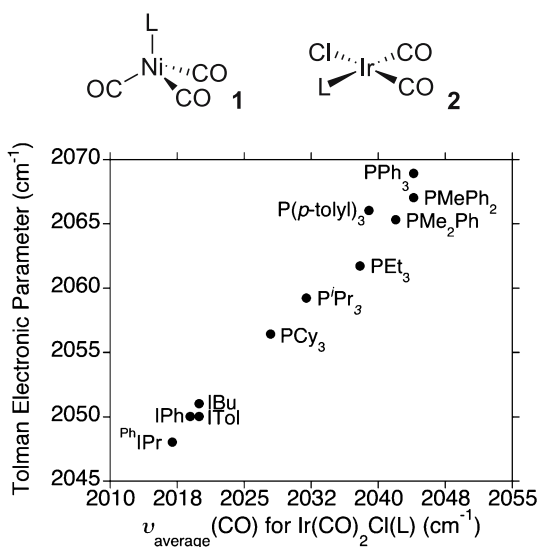


Fig. 1 Relationship between the Tolman electronic parameters and IR stretching frequencies for complex **2** (data compiled from [12, 16])

veal that NHC complexes have lower C – O stretching frequencies than their phosphine counterparts [7, 12, 16, 17]. These data, which conform to those of other studies, suggest that the NHCs are stronger σ -donors than even the most basic tertiary phosphines. Computational studies suggest that the M – C bond of NHC-metal complexes is primarily σ -bonding in character, with little contribution from π -back-bonding [4]. The strong σ -donating ability of NHCs revealed by these studies underlies the ability of NHCs to stabilize high-oxidation-state metal complexes.

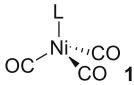
2.2

NHC–Metal Bond Strengths

Phosphines and NHCs undergo facile conversion to the corresponding phosphine oxides and ureas under oxidizing reaction conditions (cf. Eq. 1). This decomposition pathway can be slowed or eliminated by protonation of the ligand or coordination to a metal center. For example, the air sensitivity of P^tBu_3 and related trialkylphosphines may be minimized by employing the phosphonium salt, $[HPR_3]BF_4$, as a ligand precursor in catalytic reactions [18]. Despite this partial solution, phosphine ligands are seldom compatible with metal-catalyzed oxidation reactions. Dissociation of the ligand at any point during the catalytic reaction results in rapid ligand oxidation. Recent studies indicate that NHCs possess significantly higher M – L bond strengths than phosphines [9, 12–16]. This property appears to foster significantly higher ligand stability under oxidizing reaction conditions and allows NHCs to be employed in metal-catalyzed oxidation reactions.

Both steric and electronic factors contribute to M – L bond strengths. The Tolman-cone-angle measurement, used to assess the size of tertiary phosphines [19], is an inappropriate indicator of the size of NHCs because of their planar spatial orientation. Therefore, a “buried volume” parameter, $\%V_{Bur}$, has been used to compare the relative sizes of phosphine and NHC ligands [13, 17]. This calculated parameter estimates the percentage of spherical space around the metal that is consumed by a given ligand. Because it does not assume a conical ligand shape, $\%V_{Bur}$ is a more general measure of a ligand’s steric influence. Based on this parameter, the largest NHCs, I^tBu , SI^tBu and IAd , are significantly larger than even the largest tertiary phosphine, P^tBu_3 , whereas other commonly used NHCs have steric properties similar to bulky phosphines (Table 1). For ligands of comparable size, NHCs have significantly higher DFT-calculated bond dissociation energies (BDEs) than phosphines (Table 2). Only the very bulky NHCs, IAd , I^tBu and SI^tBu , exhibit BDEs lower than that of the phosphines in the four-coordinate Ni complex, **1** (Table 1) [17]. Calculations of a less hindered, three-coordinate, trigonal planar complex, $Ni(NHC)(CO)_2$, reveal that all of the NHCs possess a higher M – L bond strength than phosphines. This trend in M – L bond strengths has been attributed to the enhanced basicity (i.e., donor ability) of NHCs relative

Table 1 DFT-calculated M – NHC bond dissociation energies (kcal mol^{-1}) and % V_{Bur} for the carbene ligands in nickel-carbonyl complexes

		
Ligand	BDE of L in 1 kcal mol^{-1}	% V_{Bur}
I^tBu	24.0	37
Si^tBu	21.8	38
IAd	20.4	37
IMes	41.1	26
SiMes	40.2	27
I^iPr	38.5	29
Si^iPr	38.0	30
ICy	39.6	23
PH_3	22.7	17
PPh_3	26.7	22
P^tBu_3	28.0	30

to phosphines [20]. That NHCs undergo less facile ligand dissociation relative to phosphines provides a compelling justification for the enhanced utility of NHCs relative to phosphines in metal-catalyzed oxidation reactions.

3

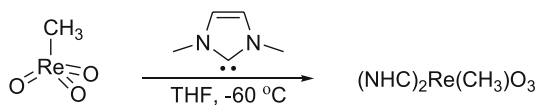
***N*-Heterocyclic Carbenes as Ligands in Fundamental Transition-Metal Oxidation Chemistry**

As phosphine analogs, *N*-heterocyclic carbenes are frequently employed as ligands for low-valent transition-metal complexes [2, 4, 6]. Significantly less is known about NHCs as ligands for high-oxidation-state metal complexes and for metals bearing oxidizing ligands such as oxides and peroxides. The following sections summarize the early developments in this area.

3.1

***N*-Heterocyclic Carbenes for the Stabilization of High-Oxidation-State Metals**

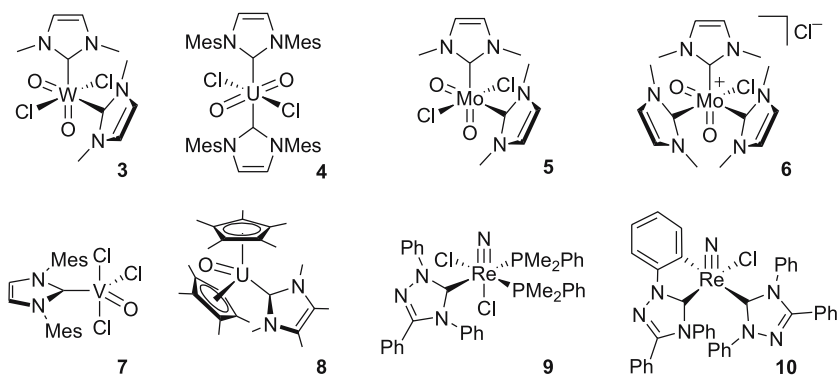
Transition-metal oxides are useful oxidizing reagents for organic molecules and often participate in oxygen-atom transfer reactions [21]. A prototypical example is CH_3ReO_3 (MTO), which serves as a versatile reagent for stoi-

**Equation 2**

chiometric and catalytic oxidation reactions [22]. The sterically unhindered NHC, 1,3-dimethylimidazolin-3-ylidene, reacts with MTO to yield a bis-NHC adduct, $(\text{NHC})_2\text{Re}(\text{CH}_3)(\text{O})_3$, at $-60\text{ }^\circ\text{C}$ (Eq. 2) in THF [23]. This complex was characterized by comparison of spectroscopic features to those of related $\text{L}_2\text{Re}(\text{CH}_3)(\text{O})_3$ complexes; however, it is unstable and decomposes when the solution is warmed above $-20\text{ }^\circ\text{C}$. Nevertheless, it is significant that the complex can be prepared without immediate NHC oxidation to the cyclic urea derivative. The analogous reaction of the NHC with Re_2O_7 led to immediate reduction of the $\text{Re}(\text{VII})$ center, presumably via NHC oxidation, although the organic reaction products were not identified. By comparison, phosphines react rapidly with MTO to yield the corresponding phosphine oxides [24, 25].

Since this initial report, NHCs have been used to stabilize a number of additional high-valent metal complexes bearing oxo and nitrido ligands (Chart 1) [26–32]. In contrast to the MTO example, these complexes and the high-valent metal precursors employed in their synthesis are not especially strong oxidants. Consequently, the preparation of these complexes often can be achieved by simple addition of the NHC to an unsaturated metal center or via displacement of a weakly coordinated solvent molecule such as THF.

Several interesting features have been noted in the studies of complexes 3–10. Cationic $\text{Mo}(\text{VI})$ complexes of the type $[\text{MoO}_2\text{ClL}_3]^+\text{Cl}^-$ were not known until the synthesis of 6 [26]. With other ligands, including DMF,

**Chart 1** NHC-coordinated high-valent metal complexes

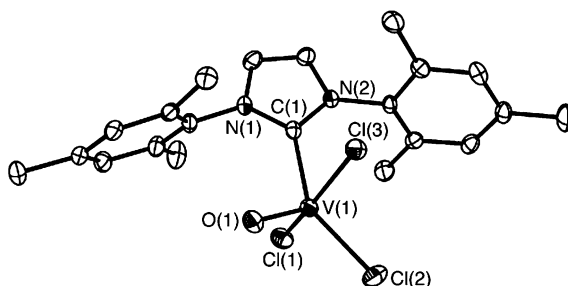


Fig. 2 X-ray structure of IMesVCl₃O, **7**

OPPh₃ and pyridine, the Mo complexes prefer the neutral formulation, MoO₂Cl₂L₂ [33–35]. This contrast probably arises from the strong donating ability of NHCs, which can stabilize the cationic metal center more effectively than other neutral ligands. The vanadium and uranium complexes, **7** and **8**, respectively (Chart 1), were the first examples of NHC-coordinated metal-oxo complexes characterized by X-ray crystallography [29, 32]. The NHC-vanadium adduct exhibits significantly greater hydrolytic stability relative to other trichloro-oxo-vanadium(V) species. Two of the V–Cl ligands orient approximately perpendicular to the plane of the heterocyclic ring (Fig. 2). Crystallographic and computational analysis supports the presence of a Cl–C_{carbene} interaction in which electrons from a chloride lone pair donate into the formally vacant p-orbital of the C_{carbene} atom. The uranium(IV) oxo **8** represents the first example of an organometallic uranium mono-oxo complex [32]. The unique nature and stability of the terminal oxo ligand has been attributed to the steric bulk of the NHC, which influences the spatial orientation of the Cp* ligands.

In addition to the metal-oxo complexes, several examples of NHC-stabilized rhenium(V)-nitrido complexes exist, e.g., **9** and **10** (Chart 1) [28]. These adducts, which feature triazole-based ligands, were prepared via displacement of phosphine ligands. The stability of both phosphine and triazole-based carbenes in these reactions suggest the nitrido ligand is relatively unreactive.

3.2

Reactions of NHC-coordinated Metal Complexes with Molecular Oxygen

Reactions between molecular oxygen and well-defined transition-metal complexes have been the subject of extensive study for decades [21]. Recent studies demonstrate the suitability of NHCs as ancillary ligands in this chemistry, and in several cases, the enhanced stability of NHCs over phosphines is noted. Certain limitations associated with NHC-ligand instability have also been identified, particularly in the study of first-row transition metals.

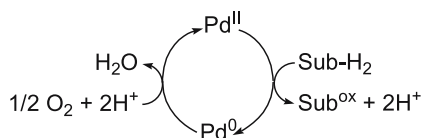
3.2.1

Palladium

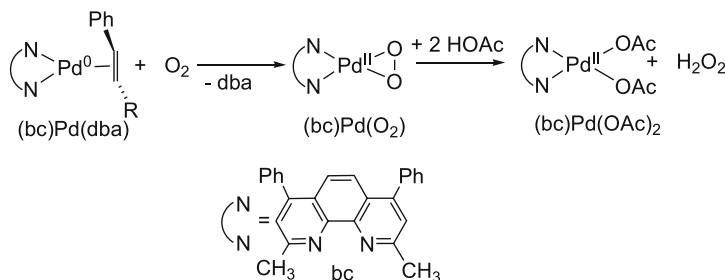
The development of palladium-catalyzed oxidation reactions has grown rapidly in recent years, and particular attention has been directed toward reactions that undergo direct dioxygen-coupled turnover (Scheme 1) [36–38]. The latter reactions are distinct from the well known Wacker process because no cocatalyst is needed to facilitate reoxidation of the reduced Pd catalyst. Recent aerobic oxidation reactions commonly feature the use of oxidatively stable ligands such as pyridine, phenanthroline and related derivatives [37]. NHC ligands are also effective (see Sect. 4.2 below) [39]. Several studies probing fundamental Pd(0)-dioxygen reactivity have been reported in recent years, including those with NHC-coordinated Pd complexes.

The first examples of well-defined reactions between dioxygen and Pd(0) complexes were reported in the late 1960s [40, 41]. η^2 -Peroxopalladium(II) complexes were prepared via direct oxygenation of Pd(0) precursors bearing phosphines and isocyanides as ancillary ligands. Both of these ligand classes are susceptible to oxidation. Indeed, homogeneous Pd is a highly efficient catalyst for the aerobic oxidation of triphenylphosphine to triphenylphosphine oxide [42].

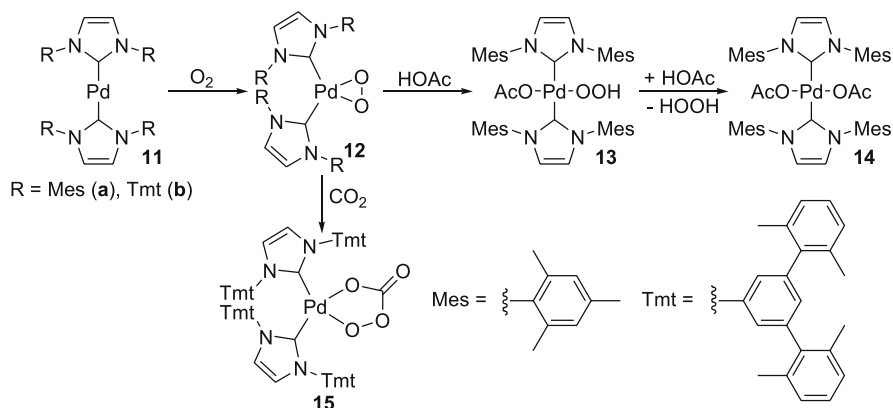
Oxygenation reactions of Pd(0) have been revisited recently in order to gain fundamental insights into this catalytically important reaction, and these studies have employed both phenanthroline and NHC ligands [43–45]. The use of bathocuproine (bc), a phenanthroline derivative, enabled isolation and crystallographic characterization of (bc)Pd(η^2 -O₂) [43] (Scheme 2). Addition



Scheme 1 General mechanism for Pd-catalyzed aerobic oxidation reaction



Scheme 2 Synthesis and isolation of bathocuproine palladium complexes



Scheme 3 Reaction of Bis-NHC palladium(0) complexes with molecular oxygen

of acetic acid to this complex results in formation of hydrogen peroxide and (bc)Pd(OAc)₂ via rapid protonolysis of both Pd – O bonds.

A somewhat different result is obtained from analogous reactions with the NHC-coordinated complex, (IMes)₂Pd⁰ (**11a**). This complex is extremely air-sensitive and reacts with dioxygen, even in the solid state, to produce the peroxo-complex, (IMes)₂Pd(η²-O₂) (**12a**). Addition of acetic acid to this complex yields the hydroperoxide complex, *trans*-(IMes)₂Pd(OAc)(OOH) (**13**). Prolonged reactions times are necessary before the second equivalent of acetic acid reacts to produce hydrogen peroxide and (IMes)₂Pd(OAc)₂ (**14**) [44] (Scheme 2). The Pd(0) complex **11b**, bearing the more-sterically-hindered NHC ligand ITmt, also reacts with molecular oxygen to produce the η²-peroxo complex [45]. If crystalline **11b** is exposed to ambient air at room temperature, the sample reacts directly to form a peroxocarbonate adduct **15** (Scheme 3). The complex results from CO₂ insertion into a Pd – O bond of **12b**. The IMes complex **12a** does not exhibit solid-state reactivity with CO₂. The difference in the reactivity of these two complexes probably arises from the different steric constraints present in the crystalline forms of **12a** and **12b**. Specifically, the ITmt ligand does not possess substituents in the ortho position of the *N*-aryl groups [45].

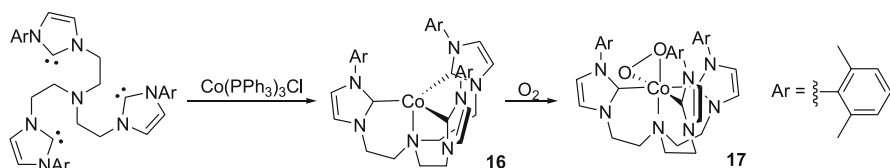
The significantly greater stability of metal-complexed NHCs relative to phosphines will permit further analysis of these fundamental reactions. On-going studies promise to provide significant insight into the aerobic oxidation of Pd(0) in Pd-catalyzed oxidation reactions.

3.2.2

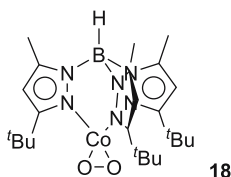
First-Row Transition Metals: Co, Ni and Cu

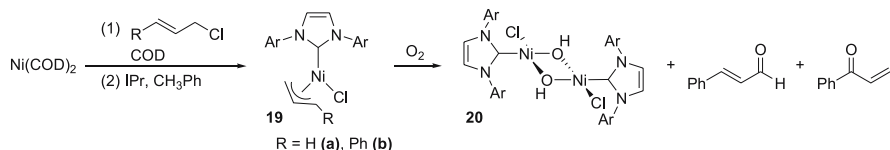
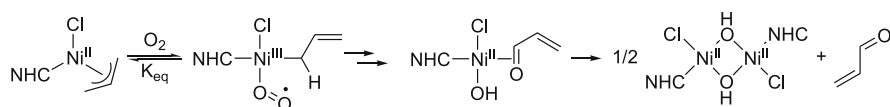
Several recent studies have probed the reactivity of dioxygen with first-row transition metals coordinated by NHC ligands. Cobalt complexes with a variety of different ligands bind dioxygen and have been investigated for use as oxygen carriers and oxidation catalysis [46, 47]. A cobalt(I) complex with a unique tripodal NHC ligand, **16**, was synthesized recently (Scheme 4). Upon reaction with molecular oxygen, it yields a pseudo-octahedral cobalt(III) η^2 -peroxo product, **17** [48]. The O – O vibrational frequency (890 cm^{-1}) and bond length [$1.429(3)\text{ \AA}$] differ significantly from the values observed for the closely related tris(pyrazolyl)borate complex $\text{Tp}'\text{Co}^{\text{III}}(\eta^2\text{-O}_2)$, **18** [961 cm^{-1} and $1.355(3)\text{ \AA}$] [49, 50]. These data, which indicate the O_2 ligand in **17** is more reduced than in **18**, suggest that the neutral NHC ligand is more electron rich than the anionic Tp' ligand. The increased electron-donating ability undoubtedly reflects the tetradentate character of the NHC ligand (one tertiary amine + three NHCs) relative to the tridentate Tp' ligand; however, the strong donor character of the NHCs probably contributes as well. The η^2 -peroxo complex **17** exhibits nucleophilic character, and reacts with electrophilic substrates such as tetracyanoethylene and benzoyl chloride.

Selective reactions of molecular oxygen with NHC-coordinated nickel(I) and nickel(II) complexes have been reported [51, 52]. π -Allyl Ni(II) complexes **19a** and **19b** were prepared via a one-pot procedure from $\text{Ni}(\text{COD})_2$ (Scheme 5). Upon exposure to an atmosphere of dioxygen, these complexes react to yield the binuclear hydroxide-bridged Ni complex **20**. Use of the phenyl-substituted allyl complex **19b** permits characterization of the organic products, which consist of a 5 : 3 ratio of cinnamaldehyde and phenyl vinyl ketone. Control experiments and ^{18}O -labeling studies demonstrated that the oxygen atoms in the Ni dimer and the organic products arise from dioxygen,



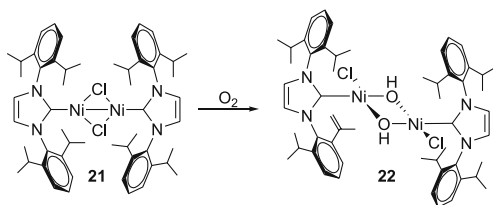
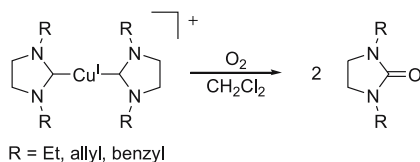
Scheme 4 Synthesis and oxygenation of Tris-carbene cobalt complex



**Scheme 5** Preparation and oxygenation of π -allylnickel NHC complexes**Scheme 6** Proposed mechanism for allylic ligand oxidation

not adventitious water. A simplified mechanistic proposal for this reaction is shown in Scheme 6. Separately, a chloride-bridged, dimeric Ni(I) complex, **21**, was prepared. This complex also undergoes reaction with molecular oxygen to yield a binuclear hydroxide-bridged Ni complex, **22** (Eq. 3). In this case, the four-electron reduction of dioxygen occurs with concomitant dehydrogenation of one isopropyl group of a single I^iPr ligand in the dimer.

The reactivity of dioxygen with nitrogen-coordinated copper(I) complexes has received extensive attention over the past two decades [53, 54]. To date, analogous reactivity has not been realized for NHC-coordinated Cu(I). Sterically unhindered bis-carbene complexes of Cu(I) undergo rapid conversion to the corresponding ureas upon exposure to air in CH_2Cl_2 solution (Eq. 4) [55]. This result suggests NHCs may not be universally applicable to metal-mediated oxidation chemistry.

**Equation 3****Equation 4**

4

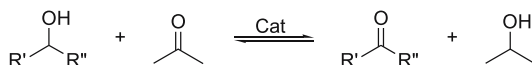
Oxidation Reactions Catalyzed by NHC-Coordinated Metal Complexes

The previous section highlighted the utility of NHC ligands in stoichiometric reactions of transition metals. NHCs have also been employed in metal-catalyzed oxidation reactions. Applications include selective alcohol, alkene and alkane oxidation reactions.

4.1

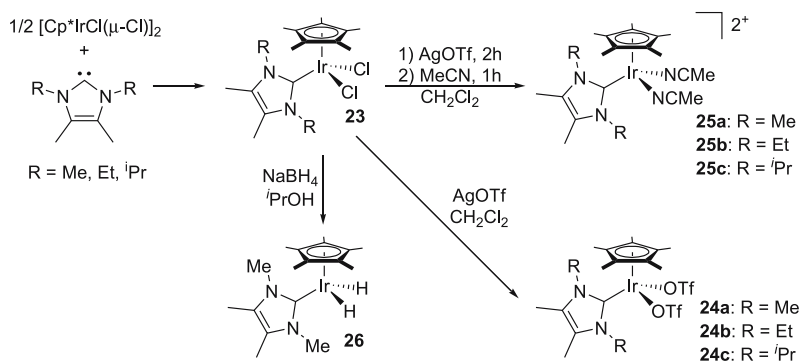
Oppenauer-Type Alcohol Oxidation

Metal-catalyzed oxidation of alcohols to aldehydes and ketones is a subject that has received significant recent attention [21, 56, 57]. One such method that utilizes NHC ligands is an Oppenauer-type oxidation with an Ir or Ru catalyst [58–62]. These alcohol oxidation reactions consist of an equilibrium process involving hydrogen transfer from the alcohol substrate to a ketone, such as acetone (Eq. 5), or an alkene. Because these reactions avoid the use of a strong oxidant, the potential oxidative instability of NHC ligands is less problematic. Consequently, these reactions represent an important target for future research into the utility of NHCs.

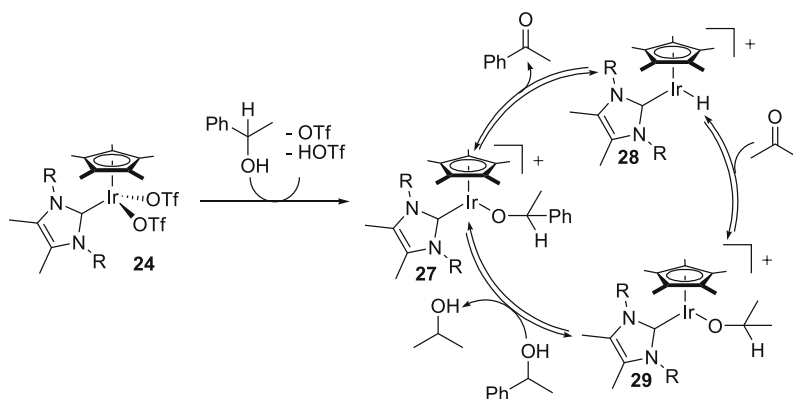


Equation 5

The Ir^{III} complex [Cp*IrCl(μ-Cl)]₂ serves as a catalyst for the oxidation of primary and secondary alcohols oxidation in acetone as the solvent [63]. The moderate effectiveness of this catalyst, however, prompted the preparation of several Ir^{III} analogs bearing an NHC ligand [58–60] (Scheme 7). It



Scheme 7 Synthesis of Cp*Ir NHC complexes



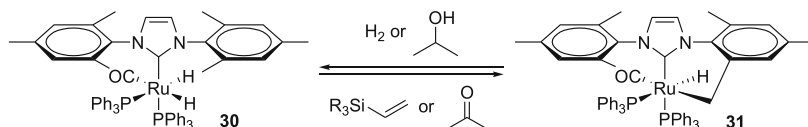
Scheme 8 Proposed mechanism for Oppenauer-type alcohol oxidation

was reasoned that NHC ligands might increase electron density at the metal center and increase the reactivity of an intermediate iridium-hydride with acetone (see intermediate **28**, Scheme 8).

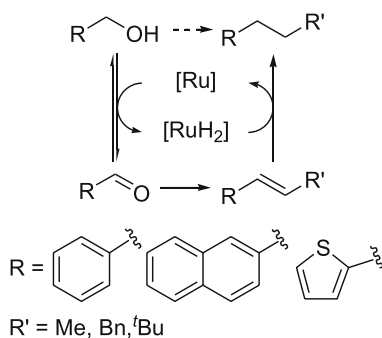
These complexes were screened in the oxidation of *sec*-phenethyl alcohol with acetone as the solvent and K_2CO_3 as a base [59]. It was found that the presence of smaller substituents on the nitrogen atoms of the NHC ligand promote catalytic activity, and the dicationic complex, **25a**, is the most active catalyst. Accordingly, use of complex **25a** enabled the catalyst loading to be lowered to 0.025 mol %, and 3200 turnovers were achieved. The utility of this catalyst was demonstrated for both primary and secondary benzylic alcohols and several aliphatic alcohols.

Analogs of **25**, wherein the NHC ligands are replaced with PPh_3 or P^nBu_3 , are almost completely inactive under comparable conditions [59]. Although a number of mechanistic details remain to be established, it is clear that including an NHC ligand in the Ir^{III} coordination sphere exerts a beneficial effect on the catalytic activity.

Ruthenium catalysts with NHC ligands, **30** and **31**, have also been employed in transfer dehydrogenation reactions [61,62]. Both acetone and alkenes have been used as the hydrogen acceptor in these reactions. When $(\text{IMes})\text{Ru}(\text{H})_2(\text{PPh}_3)_2(\text{CO})$ (**30**) reacts with acetone or an alkene, it transfers an equivalent of H_2 and undergoes C–H activation of an *ortho*-methyl group of the IMes ligand to yield a new complex $(\text{IMes}')\text{RuH}(\text{PPh}_3)_2(\text{CO})$ (**31**) (Eq. 6) [61].



Equation 6



Scheme 9 Proposed mechanism and substrate scope for tandem alcohol oxidation/Wittig reaction/alkene hydrogenation sequence

This C–H activation event is reversible, and is required to achieve catalytic turnover [62]. A series of alcohols, mostly secondary benzylic examples, have been oxidized using this catalyst. The catalytic activity does not match that of the Ir examples described above, but it has been used in several tandem reactions that feature both dehydrogenation and hydrogenation steps to achieve interesting transformations. One example is a tandem alcohol oxidation/Wittig reaction/alkene hydrogenation sequence (Scheme 9) [61, 62].

4.2

Palladium-Catalyzed Aerobic Alcohol Oxidation

Palladium-catalyzed aerobic oxidation of alcohols to aldehydes and ketones have been studied extensively in recent years, and a number of effective catalysts have been developed (Chart 2). This work has been the subject of several recent reviews [21, 36–38, 56, 64–67] and will not be summarized in depth

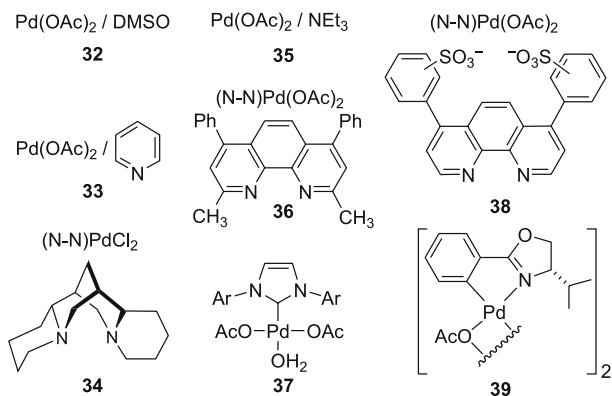


Chart 2 Palladium complexes employed in aerobic alcohol oxidation

here; however, this field highlights prospects for the use of NHC ligands in homogeneous metal-catalyzed oxidation reactions.

In 2001, two groups independently reported a PdCl₂/(-)-sparteine catalyst system **34** for the oxidative kinetic resolution of secondary alcohols [68, 69]. The reactions proceed with high selectivity for large number of substrates. Mechanistic studies revealed that (-)-sparteine serves both as a ligand for Pd and as a Brønsted base in the alcohol oxidation reaction [70, 71]. Recognition of this dual role for (-)-sparteine raised the possibility that kinetic resolution could be achieved with achiral Pd complexes, if (-)-sparteine is available as a chiral base in the reaction. This hypothesis was successfully demonstrated with NHC-coordinated Pd complexes, **40–43** (Table 2) [72]. The results obtained with enantiomeric chiral NHCs (*S,S*)-**43** and (*R,R*)-**43** reveal the presence of “matched” and “mismatched” diastereomeric interactions between the chiral NHC and (-)-sparteine during the reaction (Table 2, Entries 6 and 7). These results represent the first use of NHC ligands in aerobic oxidation catalysis. The presence of a strong Pd – NHC bond undoubtedly enhances the NHC oxidative stability and contributes to the success of these reactions.

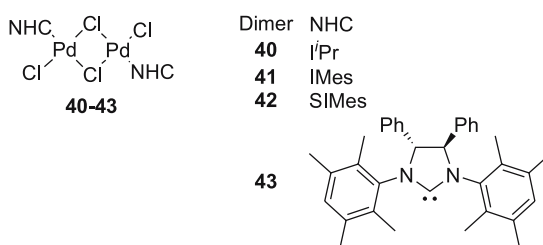


Table 2 Use of Pd(II) dimers in oxidative kinetic resolution of secondary alcohols

$ \begin{array}{c} \text{(+/-)} \begin{array}{c} \text{OH} \\ \\ \text{R}-\text{CH}-\text{Me} \end{array} \xrightarrow[\text{3\AA Molecular Sieves}]{\begin{array}{c} 1.5 \text{ mol\% Dimer} \\ 15 \text{ mol\% (-)-sparteine} \\ \text{DCE, O}_2, 65^\circ\text{C, 20h} \end{array}} \begin{array}{c} \text{OH} \\ \\ \text{R}-\text{CH}-\text{Me} \end{array} + \begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{Me} \end{array} \end{array} $				
Entry	Dimer	R	% Conversion (% ee)	<i>k</i> _{rel} ^a
1	40	C ₆ H ₅	64.5 (96.0)	11.6
2	40	2-naphthyl	52.7 (65.9)	7.8
3	40	<i>p</i> -OMeC ₆ H ₄	42.8 (58.2)	14.3
4 ^b	41	C ₆ H ₅	36.2 (34.9)	6.1
5 ^b	42	C ₆ H ₅	45.0 (54.1)	6.4
6 ^c	(<i>R,R</i>)- 43	C ₆ H ₅	39.7 (36.4)	4.5
7 ^c	(<i>S,S</i>)- 43	C ₆ H ₅	34.6 (42.0)	11.8

^a Average of multiple experiments. ^b (-)-Sparteine (20 mol%).

^c Dimer (2.5 mol%), (-)-sparteine (20 mol%).

The alcohol-oxidation catalyst systems consisting of $\text{Pd}(\text{OAc})_2/\text{pyridine}$ [73, 74] and $\text{Pd}(\text{OAc})_2/\text{NEt}_3$ [75] are perhaps the most “user-friendly” examples developed to date. Detailed mechanistic investigation of these catalyst systems revealed a common feature: key intermediates in the catalytic cycle consist of Pd complexes that possess only one neutral donor ligand (pyridine or triethylamine) [76–78]. Furthermore, excess pyridine and NEt_3 inhibit catalytic turnover by competing with the substrate for coordination sites on Pd. If the pyridine and NEt_3 concentrations are too low, however, the catalyst decomposes because facile ligand dissociation enables the aggregation of Pd metal. These observations prompted the development of a new class of NHC–Pd catalysts for alcohol oxidation, $(\text{NHC})\text{Pd}(\text{O}_2\text{CR})_2(\text{OH}_2)$ (**44**) [72, 79–82]. The NHC provides a single, strongly coordinating, neutral donor ligand to stabilize the Pd center, the carboxylate ligands are available to serve as a base in the reaction, and the water ligand can readily dissociate to provide access to the substrate.

With $(\text{I}^i\text{Pr})\text{Pd}(\text{OAc})_2(\text{OH}_2)$ (**44a**) as the catalyst, a variety of benzylic, allylic and aliphatic alcohols are oxidized efficiently (Table 3) [81]. Co-catalytic quantities of acetic acid (or, in some cases, NBu_4OAc) play a critical role in the reaction and permit the catalyst loading to be lowered to 0.5 mol %. The related catalyst $(\text{I}^i\text{Pr})\text{Pd}(\text{OPiv})_2$ (**44b**) is effective under remarkably mild con-

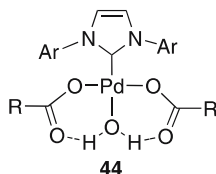


Table 3 Aerobic alcohol oxidation employing $(\text{I}^i\text{Pr})\text{Pd}(\text{OAc})_2$ and $(\text{I}^i\text{Pr})\text{Pd}(\text{OPiv})_2$ complexes

$\text{R}^1\text{CH}(\text{OH})\text{R}^2 \xrightarrow[\text{O}_2 / \text{Air}]{\text{Pd-Catalyst}} \text{R}^1\text{C}(=\text{O})\text{R}^2$ $\text{44a} = (\text{I}^i\text{Pr})\text{Pd}(\text{OAc})_2(\text{OH}_2); \text{44b} = (\text{I}^i\text{Pr})\text{Pd}(\text{OPiv})_2$							
Entry	Alcohol	Catalyst	Conversion (%)	Entry	Alcohol	Catalyst	Conversion (%)
1		0.5 mol% 44a , Air, 60 °C, 14 h 4 mol% AcOH	99	6		1 mol% 44b , Air, rt, 14 h 0.5 mol% PivOH	99
2		1 mol% 44b , Air, rt, 14 h 0.5 mol% PivOH	92	7		1 mol% 44a , O ₂ , 60 °C, 14 h 1 mol% AcOH	93
3		1 mol% 44b , Air, rt, 14 h 0.5 mol% PivOH	47	8		1 mol% 44a , O ₂ , 60 °C, 13 h 5 mol% NBu_4OAc	94
4		1 mol% 44b , Air, rt, 14 h 0.5 mol% PivOH	97	9		0.5 mol% 44a , O ₂ , 60 °C, 15 h 5 mol% NBu_4OAc	92
5		0.5 mol% 44a , O ₂ , 60 °C, 10 h 5 mol% NBu_4OAc	85	10		1 mol% 44b , Air, rt, 14 h 0.5 mol% PivOH	89

ditions (1 mol % **44b**, 0.5 mol % PivOH, ambient air as the O₂ source, room temperature), although its substrate scope is more limited than **44a** [81].

The significant influence of carboxylic acid on these reactions prompted a fundamental investigation into its role in the aerobic oxidation of 1-phenylethanol catalyzed by **44a** (0.5 mol %) [80]. At low concentrations (≤ 0.62 mol %), acetic acid has a beneficial effect on the reaction rate (Fig. 3a). Beyond this concentration, acetic acid exhibits an inhibitory effect. Acetic acid also influences the catalyst stability (Fig. 3b). In the absence of acetic acid, the reaction proceeds only to low levels of conversion. At 0.75 mol % acetic acid, the reaction begins with a high initial rate, but the time-course deviates from the expected first-order dependence on [alcohol] (Fig. 3b). The first-order dependence observed when [AcOH] is ≥ 2 mol % suggests that the catalyst is more stable (albeit somewhat less active) under these conditions.

These data have been rationalized by recognizing that acetic acid plays several roles in the catalytic mechanism (Scheme 10) [80]. In the absence of acetic acid, the Pd(0) intermediate, **49**, undergoes competitive decomposition and oxygenation. Low concentrations of acetic acid enhance the rate and minimize catalyst decomposition by trapping the reversibly formed peroxopalladium(II) intermediate, **50**. Acetic acid also can stabilize the catalyst by reversible formation of a Pd-hydride species, **48**. At high [AcOH], the reaction rate is slowed because acetic acid inhibits formation of the alkoxide intermediate **47**.

Among the significant outcomes of these studies was the demonstration that a single NHC ligand could withstand the aerobic oxidation conditions in these reactions. This ligand stability suggests that the NHC does not dissociate from the Pd center, despite numerous cycling between Pd^{II} and Pd⁰ oxidation states.

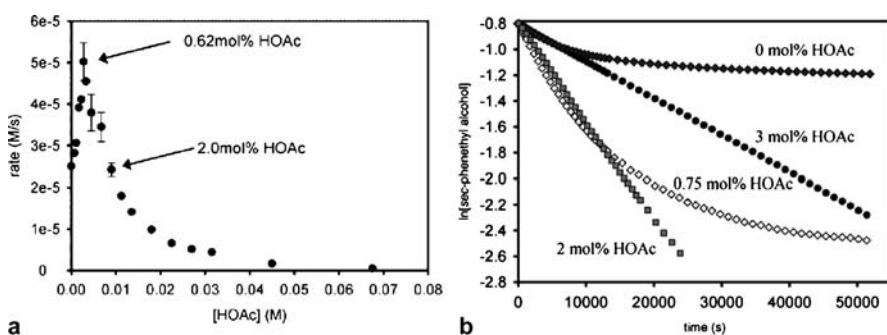
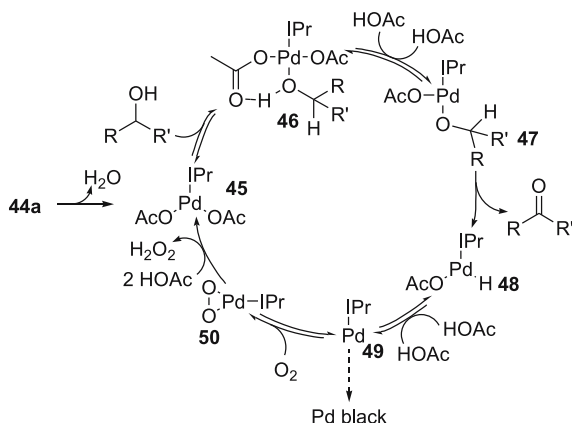


Fig. 3 **a** Rate dependence of *sec*-phenethyl alcohol oxidation using various acetic acid concentrations. **b** Natural logarithm of *sec*-phenethyl alcohol concentrations versus time at various acetic acid concentrations. Reprinted with permission from Mueller JA, Goller CP, Sigman MS (2004) *J Am Chem Soc* 126:9724, Copyright 2004, American Chemical Society

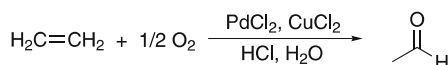


Scheme 10 Proposed mechanism for aerobic alcohol oxidation using $\text{IPrPd}(\text{OAc})_2\cdot\text{OH}_2$

4.3

Palladium-Catalyzed Oxidation of Alkenes

The field of homogeneous palladium catalysis traces its origin to the development of the Wacker process in the late 1950s (Eq. 7) [83]. Since this discovery, palladium-catalyzed reactions have evolved into some of the most versatile reactions for the synthesis of organic molecules [84, 85]. Palladium-catalyzed Wacker-type oxidation of alkenes continues to be an active field of research [86–88], and several recent applications of NHC-coordinated Pd catalysts have been reported for such reactions.



Equation 7

4.3.1

Intramolecular Oxidative Heterocyclization Reactions

Palladium(II)-promoted oxidative cyclization of alkenes bearing tethered nucleophiles represents an intramolecular variant of the Wacker reaction. These reactions, which typically generate five- and six-membered heterocycles, have been the subject of considerable interest in organic chemistry [89–96]. Contemporary interest centers on the development of enantioselective examples [95, 97] and reactions that employ dioxygen as the sole oxidant for the Pd catalyst [92–96].

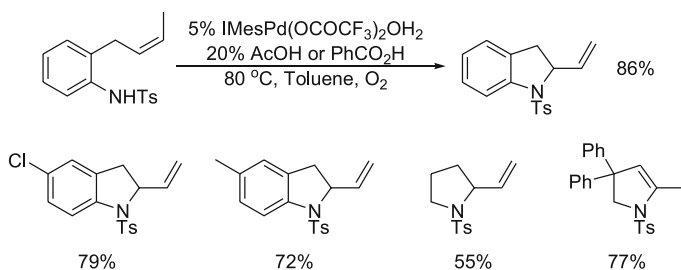
Both oxygen and nitrogen heterocycles have been prepared with mono-NHC-coordinated Pd^{II} complexes of the general structure **44**. *o*-Allylphenol

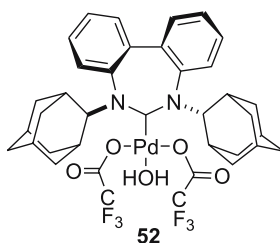
Table 4 Oxidative heterocyclization of oxygen nucleophiles

Entry	R ¹	R ²	Yield (%)
1	H	H	89
2	H	CH ₃	91
3	CH ₃	H	92
4	CH ₂	CH ₃	96

derivatives undergo efficient oxidative cyclization to yield dihydrobenzofuran derivatives under 1 atm of molecular oxygen (Table 4) [96]. The catalyst is prepared in situ by mixing 1.2 equivalents of the ligand imidazolium salt with palladium(II) trifluoroacetate. Use of the trifluoroacetate counterion is important; with acetate and chloride ions, the reaction was less efficient and produces mixtures of five- and six-membered heterocycles. The presence of base (20 mol % DMAP and 2 eq Na₂CO₃ with respect to the substrate) was reported to be necessary to avoid side reactions and maintain catalyst activity. Similarly good results were also obtained with *i*Pr and *Si*^{*i*}Pr as the NHC ligand.

Nitrogen-containing heterocycles have been prepared in a similar manner [98]. In this case, both aliphatic and aromatic Ts-protected amines cyclize to yield 5-membered heterocycles with 5 mol % (IMes)Pd(O₂CCF₃)₂(OH₂) (**51**) as the catalyst (Scheme 11). The corresponding PdCl₂ catalyst, **41**, is completely inactive, whereas the (IMes)Pd(OAc)₂(OH₂) complex is comparable to **51**. The reaction proceeds most effectively when cocatalytic quantities (10–20 mol %) of acetic acid are present. Under these conditions, the reaction is even successful with ambient air as the source of dioxygen.

**Scheme 11** Intramolecular oxidative amination



Recently, palladium(II) complexes bearing a new class of seven-membered NHC ligands was reported [99, 100]. The trifluoroacetate analog **52** catalyzes the nitrogen heterocyclization reaction with yields similar to those obtained with the IMes complex **51**, although the reactions times are somewhat longer [98]. These C_2 symmetric ligands may find future application in asymmetric catalysis once enantiomerically resolved analogs become available.

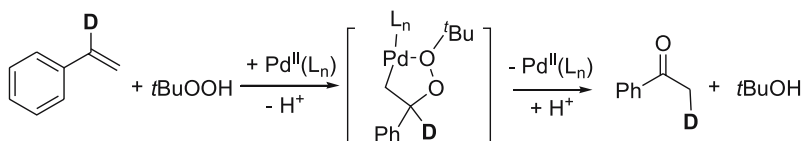
4.3.2

Intermolecular Oxidation of Alkenes

The Pd-catalyzed conversion of terminal alkenes to methyl ketones is a reaction that has found widespread use in organic chemistry [87, 88]. These reactions, as well as the industrial Wacker process, typically employ CuCl_2 as a co-catalyst or a stoichiometric oxidant. Recently Cu-free reaction conditions were identified for the Wacker-type oxidation of styrenes using $t\text{BuOOH}$ as the oxidant. An NHC-coordinated Pd complex, in-situ-generated $(\text{I}^i\text{Pr})\text{Pd}(\text{OTf})_2$, served as the catalyst (Table 5) [101]. These conditions min-

Table 5 Wacker-type oxidation of alkenes employing $(\text{I}^i\text{Pr})\text{Pd}(\text{OTf})_2$

$\text{Ar}-\text{CH}=\text{CH}_2 \xrightarrow[\substack{0.5 \text{ M in MeOH} \\ 35^\circ\text{C, air}}]{\substack{0.75 \text{ mol \% } [(\text{I}^i\text{Pr})\text{PdCl}_2]_2 \\ 3 \text{ mol \% AgOTf} \\ 5.5 \text{ equiv. TBHP}_{(\text{aq})}}} \text{Ar}-\text{C}(=\text{O})\text{CH}_3 \text{ (A)} + \text{Ar}-\text{C}(=\text{O})\text{CH}_2\text{ (B)}$				
Entry	Ar	Time (h)	Yield (%)	A:B
1	Ph	24	75	> 130:1
2	2-methylphenyl	48	79	36:1
3	3-methylphenyl	32	83	22:1
4	4-methylphenyl	16	86	22:1
5	2,4,6-trimethylphenyl	24	71	> 150:1
6	3-chlorophenyl	48	80	> 150:1



Scheme 12 Proposed hydride-shift mechanism for the Wacker oxidation of styrene catalyzed by $(1^i\text{Pr})\text{Pd}(\text{OTf})_2$

imize polymerization and oxidative cleavage of the alkene, which represent common side reactions in the Wacker oxidation of styrene.

Attempts to use molecular oxygen as the oxidant failed except in solvents that undergo efficient autooxidation to the corresponding hydroperoxide (e.g., THF). Mechanistic studies, including isotopic labeling studies, indicate that $t\text{BuOOH}$ is the source of the oxygen atom incorporated into the product, and the reaction proceeds via a hydride-shift pathway that avoids formation of an enol intermediate (Scheme 12).

4.4

Oxidative Cleavage of Alkenes

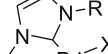
The oxidative cleavage of alkenes to aldehydes and ketones is commonly achieved via ozonolysis. Transition-metal catalysts, including RuCl_3 , RuO_4 , and OsO_4 , together with stoichiometric oxidants also may be used for this

Table 6 Oxidative cleavage of alkenes to aldehydes

	Entry	Olefin	Product	Yield (%)
	1			99
	2			58
	3			99
	4			72
	5			99
Conditions: 1 mL CDCl_3 / 0.1 mL H_2O , 1.25 equiv NaIO_4 , 1 mol% 52 . Product yields were determined by NMR.				

$$\text{CH}_4 + \text{CF}_3\text{COOH} \xrightarrow[\text{K}_2\text{S}_2\text{O}_8, 20\text{bar}]{[\text{Pd}], 80^\circ\text{C}} \text{CF}_3\text{COOCH}_3$$

$$2 \text{ KHSO}_4$$



54a: R = *t*Bu, X = Br
54b: R = *t*Bu, X = I
54c: R = Me, X = Br
54d: R = Me, X = I

Entry	[Pd]	Turnovers ^a
1	54a	5.1
2	54b	0
3	54c	9.8
4	54d	0
5	Pd(OAc) ₂	3.8
6	54c	30 ^b

^a By GC analysis, relative to Pd.
^b T = 90 °C, t = 14h, p(CH₄) = 30 bar

5

Conclusions

The results outlined above highlight significant prospects for use of *N*-heterocyclic carbenes as ligands in oxidation chemistry. Nevertheless, this field remains in the early stages of development. With strong sigma-donor properties, NHCs are well suited to stabilize high-oxidation-state metal complexes; however, the number of complexes that have been prepared to date is quite small and very little has been described concerning the oxidizing properties of these complexes. Significant opportunities exist to expand the use of NHCs as ancillary ligands in metal-catalyzed oxidation reactions. The relatively high NHC – metal bond strength slows ligand dissociation and helps to prevent oxidative decomposition of the NHC ligand. Further studies are needed to probe the scope (and limitations) of metal complexes, catalysts, oxidizing agents, and reaction conditions that are compatible with the use of NHCs as ancillary ligands.

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References

1. Arduengo AJ III, Harlow RL, Kline M (1991) *J Am Chem Soc* 113:361
2. Cardin DJ, Cetinkay AB, Lappert MF (1972) *Chem Rev* 72:545
3. Herrmann WA, Köcher C (1997) *Angew Chem Int Ed* 36:2162
4. Herrmann WA (2002) *Angew Chem Int Ed* 41:1290
5. Peris E, Crabtree RH (2004) *Coord Chem Rev* 248:2239
6. Crudden CM, Allen DP (2004) *Coord Chem Rev* 248:2247
7. Scott NM, Nolan SP (2005) *Eur J Inorg Chem* p 1815
8. Öfele K, Herrmann WA, Mihalios D, Elison M, Herdtweck E, Scherer W, Mink J (1993) *J Organomet Chem* 459:177
9. Huang J, Schanz H-J, Stevens ED, Nolan SP (1999) *Organometallics* 18:2370
10. Perrin L, Clot E, Eisenstein O, Loch J, Crabtree RH (2001) *Inorg Chem* 40:5806
11. Denk K, Sirsch P, Herrmann WA (2002) *J Organomet Chem* 649:219
12. Chianese AR, Li X, Janzen MC, Faller JW, Crabtree RH (2003) *Organometallics* 22:1663
13. Hillier AC, Sommer WJ, Yong BS, Petersen JL, Cavallo L, Nolan SP (2003) *Organometallics* 22:4322
14. Lee M-T, Hu C-H (2004) *Organometallics* 23:976
15. Crabtree RH (2005) *J Organomet Chem* 690:5451
16. Chianese AR, Kovacevic A, Zeglis BM, Faller JW, Crabtree RH (2004) *Organometallics* 23:2461
17. Dorta R, Stevens ED, Scott NM, Costabile C, Cavallo L, Hoff CD, Nolan SP (2005) *J Am Chem Soc* 127:2485

18. Netherton MR, Fu GC (2001) *Org Lett* 3:4295
19. Tolman CA (1977) *Chem Rev* 77:313
20. Magill AM, Cavell KJ, Yates BF (2004) *J Am Chem Soc* 126:8717
21. Sheldon RA, Kochi JK (1981) *Metal-Catalyzed Oxidations of Organic Compounds*. Academic Press, New York
22. Romão CC, Kühn FE, Herrmann WA (1997) *Chem Rev* 97:3197
23. Herrmann WA, Öfele K, Elison M, Kühn FE, Roesky PW (1994) *J Organomet Chem* 480:C7
24. Felixberger JK, Kuchler JG, Herdtweck E, Paciello RA, Herrmann WA (1988) *Angew Chem Int Ed* 27:946
25. Al-Ajlouni AM, Espenson JH (1995) *J Am Chem Soc* 117:9243
26. Herrmann WA, Lobmaier GM, Elison M (1996) *J Organomet Chem* 520:231
27. Oldham WJ Jr, Oldham SM, Scott BL, Abney KD, Smith WH, Costa DA (2001) *Chem Commun* p 1348
28. Braband H, Abram U (2003) *Chem Commun* p 2436
29. Abernethy CD, Codd GM, Spicer MD, Taylor MK (2003) *J Am Chem Soc* 125:1128
30. Braband H, Zahn TI, Abram U (2003) *Inorg Chem* 42:6160
31. Kückmann TI, Abram U (2004) *Inorg Chem* 43:7068
32. Evans WJ, Kozimor SA, Ziller JW (2004) *Polyhedron* 23:2689
33. Horner SM, Tyree SY Jr (1962) *Inorg Chem* 1:122
34. Florian LR, Corey ER (1968) *Inorg Chem* 7:722
35. Butcher RJ, Powell HKJ, Wilkins CJ, Yong SH (1976) *J Chem Soc, Dalton Trans* p 356
36. Stahl SS (2005) *Science* 309:1824
37. Stahl SS (2004) *Angew Chem Int Ed* 43:3400
38. Sigman MS, Jensen DR, Rajaram S (2002) *Curr Opin Drug Discovery Dev* 5:860
39. Jensen DR, Schultz MJ, Mueller JA, Sigman MS (2003) *Angew Chem Int Ed* 42:3810
40. Wilke G, Schott H, Heimbach P (1967) *Angew Chem Int Ed* 6:92
41. Otsuka S, Nakamura A, Tatsuno Y (1969) *J Am Chem Soc* 91:6994
42. Hikichi S, Akita M, Moro-oka Y (2000) *Coord Chem Rev* 198:61
43. Stahl SS, Thorman JL, Nelson RC, Kozee MA (2001) *J Am Chem Soc* 123:7188
44. Konnick MM, Guzei IA, Stahl SS (2004) *J Am Chem Soc* 126:10212
45. Yamashita M, Goto K, Kawashima T (2005) *J Am Chem Soc* 127:7294
46. Bianchini C, Zoellner RW (1997) In: Sykes AG (ed) *Advances in Inorganic Chemistry*, vol 44. Academic Press, San Diego, pp 263–339
47. Busch DH, Alcock NW (1994) *Chem Rev* 94:585
48. Hu X, Castro-Rodriguez I, Meyer K (2004) *J Am Chem Soc* 126:13464
49. Egan JW Jr, Haggerty BS, Rheingold AL, Sendlinger SC, Theopold KH (1990) *J Am Chem Soc* 112:2445
50. Cramer CJ, Tolman WB, Theopold KH, Rheingold AL (2003) *Proc Natl Acad Sci USA* 100:3635
51. Dible BR, Sigman MS (2003) *J Am Chem Soc* 125:872
52. Dible BR, Sigman MS, Arif AM (2005) *Inorg Chem* 44:3774
53. Mirica LM, Ottenwaelder X, Stack TDP (2004) *Chem Rev* 104:1013
54. Lewis EA, Tolman WB (2004) *Chem Rev* 104:1047
55. Ku R-Z, Huang J-C, Cho J-Y, Kiang F-M, Reddy KR, Chen Y-C, Lee K-J, Lee J-H, Lee G-H, Peng S-M, Liu S-T (1999) *Organometallics* 18:2145
56. Sheldon RA, Arends IWCE (2003) In: Simándi II (ed) *Advances in Catalytic Activation of Dioxygen by Metal Complexes*. Kluwer Academic Press, Dordrecht, pp 123–155

57. Besson M, Gallezot P (2000) *Catal Today* 57:127
58. Hanasaka F, Fujita K, Yamaguchi R (2004) *Organometallics* 23:1490
59. Hanasaka F, Fujita K, Yamaguchi R (2005) *Organometallics* 24:3422
60. Fujita K, Yamaguchi R (2005) *Synlett* p 560
61. Edwards MG, Jazzar RFR, Paine BM, Shermer DJ, Whittlesey MK, Williams MJ, Edney DD (2004) *Chem Commun* p 90
62. Burling S, Whittlesey MK, Williams MJ (2005) *Adv Synth Catal* 347:591
63. Fujita K, Furukawa S, Yamaguchi R (2002) *J Organomet Chem* 649:289
64. Muzart J (2003) *Tetrahedron* 59:5789
65. Sheldon RA, Arends IWCE, Dijkstra A (2000) *Catal Today* 57:157
66. Nishimura T, Uemura S (2004) *Synlett* p 201
67. Stoltz BM (2004) *Chem Lett* 33:362
68. Jensen DR, Pugsley JS, Sigman MS (2001) *J Am Chem Soc* 123:7475
69. Ferreira EM, Stoltz BM (2001) *J Am Chem Soc* 123:7725
70. Mueller JA, Jensen DR, Sigman MS (2002) *J Am Chem Soc* 124:8202
71. Mandal SK, Sigman MS (2003) *J Org Chem* 68:7535
72. Jensen DR, Sigman MS (2003) *Org Lett* 5:63
73. Nishimura T, Onoue T, Ohe K, Uemura S (1998) *Tetrahedron Lett* 39:6011
74. Nishimura T, Onoue T, Ohe K, Uemura S (1999) *J Org Chem* 64:6750
75. Schultz MJ, Park CC, Sigman MS (2002) *Chem Commun* p 3034
76. Steinhoff BA, Stahl SS (2002) *Org Lett* 4:4179
77. Steinhoff BA, Guzei IA, Stahl SS (2004) *J Am Chem Soc* 126:11268
78. Schultz MJ, Adler RS, Zierkiewicz W, Privalov T, Sigman MS (2005) *J Am Chem Soc* 127:8499
79. Jensen DR, Schultz MJ, Mueller JA, Sigman MS (2003) *Angew Chem Int Ed* 42:3810
80. Mueller JA, Goller CP, Sigman MS (2004) *J Am Chem Soc* 126:9724
81. Schultz MJ, Hamilton SS, Jensen DR, Sigman MS (2005) *J Org Chem* 70:3343
82. Privalov T, Linde C, Zetterberg K, Moberg C (2005) *Organometallics* 24:885
83. Smidt J, Hafner W, Jira R, Sedlmeier J, Sieber R, Rüttinger R, Kojer H (1959) *Angew Chem* 71:176
84. Henry PM (1980) *Palladium Catalyzed Oxidation of Hydrocarbons*. D. Reidel Publishing Company, Hingham
85. Tsuji J (1995) *Palladium Reagents and Catalysis: Innovations in Organic Synthesis*. Wiley, Chichester
86. Hintermann L (2004) In: Beller M, Bolm C (eds) *Transition Metal for Organic Synthesis: Building Blocks and Fine Chemicals*, vol 2. Wiley, Weinheim, pp 379–388
87. Henry PM (2002) In: Negishi E, de Meijere A (eds) *Handbook of Organopalladium Chemistry for Organic Synthesis*, vol 2. Wiley, New York, pp 2119–2139
88. Takacs JM, Jiang X (2003) *Curr Org Chem* 7:369
89. Hosokawa T (2002) In: Negishi E, de Meijere A (eds) *Handbook of Organopalladium Chemistry for Organic Synthesis*, vol 2. Wiley, New York, pp 2211–2225
90. Hosokawa T, Uno T, Inui S, Murahashi S-I (1981) *J Am Chem Soc* 103:2318
91. Larock RC, Hightower TR (1993) *J Org Chem* 58:5298
92. Rönn M, Bäckvall J-E, Andersson PG (1995) *Tetrahedron Lett* 36:7749
93. Larock RC, Hightower TR, Hasvold LA, Peterson KP (1996) *J Org Chem* 61:3584
94. Fix SR, Brice JL, Stahl SS (2002) *Angew Chem Int Ed* 41:164
95. Trend RM, Ramtohul YK, Ferreira EM, Stoltz BM (2003) *Angew Chem Int Ed* 42:2892
96. Muñoz K (2004) *Adv Synth Catal* 346:1425
97. Uozumi Y, Kato K, Hayashi T (1997) *J Am Chem Soc* 119:5063
98. Rogers MM, Wendlendt JE, Guzei IA, Stahl SS (2006) *Org Lett* 8:2257

-
99. Scarborough CC, Grady MJW, Guzei IA, Gandhi BA, Bunel EE, Stahl SS (2005) *Angew Chem Int Ed* 44:5269
 100. Scarborough CC, Popp BV, Guzei IA, Stahl SS (2005) *J Organomet Chem* 690:6143
 101. Cornell CN, Sigman MS (2005) *J Am Chem Soc* 127:2796
 102. Lee DG, Chen T (1991) In: Trost BM, Fleming I, Ley SV (eds) *Comprehensive Organic Synthesis: Selectivity, Strategy and Efficiency in Modern Organic Chemistry*, vol 7. Pergamon Press, Elmsford, pp 541–591
 103. Kühn FE, Fischer RW, Herrmann WA, Weskamp T (2004) In: Beller M, Bolm C (eds) *Transition Metals for Organic Synthesis*, vol 2. Wiley, Weinheim, pp 427–436
 104. Poyatos M, Mata JA, Falomir E, Crabtree RH, Peris E (2003) *Organometallics* 22:1110
 105. Shilov AE, Shul'pin GB (1997) *Chem Rev* 97:2879
 106. Sen A (1998) *Acc Chem Res* 31:550
 107. Stahl SS, Labinger JA, Bercaw JE (1998) *Angew Chem Int Ed* 37:2180
 108. Jia C, Piao D, Oyamada J, Lu W, Kitamura T, Fujiwara Y (2000) *Chemtracts: Org Chem* 13:491
 109. Periana RA, Taube DJ, Gamble S, Taube H, Satoh T, Fujii H (1998) *Science* 280:560
 110. Muehlhofer M, Strassner T, Herrmann WA (2002) *Angew Chem Int Ed* 41:1745
 111. Strassner T, Muehlhofer M, Zeller A, Herdtweck E, Herrmann WA (2004) *J Organomet Chem* 689:1418