CHEMICAL REVIEWS

REVIEW

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Organic Synthesis Involving Iridium-Catalyzed Oxidation

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1. INTRODUCTION

Oxidation of organic compounds is one of the most fundamental technologies for organic synthesis. Traditional methods, however, use stoichiometric quantities of toxic heavy metal oxidants and produce large amounts of inorganic salts along with the target compounds. During recent years, the development of environmentally friendly processes has attracted much attention.[1] From an environmentally benign point of view, synthetic methods should be developed with a high atom economy. Nontoxic and recyclable reagents are also preferred. Oxidations with molecular oxygen or hydrogen peroxide are high-atom economical methodologies relying on such nontoxic oxidants. In 'green' processes, the use of an auxiliary solvent, especially halogenated solvents, should also be avoided. Ambient temperature and pressure is ideal for energy saving. High yield and high stereoselectivity, including regioselectivity, diastereoselectivity, and enantioselectivity, contribute to the environmental value as well as the economic importance. Chemoselective processes with high functional group tolerance supply protecting group free syntheses. The key to achieving the above-mentioned points is the development of excellent catalytic methodologies. For example, the oxidation of alcohols with H_2O_2 or O_2 has been developed using a transition-metal catalyst such as Pd, Cu, and Ru.[2] The application of iridium catalysts for oxidation reactions is less well known than the use of other transition metals. In general, the iridium complex is more stable than the rhodium and cobalt complexes. The stability has been utilized for the mechanistic study using stoichiometric reactions. However, research using Ir catalyst has made tremendous progress since the report of the Crabtree hydrogenation catalyst.[3] Many oxidations utilizing the hydrogen transfer process have been developed in the last few decades.[4] The stable character of the Ir complex can be effective for the severe thermal condition or basic condition. This unique feature of the Ir complex provides access to the new tandem reaction world. This review covers studies up to October 2010.

2. OXIDATION OF ALCOHOLS AND CARBONYL COMPOUNDS

2.1. Oxidation of Secondary Alcohols to Ketones

The first example of a transition-metal-catalyzed hydrogen transfer reaction was reported by Henbest in the 1960s.[5] $IrCl_3(dmso)_3$ or $HIrCl_2(dmso)_3$ catalyzed the transfer hydrogenation of cyclohexanone or chalcone in the presence of 2-propanol, giving the cyclohexanol and dihydrochalcone, respectively. Later, Zassinovich developed the more active transfer hydrogenation catalyst [Ir(Phen)(cod)]Cl, which has been shown to have a turnover number of more than 5000.[6]

After these successes with iridium-catalyzed transfer hydrogenation, Ajjiou reported the oxidation of secondary alcohols using $[Ir(cod)Cl]_2$/BQC as the catalyst and acetone as the oxidant (eq 1).[7] This catalyst system is soluble in water, and recycling the aqueous phase for repeated catalysis was carried out three times. Interestingly, when the oxidation was performed with $[Ir(cod)Cl]_2$ alone or combined with 2.2% biquinoline (BQ) in acetone containing only 0.5% water, very low yields were obtained (~5%).

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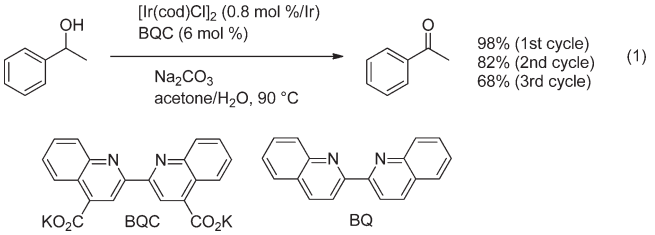


The oxidation of 3-methyl-2-cyclohexenol proceeded with full conversion to the corresponding unsaturated ketone (Table 1, entry 1).[7b] However, 1-octen-3-ol and 1-phenyl-2-propen-1-ol underwent quantitative isomerization to give saturated carbonyl compounds (entries 2 and 3).

Fujita and Yamaguchi reported that $[Cp^*IrCl_2]_2$ with K_2CO_3 also catalyzes oxidations with acetone as an oxidant (Table 2).[8] They found that the introduction of N-heterocyclic carbene (NHC) ligands enhanced the catalytic activity. In the oxidation of 1-phenylethanol and cyclopentanol, turnover numbers reached 3200 and 6640, respectively.[8c,d] Enhancement of the catalytic activity by NHC ligands was explained to result from the increased nucleophilicity of the iridium hydride.

Gelman reported the oxidation of secondary alcohols using an air-stable Ir pincer complex (eq 2).[9] The manipulations were carried out in air, and no advantage was observed when the reaction was performed under a nitrogen atmosphere. Various aromatic ketones including benzophenone can be synthesized. The reaction of benzylalcohol produced Tishchenko product along with minute quantities of the desired aldehyde.

Table 1. Reaction of Allylic Alcohols by Acetone Using $[Ir(cod)Cl]_2$/BQC]

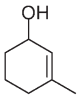
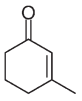
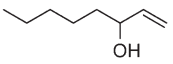
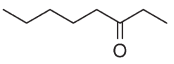
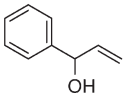
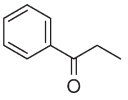
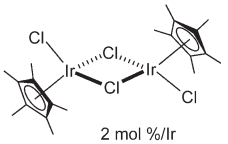
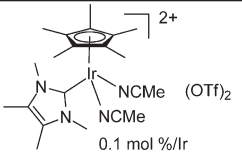
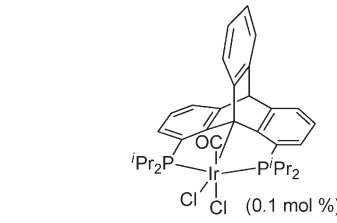
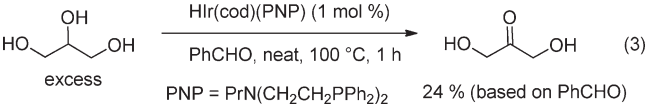
entry	substrate	time (h)	product	yield(%)
1		17		100
2		1		100
3		1.5		100

Table 2. Oxidation of Secondary Alcohols by Acetone Using Cp*Ir Catalysts

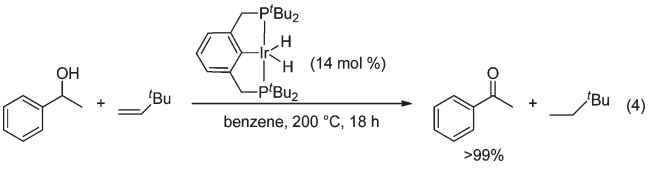
catalyst / substrate	 2 mol %/Ir	 0.1 mol %/Ir
	94 % yield	95 % (TON 950) 80 % (TON 3200)* *0.025 mol%/Ir
	100 % yield	90% (TON 900) 83% (TON 6640)* *0.0125 mol %



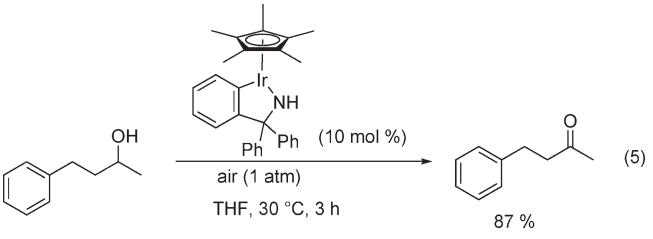
Crotti and Farnetti showed regioselective oxidation of glycerol to dihydroxyacetone (DHA) (eq 3).[10] HIr(cod)(PNP) gave DHA using benzaldehyde in the absence of a basic cocatalyst in order to avoid decomposition of the desired product.[10b]



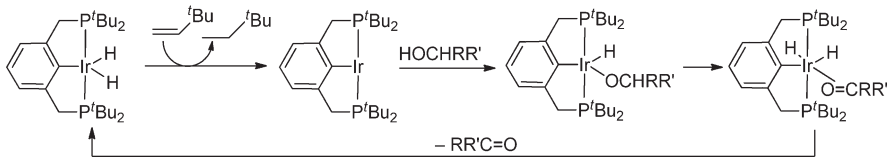
Jensen developed a dihydride iridium PCP pincer complex and applied it to the oxidation of phenylethanol in the presence of *tert*-butylethylene (tbe) as an oxidant (eq 4).[11] O−H oxidative addition of the alcohol to the 14 e Ir(I) complex, which is generated by reaction of Ir dihydride and tbe, was proposed. β-Elimination from the alkoxide produces the ketone and the dihydride complex (Scheme 1).



Ikariya reported the mild aerobic oxidation of secondary alcohols with bifunctional Ir catalysts bearing C−N chelating ligands (eq 5). The catalyst facilitates the aerobic oxidation of alcohols under mild conditions of atmospheric pressure and ambient temperature. The oxidation of unsaturated 2-cyclohexen-1-ol gave 2-cyclohexenone in 47% yield.[12]

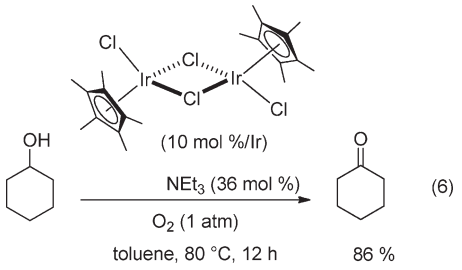


Scheme 1

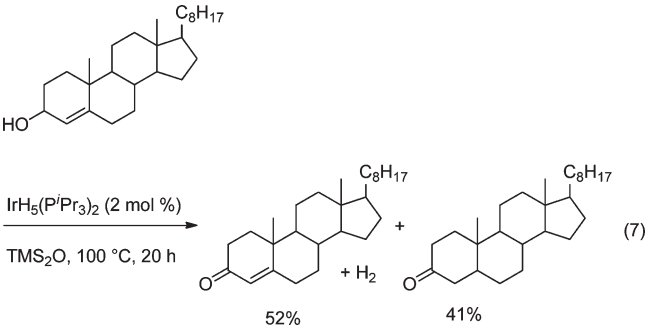


dx.doi.org/10.1021/cr100378r |*Chem. Rev.* 2011, 111, 1825–1845

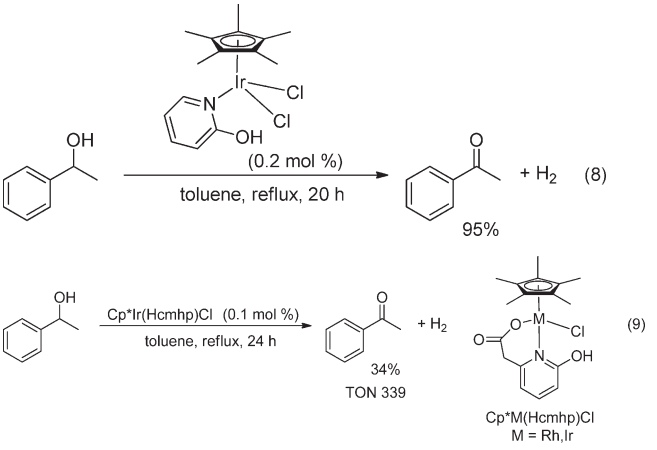
Ison showed that $[Cp^*IrCl_2]_2$ can catalyze the oxidation of secondary alcohols with O_2 as the oxidant (eq 6).[13] The role of Et_3N in the catalytic reaction is to promote β-hydride elimination of the coordinated alcohol and formation of $[(Cp^*IrCl)_2HCl]$. Reaction of $[(Cp^*IrCl)_2HCl]$ with O_2 is the turnover limiting step. The reaction occurs with Ir in a +3 oxidation state throughout the catalytic cycle.



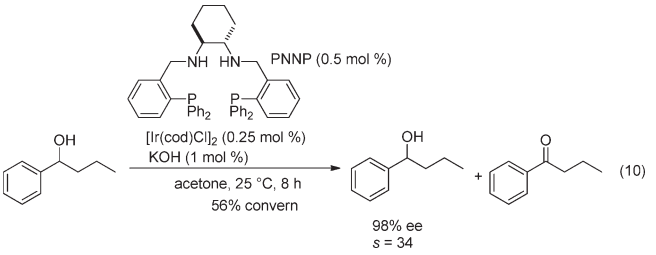
Iridium-catalyzed dehydrogenation without a hydrogen acceptor was reported by Lu in 1987.[14] $IrH_5(P^iPr_3)_2$ was used as the catalyst in hexamethyldisiloxane (TMS_2O) at 100 °C (eq 7). The catalytic turnover number reached 150 for the dehydrogenation of cyclohexanol. Dehydrogenation of an allylic steroidal alcohol gave 52% of the desired unsaturated ketone and 41% of the saturated ketone.



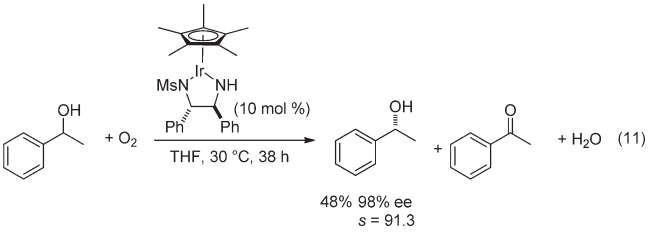
Fujita and Yamaguchi reported that a Cp*Ir catalyst bearing a 2-hydroxypyridine ligand is effective for the dehydrogenation of secondary alcohols (eq 8). A high turnover number (2120) was noted for the reaction run in xylene for 100 h with 0.025 mol % catalyst.[15] Rauchfuss and Wilson reported dehydrogenation of 2-phenylethanol with Cp*Ir(Hcmhp)Cl (eq 9).[16] A 2-hydroxy substituent in the pyridine ring enhances the catalytic reactivity. Although the structure of the corresponding Rh complex was determined by single-crystal X-ray diffraction analysis, the complex is not sufficiently robust thermally.



Oxidative kinetic resolution of secondary alcohols is one approach for obtaining optically active alcohols. Gao found that a chiral diaminodiphosphine (PNNP) Ir complex efficiently catalyzed enantioselective oxidation of racemic secondary alcohols in acetone. In the presence of KOH, oxidative kinetic resolution of the alcohols proceeded smoothly and the best selectivity factor (s = [rate of fast-reacting enantiomer]/[rate of slow-reacting enantiomer]) was up to 34 (eq 10).[17]

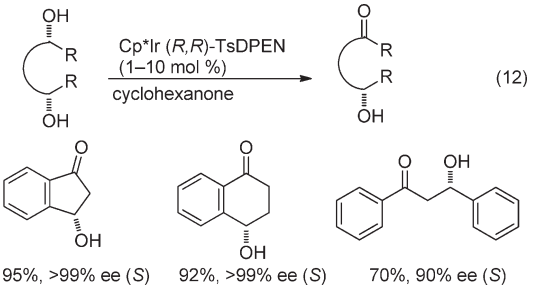


The first aerobic oxidative kinetic resolution of secondary alcohols was reported by Ikariya. Cp*Ir((*S*,*S*)-Msdpen) also showed a high selectivity factor (eq 11).[18] Similarly, the *R* enantiomers with >99% ee and with 46−50% yields were readily obtainable from reactions of 1-indanol and 1-tetralol at ambient temperature.



A mechanistic study of the aerobic oxidation using Cp*IrTsDPEN was carried out by Rauchfuss. His group proposed a catalytic cycle involving regeneration of the 16e catalyst via IrOOH and IrOH intermediates (Scheme 2, path a).[19] Ikariya suggested direct regeneration of the catalyst from IrOOH with H_2O_2 (path b). H_2O_2 reacts with IrH to provide the 16e catalyst and H_2O.[18]

Suzuki reported the oxidative desymmetrization of *meso*-diols using an Ir aminoalkoxide or Cp*IrTsDPEN catalyst (eq 12).[20] High yields and selectivities were achieved using cyclohexanone as an oxidant. In particular, the reaction is effective for the cyclic diols to give the corresponding hydroxy ketones with >99% ee.



This oxidative desymmetrization reaction was applied to the synthesis of otteliones, compounds that exhibit antitumor activity (Scheme 3).[20b] In the absence of base, low conversion to the desired compound was observed.

2.2. Oxidation of Primary Alcohols to Aldehydes

Selective oxidation of primary alcohols to aldehydes is one of the fundamental reactions in organic synthesis. Jensen's iridium PCP

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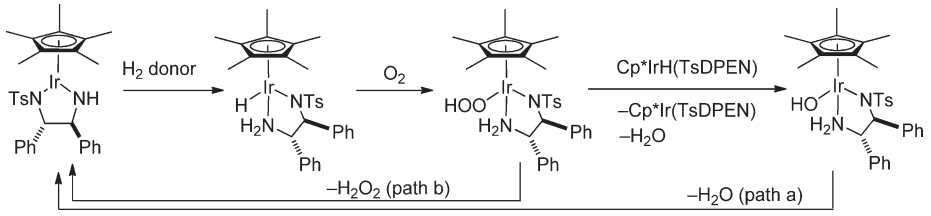
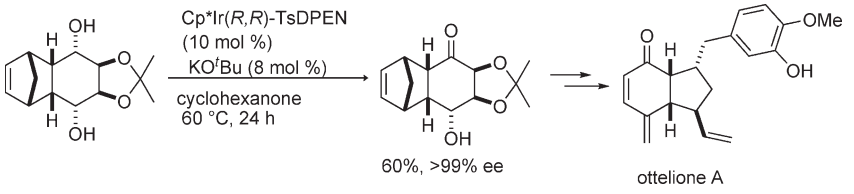
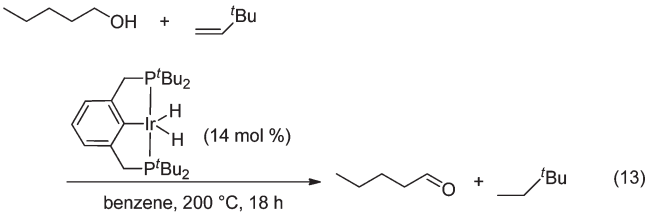
Scheme 2



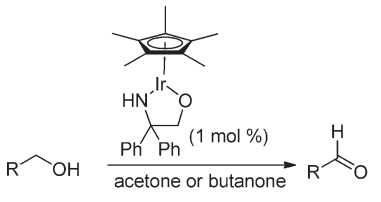
Scheme 3



pincer complex converts aliphatic primary alcohols and benzylic alcohols to the corresponding aldehydes in the presence of *tert*-butylethylene as the oxidant (eq 13).[11] The reaction of methanol, however, gave the carbonyl complex $Ir(CO)[C_6H_3\text{-}2,6\text{-}(CH_2P^tBu_2)_2]$.

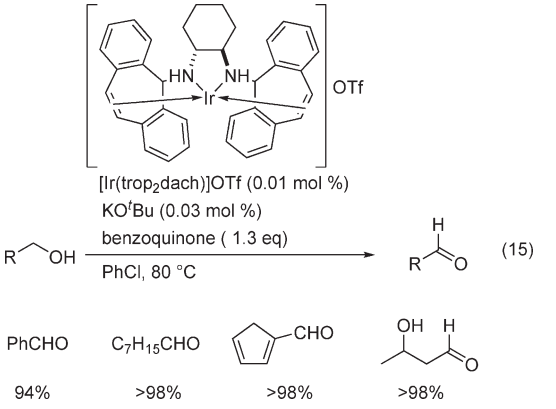


Fujita and Yamaguchi reported for the first time an Oppenauer-type oxidation of primary alcohols using $[Cp^*IrCl_2]_2$ and K_2CO_3.[8a] The use of $[Cp^*Ir(NHC)(MeCN)_2][OTf]_2$ or an Ir NHC complex bearing functionalized Cp* ligands gave high turnover numbers for benzyl alcohol.[8b,d] Suzuki reported the Oppenauer-type oxidation of primary alcohols using an Ir aminoalkoxide complex (eq 14).[21] Reaction of alcohols bearing an easily oxidizable sulfide substituent proceeded with no problem. Reaction of cinnamyl alcohol gave cinnamaldehyde without formation of any saturated aldehyde. When these Oppenauer-type reactions were carried out with acetone or butanone as the oxidant, however, low yields of aliphatic primary alcohols were obtained due to the lower oxidation potential of the oxidants.

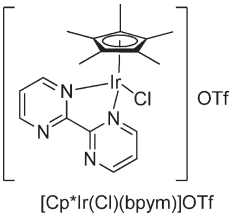


alcohol	yield
p-$MeOC_6H_4CH_2OH$	91%
p-$MeSC_6H_4CH_2OH$	81%
(*E*)-PhCH=$CHCH_2OH$	72%

Grützmacher developed a process for the selective oxidation of primary alcohols using an iridium amido complex with 1,4-benzoquinone as the oxidant (eq 15).[22a,b] Oxidation of aliphatic, aromatic, and allylic alcohols proceeds with 0.01 mol % catalyst. Moreover, selective oxidation of 1,3-butanediol gives 3-hydroxybutanal exclusively. An iridium aminyl radical species plays an important role in the proposed mechanism.



Gabrielsson reported the first aerobic oxidation of alcohols using an iridium catalyst in 2006.[23] $[Cp^*Ir(Cl)(bpym)]OTf$ catalyzed the oxidation of benzyl alcohol containing aq. Na_2CO_3 at 70 °C in a vial open to air with an observed turnover number of 70. Ison reported a mechanistic study of the aerobic oxidation of primary alcohols using $[Cp^*IrCl_2]_2$ (5−10 mol % as Ir) with 20 mol % NEt_3.[13] Benzyl alcohol derivatives are oxidized at 80 °C. A dimeric $[(Cp^*IrCl)_2(\mu HCl)]$ complex was suggested to be a key intermediate.



2.3. Oxidation of Primary Alcohols to Esters

For the synthesis of dimeric esters, oxidative dimerization is an important method, as is the Tishchenko reaction of aldehydes.

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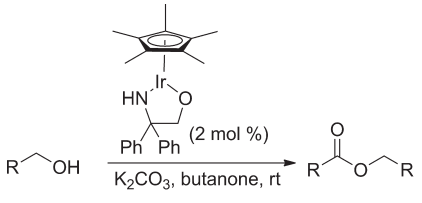
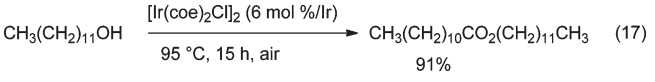
Suzuki developed the mild oxidative dimerization of alcohols using an iridium aminoalkoxide catalyst.[24] Dimerization of aliphatic or benzylic primary alcohols proceeds at room temperature with 2 mol % catalyst using butanone as an oxidant in the presence of K_2CO_3 (eq 16).



(16)

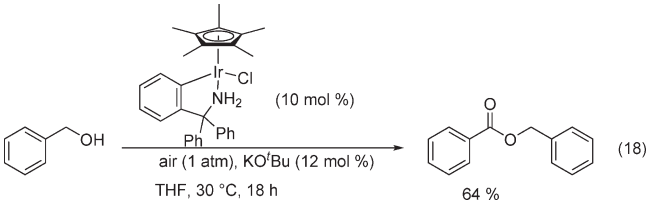
alcohol	yield
$Ph(CH_2)_3OH$	89%
p-$MeSC_6H_4CH_2OH$	87%
$PhCH_2OH$	93%

Aerobic oxidative dimerization using $[IrCl(coe)_2]_2$ at 95 °C was reported by Ishii (eq 17).[25] This is the first successful Ir-catalyzed oxidative dimerization of primary alcohols to esters using air as an oxidant. Aliphatic primary alcohols can be converted to the corresponding dimeric esters without the need for any base or solvent.



(17)

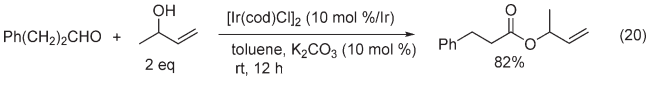
Ikariya reported the mild aerobic oxidative dimerization of primary benzylic or aliphatic alcohols with bifunctional Ir catalysts bearing C−N chelating ligands (eq 18).[12] KO^{t}Bu is required for not only generation of the Ir amido complex but also intermediate formation of the hemiacetal. In the oxidation of aliphatic alcohols, esters were produced in moderate yields and with good selectivities.



(18)

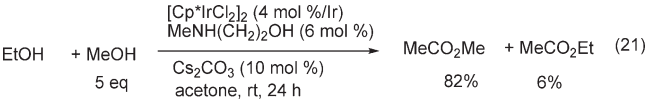
Kiyooka reported oxidative esterification of aldehydes with alcohols using an $[Ir(cod)Cl]_2$ catalyst (eq 19).[26] The oxidative esterifications are accompanied by formation of the reduction product of the aldehyde. However, the reaction with secondary allylic alcohols proceeds in high yield (eq 20).

(19)



(20)

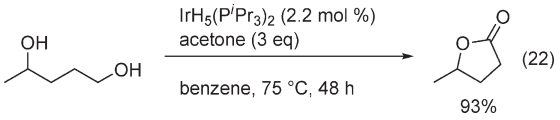
Ishii reported the ethyl and methyl esterification of ethanol using an iridium aminoalcohol complex with acetone as oxidant.[27] The methyl ester was preferentially obtained in 82% yield (eq 21). This is the first Ir-catalyzed direct route to ethyl and methyl acetates from ethanol.



(21)

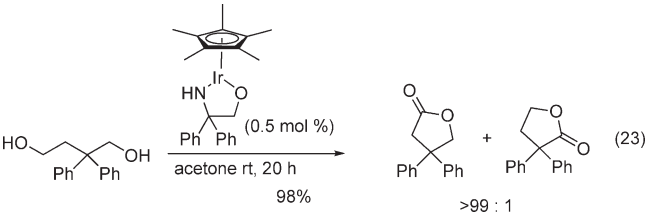
2.4. Oxidation of Diols to Lactones

Lin reported the oxidative lactonization of 1,4- and 1,5-diols using $IrH_5(P\text{-}iPr_3)_2$ with acetone as the oxidant.[28] Selective oxidation proceeds with 1,4-pentanediol to give γ-valerolactone in 93% yield (eq 22). This indicates that the primary hydroxy group was dehydrogenated in preference to the secondary hydroxy group. Oxidative lactonization without a hydrogen acceptor was observed for 1,4- butanediol to give γ-butyrolactone in 54% yield.



(22)

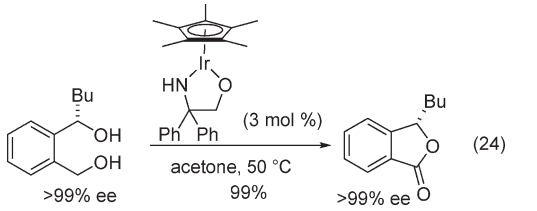
Suzuki developed a mild oxidative lactonization using a Cp*Ir aminoalkoxide catalyst with acetone as the oxidant.[29] The reaction proceeds in high yield with high functional group tolerance. The oxidation of unsymmetrical diols occurs at the less hindered hydroxy group (eq 23). The same catalyst was used for the synthesis of isocoumarin via the oxidative lactonization of *o*-acetonyl benzaldehyde and for the synthesis of a pheromone of *Biprorulus bibax*.[29b,c]



(23)

Galano synthesized isoprostane employing the selective oxidation reaction using a Cp*Ir aminoalkoxide catalyst (Scheme 4).[30] The same reaction using PDC or IBX (1.2 equiv) only provides the inseparable lactones in a 1:1 ratio.

Harada succeeded in the synthesis of enantiopure phthalides from optically pure diols (eq 24).[31] The oxidative lactonization using Cp*Ir aminoalkoxide proceeds without racemization. Even 3-(4-methoxyphenyl)phthalide is also obtained in 80% yield with an enantiopure form.



(24)

Grützmacher developed a highly active oxidative lactonization of primary alcohols using an iridium amido complex with 1,4-benzoquinone as the oxidant (eq 25).[22b] The oxidation of

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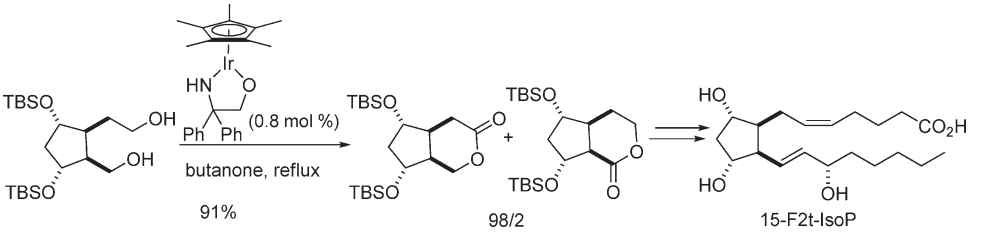
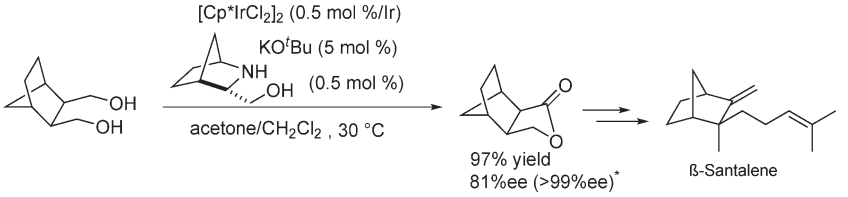
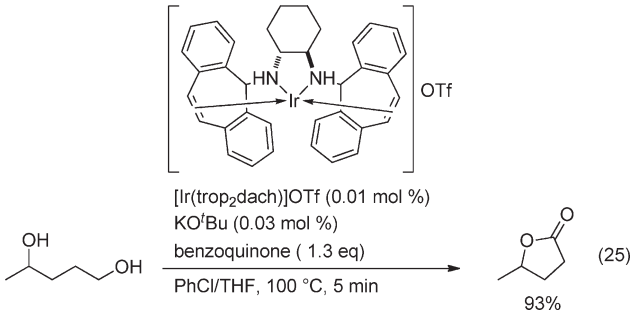
Scheme 4



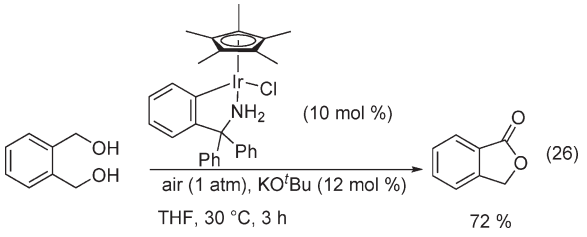
Scheme 5



1,4-pentanediol or *cis*-1,2-bis(hydroxymethyl)cyclohexane proceeds with 0.01 mol % catalyst.



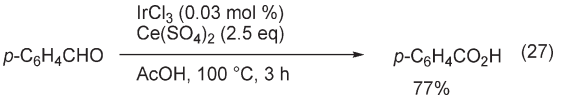
Ikariya reported the mild aerobic oxidative lactonization with bifunctional Ir catalysts bearing C−N chelating ligands (eq 26).[12] The oxidation of 1,2-benzenedimethanol afforded phthalide in 72% yield.



Suzuki developed the asymmetric oxidative lactonizations using the Ir complexes prepared from a chiral aminoalcohols to give 81% ee of the lactone that is an intermediate of β-santalene (Scheme 5).[32] Optically pure lactone was obtained after a single recrystallization.

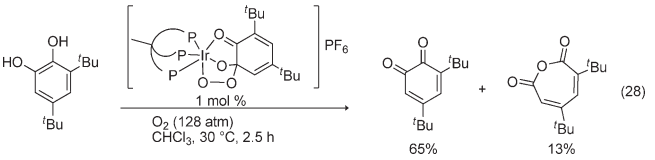
2.5. Oxidation of Secondary Alcohols or Carbonyl Compounds to Carboxylic Acids

Oxidation of acyclic ketones and aldehydes by Ce(IV) gives carboxylic acids in the presence of $IrCl_3$ as catalyst (eq 27).[33] Oxidation of glycols by $K_3Fe(CN)_6$ or sugars by KIO_3 yields the corresponding carboxylic acids with the $IrCl_3$ catalyst.[34]

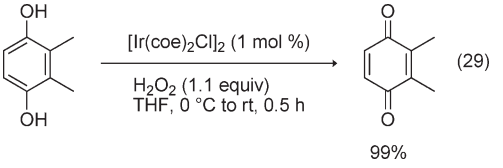


3. OXIDATION OF PHENOLS AND ETHERS

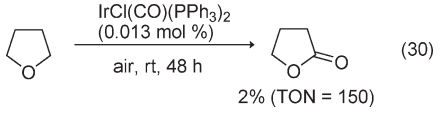
Bianchini reported aerobic oxidation of 3,5-di-*tert*-butylcatechol to the corresponding benzoquinone catalyzed by an Ir catecholate complex bearing a triphos ligand (eq 28).[35] Muconic acid anhydrides are also produced at higher O_2 pressure.



Iwasa reported the oxidation of catechol or hydroquinone with hydrogen peroxide using Ir complexes (eq 29).[36] $[Ir(coe)_2Cl]_2$ is more reactive than $[Ir(cod)Cl]_2$. Although the Ru complex is more active for the above reaction and is applicable for the methoxybenzene derivatives, the Ir complex is not effective for them.



Shi reported that γ-butyrolactone was formed along with a trace amount of lactol and 4-hydroxybutyraldehyde when stirring a THF solution of Vaska's complex under an aerobic atmosphere (eq 30).[37] The corresponding Rh complex showed 94 of TON (turnover numbers) in the same reaction.



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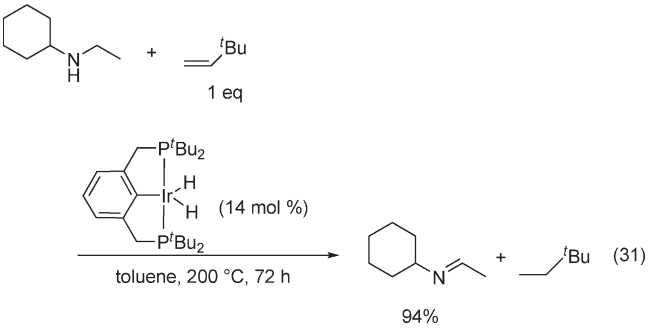
4. OXIDATION OF NITROGEN AND PHOSPHORUS COMPOUNDS

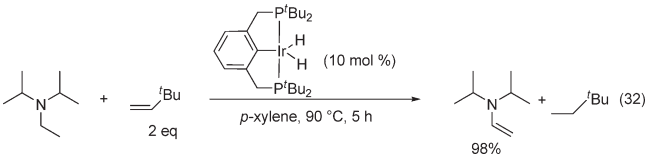
4.1. Oxidation of Amines

Jensen reported the dehydrogenation of secondary amines to imines catalyzed by the iridium PCP pincer complex (eq 31).[38] Greater than 99% regioselectivity was observed in the dehydrogenation of the asymmetric substrates cyclohexylethylamine and benzylpropyl amine, which underwent dehydrogenation to *N*-ethylidenecyclohexylamine and *N*-benzylidenepropylamine, respectively.



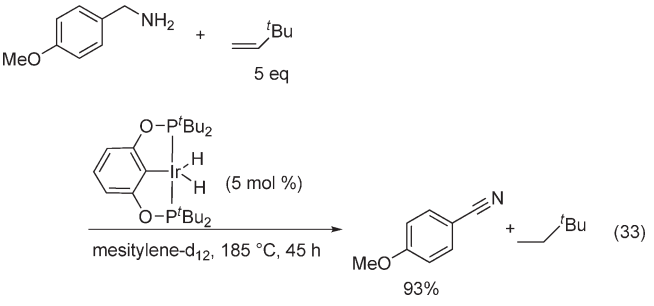
(31)

Knapp and Goldman reported the dehydrogenation of tertiary amines catalyzed by the same Ir PCP complex to give enamines.[39] *N*,*N*-Diisopropylvinylamine was selectively formed from the corresponding amine (eq 32). The use of an excess amount of *tert*-butyl ethylene caused formation of the didehydrogenated product. *N*,*N*-Divinylethylamine (25%) is obtained in addition to *N*,*N*-diethylvinylamine (54%) in the reaction of triethylamine.



(32)

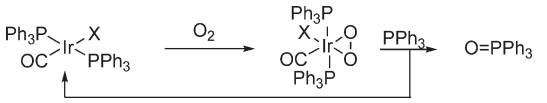
Brookhart reported the dehydrogenation of primary amines using $[C_6H_3\text{-}2,6\text{-}(OP^tBu_2)_2]IrH_2$ (eq 33).[40] Isobutylamine and several benzylamines can be converted to the corresponding nitriles. The mechanism of amine dehydrogenation is proposed to proceed from an iridium(I) nitrile complex, the catalyst resting state, via two preturnover-limiting equilibria, followed by a slow β-hydride elimination event from a transient iridium(III) amido hydride species.



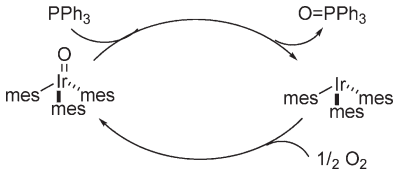
(33)

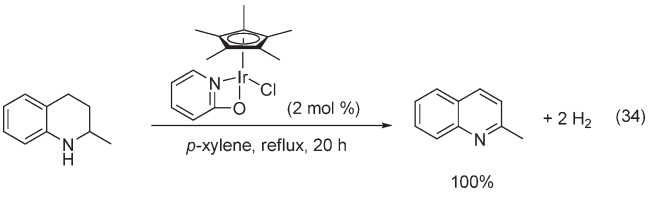
Yamaguchi and Fujita reported dehydrogenation of tetrahydroquinolines using a Cp*Ir complex prepared from 2-hydroxypyridine (eq 34).[41] The reaction proceeds without a hydrogen acceptor. The reverse reaction, i.e., hydrogenation of quinoline to tetrahydroquinoline, also proceeded under hydrogen (1 atm) in the presence of the same catalyst at 110 °C in *p*-xylene in quantitative yield.

Scheme 6



Scheme 7





(34)

4.2. Oxidation of Phosphines

Oxidation of triphenylphosphine using Vaska's complex with O_2 was studied by Teranishi in early 1970.[62] An Ir−O_2 complex[42] was suggested as the active species (Scheme 6).

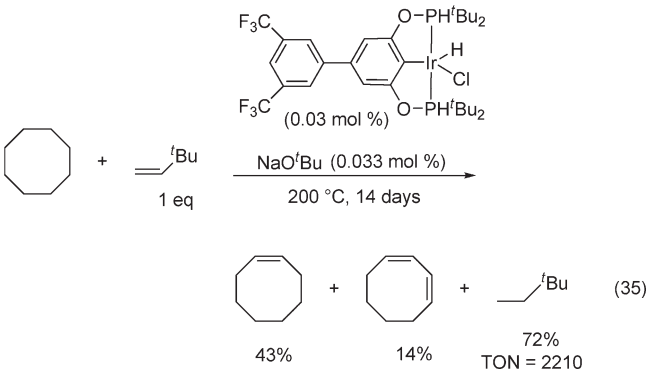
Trimesityliridium(III) (mesityl =2,4,6-trimethylphenyl) catalyzes the oxidation of triphenylphosphine and triphenylarsine (Scheme 7).[43] The reaction proceeds at room temperature and atmospheric pressure with an overall activity of ~60 turnovers/h. Aerobic oxidation by oxotrimesityliridium(V) was proposed by Brown. Triphenylarsine is also oxidized, though over an order of magnitude more slowly.

5. OXIDATION OF ALKANES, ALKENES, AND AROMATIC COMPOUNDS

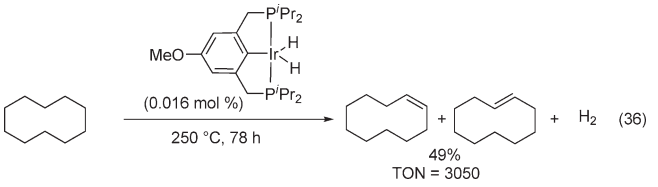
5.1. Oxidation of Alkanes

The dehydrogenation of alkanes is one of the significant goals in the field of homogeneous catalysis. Crabtree first reported in 1979 the stoichiometric dehydrogenation of alkanes using $[IrH_2(acetone)_2(PPh_3)_2]BF_4$ with tbe as the hydrogen acceptor.[44] Later, thermal and photochemical catalytic dehydrogenation of alkanes were developed, but turnover numbers were limited by catalyst decomposition.[45] A key breakthrough was achieved by Kaska and Jensen with the robust pincer-ligated iridium complex $(^tBu_4PCP)IrH_2$, which catalyzes the transfer dehydrogenation of cyclooctane to cyclooctene at a rate of 12 turnovers per min.[46] The PCP complex catalyzes transfer dehydrogenation of ethylbenzene,[47] tetrahydrofuran,[47] *n*-alkanes,[48] and polyofefins.[49] Transfer dehydrogenation of cyclohexane and decalins gave benzene and naphthalenes, respectively.[50] Brookhart found that *p*-XPCP pincer complexes exhibited high catalytic activity for transfer dehydrogenation (eq 35).[51] Koridze developed an Ir PCP complex based on ferrocene that shows a high turnover number (3300) for the transfer dehydrogenation of cyclooctane.[52]

dx.doi.org/10.1021/cr100378r |*Chem. Rev.* 2011, 111, 1825–1845



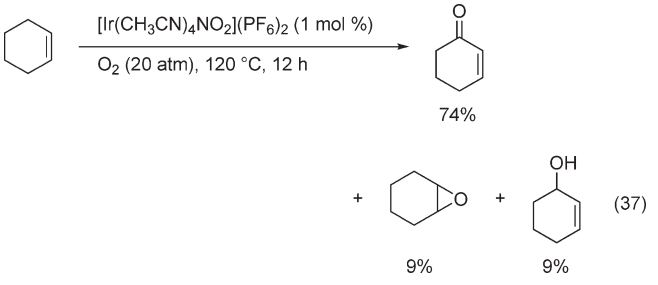
Jensen and Goldman first found that the robust Ir PCP complex catalyzes the dehydrogenation of cycloalkanes under reflux without the need for a hydrogen acceptor.[53] Several Ir PCP complexes[54] or Ir CCC-pincer *N*-heterocyclic carbine complexes[55] have been synthesized for acceptorless dehydrogenation. A high turnover number of 3050 was obtained for the dehydrogenation of cyclodecane by Krogh-Jespersen and Goldman (eq 36).[54c]



Oxidation of cyclohexane by Ce(IV) sulfate catalyzed by $IrCl_3$ at 100 °C was found to give a 44% yield of cyclohexanone.[56] The electrooxidation of cyclohexane to cyclohexanone using Ir(acac)$_3$ supported on a carbon fiber anode was reported by Yamanaka.[57]

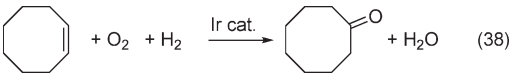
5.2. Oxidation of Alkenes

Allylic oxidation is a fundamental transformation in organic synthesis. In 1967, Collman first reported that the allylic oxidation of cyclohexene catalyzed by $IrI(CO)(PPh_3)_2$ under oxygen (1−2.5 atm) gave cyclohexenone.[58] This process was found to occur via the radical autoxidation of cyclohexene by low oxidation state phosphine complexes.[59]An iridium nitro complex also catalyzes the oxidation of cyclohexene to give cyclohexenone as a major product (eq 37). Severe reaction conditions are required for high conversion though.[60] Polyoxoanion-supported Ir complexes were also investigated for oxidation reactions by Finke.[61]

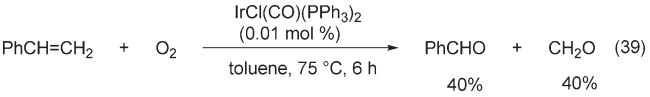


Epoxides are important synthetic intermediates for organic synthesis. In early studies of the oxidation of cyclohexene and styrene by Collman and Takao, epoxides were obtained as minor products.[58,62] Lyons reported that the oxidation of tetramethylethylene with $IrCl(CO)(PPh_3)_2$ gives 2,3-dimethyl-2,3-epoxybutane and 2,3-dimethyl-3-hydroxy-1-butene.[63] The reaction initiates autoxidation of the olefin to form an allylic hydroperoxide, and the subsequent epoxidation step is catalyzed by $IrCl(CO)(PPh_3)_2$. The iridium nitro complex $[Ir(CH_3CN)_5(NO_2)](PF_6)_2$ catalyzes the epoxidation of 1-hexene selectively but with low conversion.[60]

James reported that $[IrHCl_2(cod)]_2$ and $[Ir(cod)Cl]_2$ with hydrogen chloride catalyze the oxidation of cyclooctene to cyclooctanone and water using oxygen and hydrogen mixtures (eq 38).[64]



Olefin cleavage was observed by Takao in 1970 in the oxidation of styrene with $IrCl_3$ or $IrClCO(PPh_3)_2$ under O_2 bubbling.[62] Lyons reported that the initial step in styrene oxidation is radical-initiated autoxidation; a 40% yield of benzaldehyde and formaldehyde was obtained with 0.01 mol % $IrCl(CO)(PPh_3)_2$ (eq 39).[65]



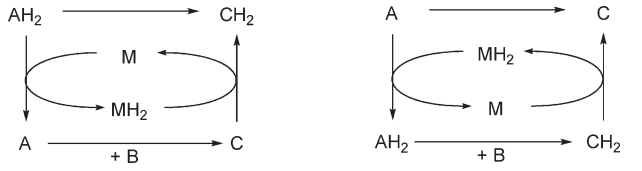
5.3. Oxidation of Aromatic Compounds

Oxidation of anthracene to anthraquinone catalyzed by $IrCl(CO)(PPh_3)_2$ with *tert*-butylhydroperoxide proceeds in 15% yield. The same reaction is efficiently promoted by $RhCl(PPh_3)_3$ in 96% yield.[66] Oxidation of naphthalene by cerium sulfate in the presence of $IrCl_3$ catalyst provides α-naphthol in 34% yield.[67] The same catalyst system oxidizes *p*-cresol to *p*-hydroxybenzaldehyde in 96% yield.

6. TANDEM REACTIONS

Tandem reactions are a very attractive strategy since they involve multistep transformations that allow for a rapid increase in molecular complexity from readily available starting compounds. In particular, 'borrowing hydrogen methodology'[68] or 'hydrogen autotransfer processes'[69] is an example of an attractive method for synthesizing complex molecules.[70] In this reaction substrate is activated by the redox process and the activated substrate leads to the next reaction and the final product was produced by the redox process. Thus, it is a totally redox-neutral process. This method can be classified into two types based on the order of the redox steps (Scheme 8). The first begins with oxidative activation followed by reaction with component B, with resulting intermediate C reduced to the final product. The second type involves an initial reductive activation followed by reaction with component B and final oxidation of intermediate C to yield the desired product.

Scheme 8



6.1. Synthesis of Esters, Lactones, and Amides

Williams reported the synthesis of homologated esters from alcohols (Scheme 9).[71] The alcohol is first oxidized to the

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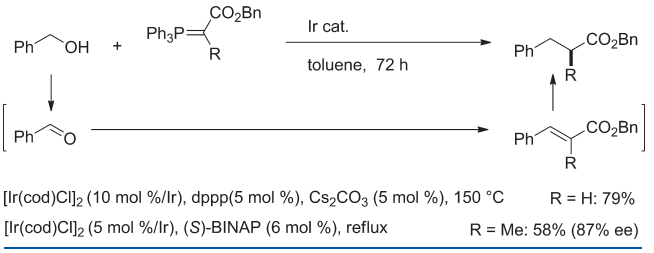
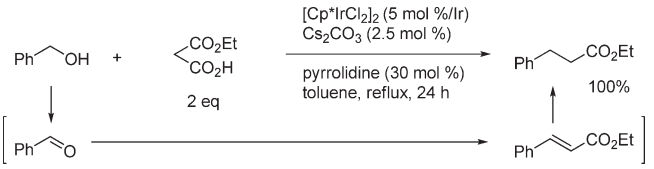
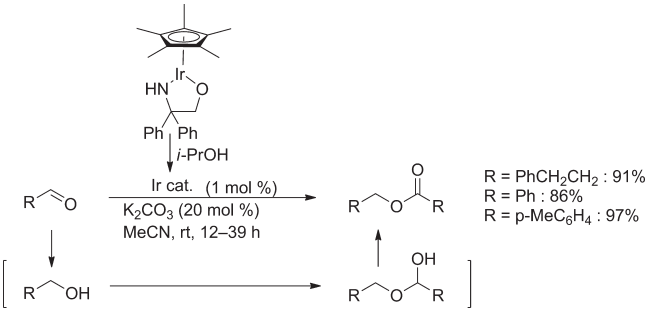
Scheme 9



Scheme 10



Scheme 11



aldehyde, which is then converted to the unsaturated ester via Wittig olefination. Reduction of the alkene yields the final homologated ester. 2-Substituted propanoate was successfully obtained with 87% ee in the presence of (*S*)-BINAP. Combination with the Hornor−Wadsworth−Emmons reaction gave moderate yields.[72]

Homologated esters can also be synthesized by combining the reaction with the decarboxylative Knoevenagel reaction (Scheme 10).[73] Pyrrolidine was used as the organocatalyst for the decarboxylative Knoevenagel reaction. The catalyst loading is reduced to 2.5 mol % by using Ru $(PPh_3)_3Cl_2$.

Suzuki reported a mild Tishchenko-type reaction using an iridium aminoalkoxide catalyst (Scheme 11).[74] Both aliphatic and aromatic aldehydes could be converted to the corresponding dimeric esters in high yields. In the presence of Ir hydride catalyst, the aldehyde is reductively activated to the alcohol, which reacts with another aldehyde to produce a hemiacetal, which in turn is oxidized to the final dimeric ester.

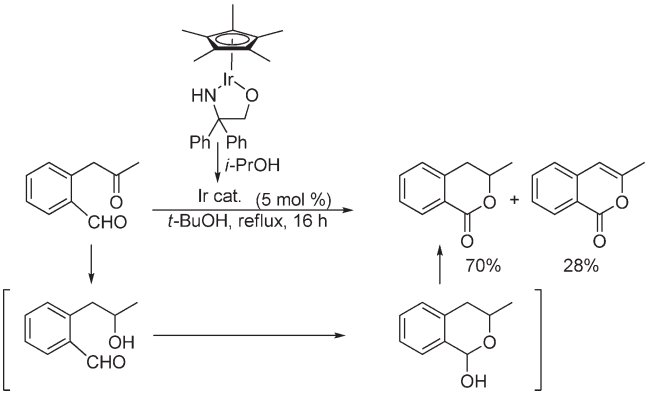
Similarly, intramolecular Tishchenko-type reactions of δ-ketoaldehydes give 3,4-dihydroisocoumarins in 70% yield (Scheme 12).[29b] Isocoumarin was also obtained in 28% yield under the conditions, although no extra cooxidant was added to the reaction mixture.

Williams reported the one-pot synthesis of amides from alcohols (Scheme 13).[75] This synthesis does not involve the borrowing hydrogen methodology but consists of Ir-catalyzed oxidation, oxime formation, and Ir-catalyzed rearrangement.

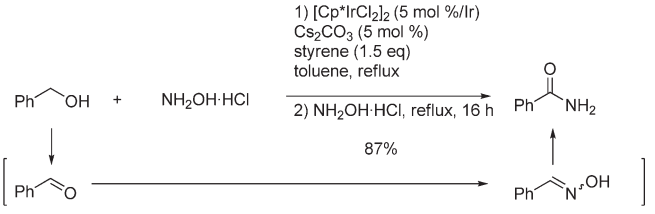
6.2. Alkylation of Ketones, Nitriles, Nitro Compounds, and Esters

Ishii reported direct α-alkylation of ketones with primary alcohols catalyzed by an $[Ir(cod)Cl]_2/PPh_3/KOH$ system

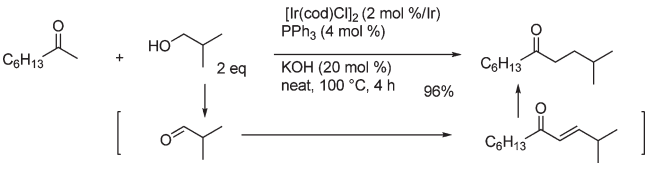
Scheme 12



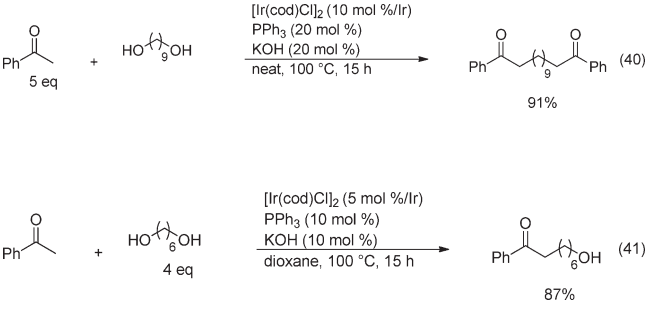
Scheme 13



Scheme 14



without solvent (Scheme 14).[76] After initial oxidation of the primary alcohol, base-catalyzed aldol condensation takes place with complete regioselectivity at the less hindered side of the ketone. Selective hydrogenation of the α,β-unsaturated ketones by an iridium dihydride complex leads to the α-alkylated ketones. The reaction of methyl ketone and α,ω-diols can be utilized for the synthesis of diketones or ω-hydroxy ketones (eqs 40 and 41).[77]



This reaction was applied by Nishibayashi to the synthesis of optically active alcohols in a one-pot process (Scheme 15).[78] Iridium complex, PPh_3, and KOH did not interfere with the final reduction step of the ketone intermediate. The iridium

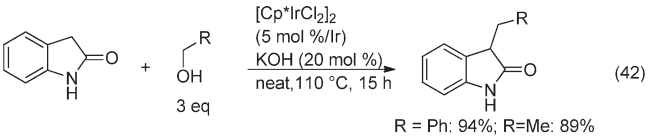
dx.doi.org/10.1021/cr100378r |*Chem. Rev.* 2011, 111, 1825–1845

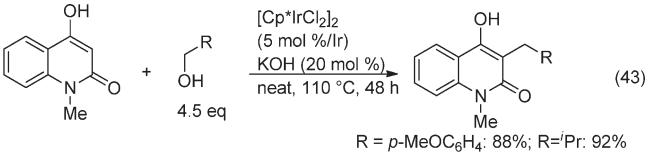
and ruthenium complexes play their roles independently in each step.

Grigg reported the solvent-free selective alkylation of arylacetonitriles with alcohols catalyzed by $[Cp^*IrCl_2]_2$ (Scheme 16).[79] The reaction is selective for the monoalkylated product, as in the second Knoevenagel condensation there is no α proton to the OH group to be eliminated as water. The reaction time can be reduced with microwave heating.

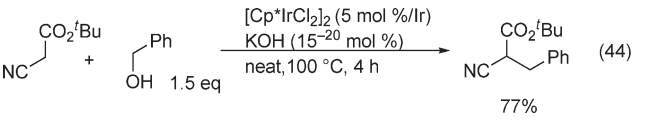
Williams investigated the alkylation of nitroalkanes, β-diketones, malonate esters, and α-cyanoketones, achieving moderate yields (Scheme 17).[72] The high temperature required for the crossover transfer hydrogenation process is almost certainly responsible for the lack of selectivity.

Grigg reported the one-pot bisalkylation of 1,3-dimethylbarbituric acid sequentially using iridium and palladium catalysts (Scheme 18)[80] Oxidation of the alcohol is first catalyzed by iridium, followed by Pd-catalyzed three-component coupling. Alkylation of oxindole with various alcohols under solvent-free thermal or microwave conditions afforded the corresponding C-3-monoalkylated products in high yield (eq 42).[81] In a similar manner, 4-hydroxy-quinolones, coumarin, and 4-(1*H*)-quinolone were successfully *C*-alkylated with a range of substituted benzyl and aliphatic alcohols (eq 43).[82]





Ishii reported the alkylation of α-cyanoesters with alcohols catalyzed by an iridium phosphine complex (Scheme 19).[83] This system functions without added base to give the corresponding saturated α-alkylated products in good yields. Grigg reported alkylation of *tert*-butyl cyanoacetate using $[Cp^*IrCl_2]_2$ under solvent-free conditions (eq 44).[84] Extended reaction time leads to some product degradation via hydrolysis and decarboxylation.

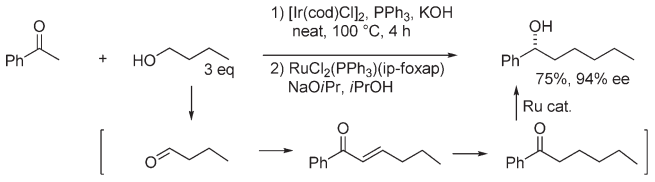


Alkylation of acetates with primary alcohols has also been reported by Ishii (Scheme 20).[85] This alkylation is influenced by the base employed. No alkylation is induced by KOH, which is the efficient additive for the alkylation of ketones. Notably, alkylation with secondary alcohols such as 2-butanol do not occur under these conditions.

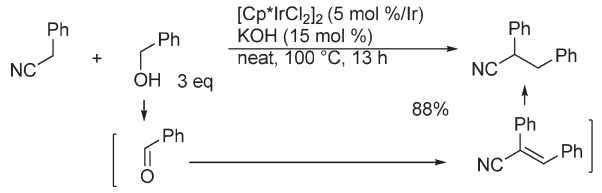
6.3. Synthesis of Alcohols

Fujita and Yamaguchi reported direct β-alkylation of secondary alcohols with primary alcohols catalyzed by a Cp*Ir complex (Scheme 21).[86] The reaction involves the oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones followed by cross-aldol condensation between them. Successive transfer hydrogenations of the C═C and C═O

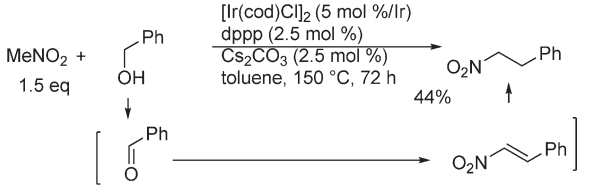
Scheme 15



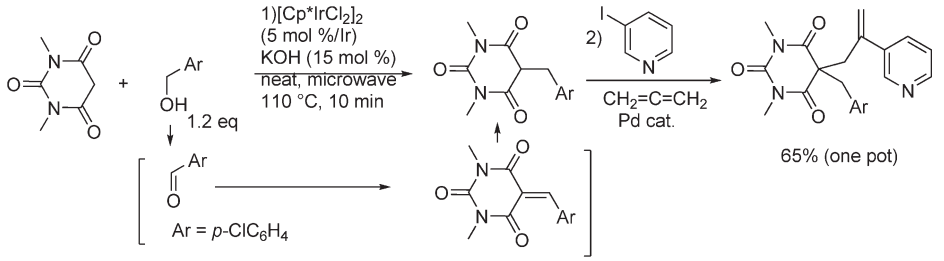
Scheme 16



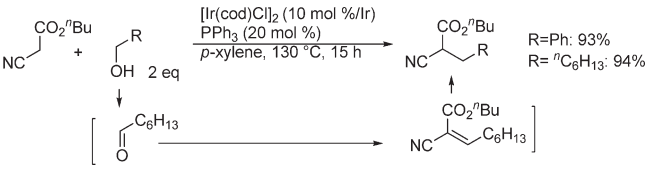
Scheme 17



Scheme 18

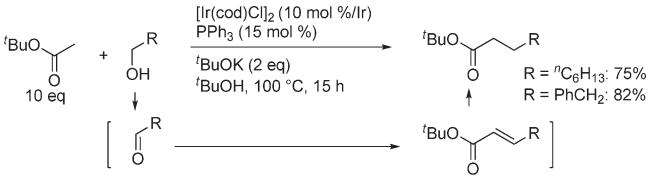


Scheme 19

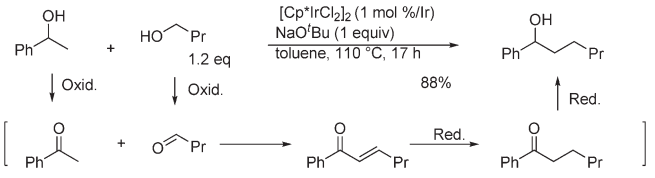


dx.doi.org/10.1021/cr100378r |*Chem. Rev.* 2011, 111, 1825–1845

Scheme 20



Scheme 21



double bonds of the intermediate α,β-unsaturated ketone lead to the final product.

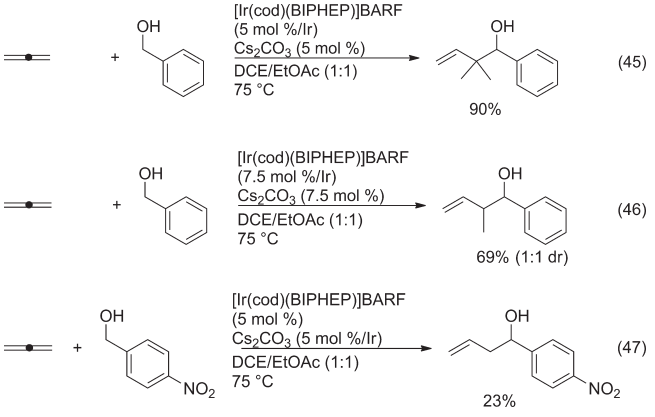
Tejeda, Peris, and Royo studied the β-alkylation of secondary alcohols with a Cp*-functionalized *N*-heterocyclic carbene Ir complex,[87] and Crabtree investigated similar reactions with chelating NHC complexes[88] and an Ir terpyridine complex[89] (Table 3). The Ir terpyridine complex can operate effectively under neat conditions.

Ishii reported the Guerbet reaction of primary alcohols catalyzed by $[Ir(cod)Cl]_2$ and $[Cp^*IrCl_2]_2$ (Scheme 22).[90] The Guerbet reaction of ethanol also proceeds in the presence of a catalytic amount of [Ir(acac)(cod)], 1,7-octadiene, and NaOEt to give *n*-butanol.[91] A turnover number of 1220 was obtained.

6.4. Synthesis of Homoallylic Alcohols and Related Compounds[92]

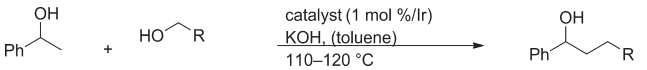
In 2007, Krische developed a new type of autotransfer reaction that involves carbonyl allylation (Scheme 23).[93] His group utilized the metal hydride complex formed in the alcohol dehydrogenation for generation of the allyl metal species.

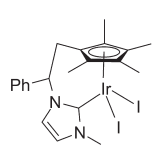
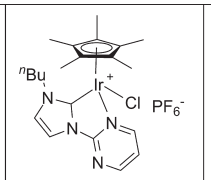
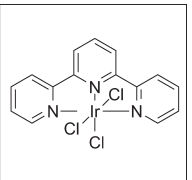
The reaction of alcohols and allenes proceeds in the presence of the [Ir(cod)(BIPHEP)]BARF complex. Prenylation, crotylation, and allylation products were obtained without over reduction of the olefinic substituent (eqs 45−47).



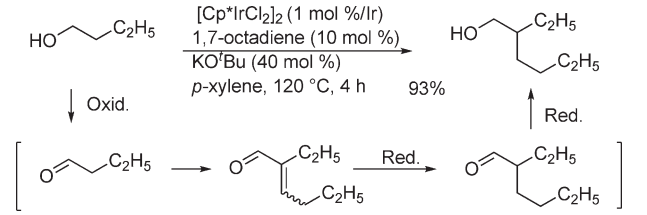
Krische also developed enantioselective carbonyl prenylation from alcohols and 1,1-dimethylallene (eq 48).[94] The Ir complex prepared from allyl acetate, *m*-nitrobenzoic acid, and (*S*)-SEGPHOS shows good to excellent isolated yields and enantioselectivities.

Table 3. Ir-Catalyzed β-Alkylation of Secondary Alcohols with Primary Alcohols

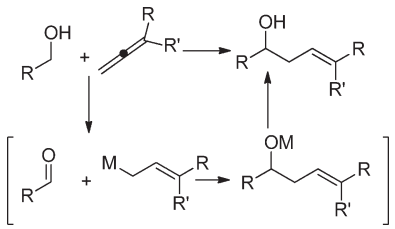


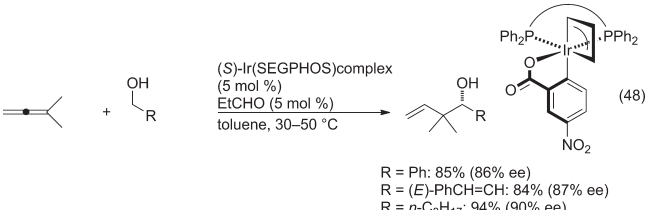
R \ catalyst			
Ph	91	93	95
Pr	80	60	65

Scheme 22

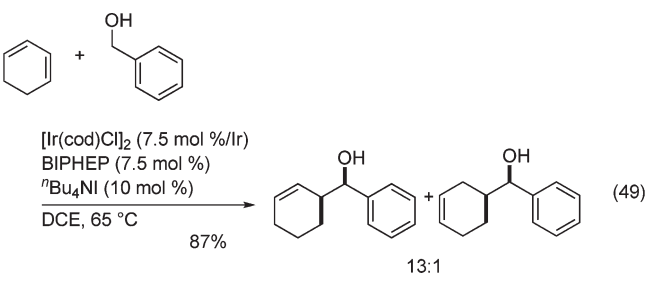


Scheme 23





The reaction of 1,3-cyclohexadiene and primary alcohols also proceeds with an Ir phosphine catalyst (eq 49).[95] Addition of $^nBu_4NI$ has an effect on the diastereoselectivity and suppression of the regioisomeric product.



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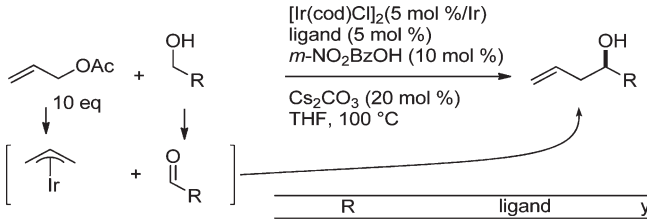
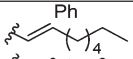
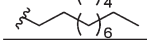
Scheme 24

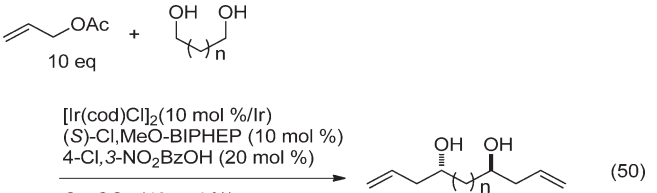


R	ligand	yield (%)	ee (%)
Ph	(*R*)-BINAP	62	93
	(*R*)-Cl,MeO-BIPHEP	72	91
	(*R*)-Cl,MeO-BIPHEP	78	95

Krische found that allyl acetate can be used as an allyl donor for enantioselective carbonyl allylation with alcohols. In contrast to Ir-catalyzed allylic substitution (*O*-alkylation) reactions employing an alcohol nucleophile where an Ir allyl intermediate functions as an electrophile in this system the allyl intermediate acts as a nucleophile.[96] The reaction with allylic alcohols or aliphatic alcohols also gives the allylation products with high ees (Scheme 24).[97] The use of Cs_2CO_3 and *m*-nitrobenzoic acid is effective for both conversion and enantioselection. They suggest that the active catalyst is *ortho*-cyclometalated complex as shown in eq 48.

Thus, the reaction is quite practical. In fact, O'Doherty used this allylation method in the synthesis of (+)-goniothalamin.[98] The allylation is also applicable to furan methanol derivatives.[99] Krische succeeded in the elongation of 1,3-polyols via iterative enantioselective carbonyl allylation (Scheme 25).[101b] High levels of catalyst-directed enantioselectivity and diastereoselectivity were attained.

Reactions with 1,3-, 1,4-, and 1,5-diols give doubly allylated products with high enantio- and diastereoselectivities (eq 50).[100] Thus, 1,*n*-glycols can be used instead of the corresponding unstable dialdehydes. This reaction was useful in the concise synthesis of the bryostatin A-ring.[101a]

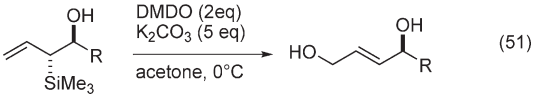


(50)

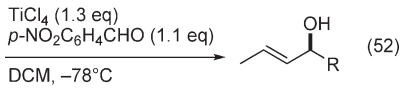
n	yield (%)	ee (%)	d.r.
1	70	>99	>30:1
2	68	>99	>30:1
3	56	>99	>30:1

Krische reported *anti*-diastereo- and enantioselective carbonyl crotylations from alcohols (Scheme 26). A broad range of alcohols can be crotylated with high ee.[102] This method avoids the use of chirally modified crotylmetal reagents or metallic terminal reductants and, consequently, keeps away from generation of stoichiometric metallic byproducts.

The reaction of α-(trimethylsilyl)allyl acetate with alcohols under similar conditions gave (trimethylsilyl)allylation products with high enantioselectivity and *anti*-diastereoselectivity (Scheme 27).[103] The use of K_3PO_4 was effective for suppressing the Peterson olefination. Trimethylsilyl allylated products can be converted to 1,4-ene-diols via DMDO-mediated oxidative elimination (eq 51). Protodesilylation was also achieved using $TiCl_4$ in the presence of exogeneous aldehydes to give allylic alcohols (eq 52).

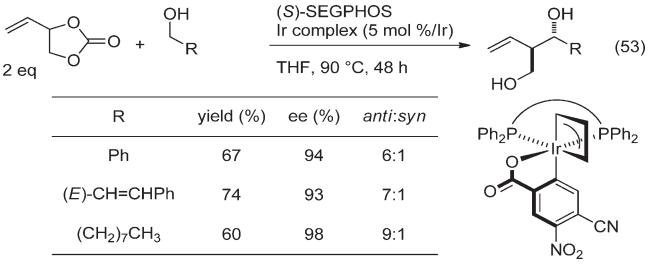


(51)



(52)

The reaction with cyclic carbonates and alcohols produces *anti*-selective (hydroxymethyl)allylation products (eq 53).[104] This method is the first general method for enantioselective carbonyl (hydroxymethyl)allylation. The reaction can be used for a broad range of alcohols.



(53)

R	yield (%)	ee (%)	*anti*:*syn*
Ph	67	94	6:1
(*E*)-CH=CHPh	74	93	7:1
$(CH_2)_7CH_3$	60	98	9:1

Obora and Ishii reported the coupling of 1-aryl-1-propynes with primary alcohols using an $[Ir(cod)OH]_2$ and P(*n*-Oct)$_3$ catalyst system to give homoallylic alcohols (Scheme 28).[105] A (π-allyl)iridium hydride species is proposed as an intermediate. On the other hand, coupling with the $[Ir(cod)Cl]_2$ and P(*n*-Oct)$_3$ catalyst system gives α,β-unsaturated ketones (Scheme 29).[106] The reaction proceeds through the initial formation of homoallylic alcohols followed by dehydrogenation to β,γ-unsaturated ketones and then isomerization.

6.5. Synthesis of Amines and Related Compounds

In 1981, Grigg reported the *N*-alkylation of amines with primary and secondary alcohols in the presence of transition-metal complexes such as Rh, Ir, and Ru (Scheme 30).[107] Iridium-(I), -(III), and -(IV) chloride phosphine catalyst systems catalyze the *N*-alkylation of pyrrolidine.

In 1992, Tanaka reported the *N*-alkylation of azole with alcohols catalyzed by transition-metal complexes (Ru, Rh, Ir).[108] The $IrCl_3$−P(O^{n}Bu)$_3$ catalyst system can catalyze the

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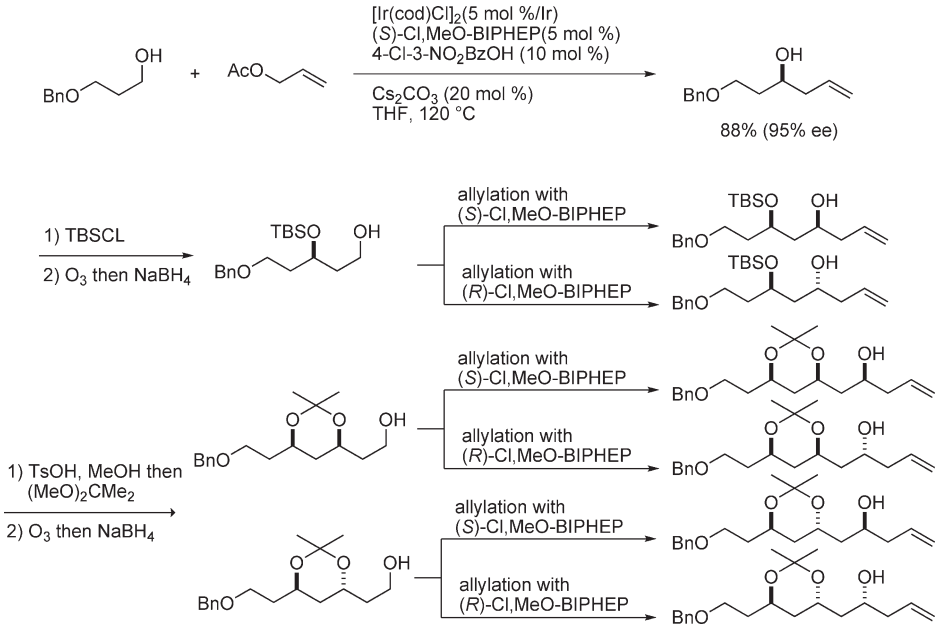
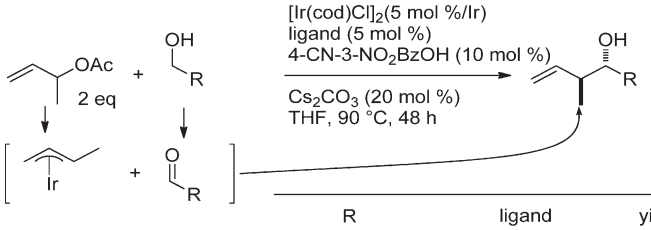
Scheme 25

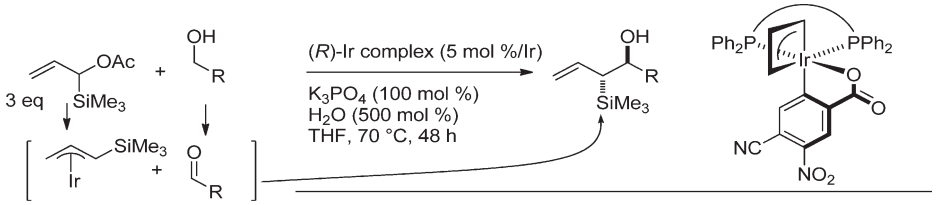


Scheme 26



R	ligand	yield (%)	ee (%)	*anti*:*syn*
Ph	(*S*)-SEGPHOS	65	95	6:1
(*E*)-CH=CHPh	(*S*)-C3-TUNEPHOS	63	90	6:1
$(CH_2)_7CH_3$	(*S*)-SEGPHOS	69	97	7:1

Scheme 27



R	ligand	yield (%)	ee (%)	*anti*:*syn*
Ph	(*R*)-SEGPHOS	69	96	>99:1
(*E*)-CH=CHPh	(*R*)-C3-TUNEPHOS	70	92	>99:1
$(CH_2)_7CH_3$	(*R*)-SEGPHOS	67	95	>99:1

N-methylation of 3,5-dimethlpyrazole by methanol under high-pressure conditions (Scheme 31).

Fujita and Yamaguchi reported that $[Cp^*IrCl_2]_2/K_2CO_3$ or $NaHCO_3$ catalyzes the *N*-alkylation of primary and secondary amines (eqs 54−56).[109] A wide range of secondary and tertiary amines can be synthesized in good yield. The mechanism of this reaction has been studied by Eisenstein using DFT calculations.[110] The involvement of ancillary carbonate

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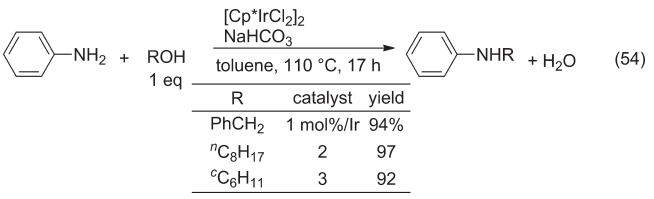
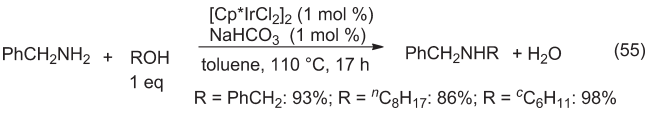
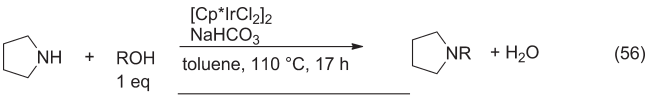
ligands on the Ir for the hydrogen transfer reaction is proposed.



R	catalyst	yield
$PhCH_2$	1 mol%/Ir	94%
$^nC_8H_{17}$	2	97
$^cC_6H_{11}$	3	92





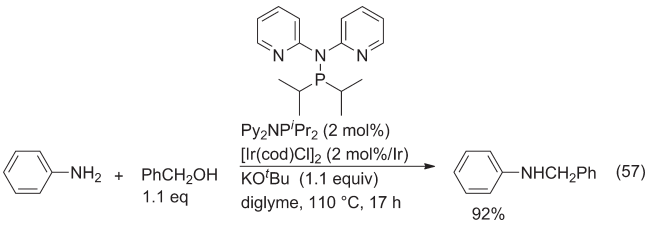
R	catalyst	yield
$PhCH_2$	1mol%/Ir	92%
$^nC_8H_{17}$	2	96
$^cC_6H_{11}$	5	88

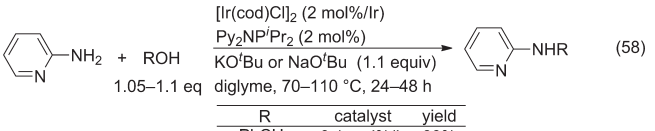
Williams reported the *N*-alkylation of amines with alcohols in water in the absence of base using $[Cp^*IrI_2]_2$.[111] The reaction has also been investigated in an ionic liquid using $[Cp^*IrI_2]_2$.[112]

N-Alkylations of aniline or primary amines with alcohols using NHC−iridium complexes have also been examined by several groups.[87,88,113] The catalyst system consisting of $[Cp^*IrCl_2(NH\text{-}C)]$ and AgOTf promotes *N*-alkylation in the absence of base.[113a]

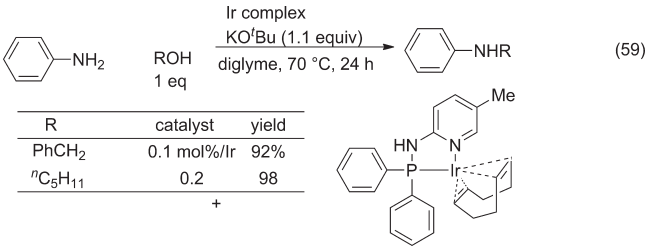
Williams reported that *N*-alkylation of phenylethylamine and tryptamine with alcohols proceeds with the $[Ir(cod)Cl]_2$−dppf catalyst system.[114] The conversion of alcohols into *N*-alkylamines via aza-Wittig reactions using $Ph_3P{=}NPh$ and $[Ir(cod)Cl]_2$−dppf catalyst system has also been reported by the same author.[115]

Kempe developed the $[Ir(cod)Cl]_2$−Py_2NP^iPr catalyst system, which shows high activity for the selective monoalkylation of anilines with primary alcohols (eq 57).[116] The reaction of aliphatic amines such as benzylamine, *n*-butylamine, and cyclohexylamine with benzylalcohol barely proceeded, however. This catalyst system works well, though, for aminopyridines, and aminoalcohols can be used as the aminoalkyl source to give mono-*N*-arylated aliphatic diamines (eq 58). Using careful NMR observations, the researchers recently developed an aminopyridine-based ligand and succeeded in lowering the catalyst loading using a preformed catalyst (eq 59).[117] P,N-ligand-stabilized iridium catalyst also promotes the alkylation of methyl-*N*-heteroaromatics (eq 60).[118] The alkylation of 2- and 4-picoline is possible in moderate yield.





R	catalyst	yield
$PhCH_2$	0.1 mol%/Ir	93%
$^nC_4H_9$	2	83
$(CH_2)_2NH_2$	1	71
$(CH_2)_3NH_2$	1	91



R	catalyst	yield
$PhCH_2$	0.1 mol%/Ir	92%
$^nC_5H_{11}$	0.2	98

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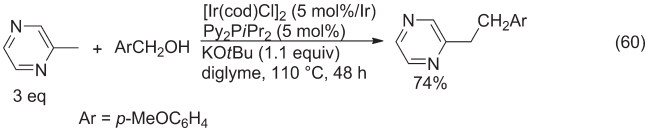
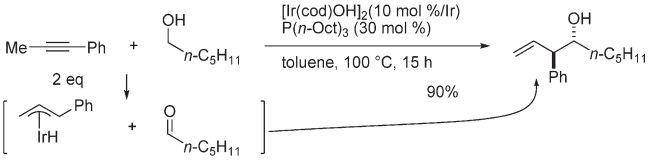
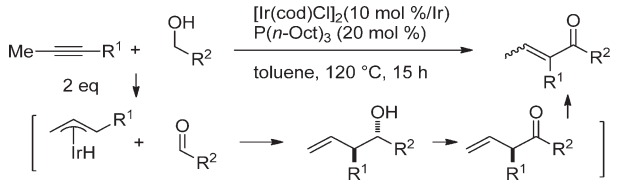


The reaction of nitroarenes and primary alcohols affords the imine by $[Cp^*IrCl_2]_2$ or Ir/Pd heterobimetallic complex

Scheme 28

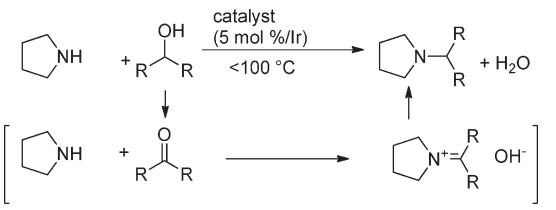


Scheme 29



R^1	R^2	yield (%)	*E*:*Z*
Ph	Ph	70	16:84
Me	Ph	94	66:34
Me	(*E*)-PhCH=CH	63	79:21

Scheme 30



R	catalyst	time	yield
H	$IrCl(PPh_3)_3$	5 h	87%
Me	$IrCl_3{\cdot}3H_2O$–PPh_3	240 h	37%

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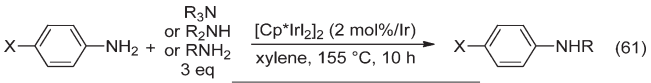
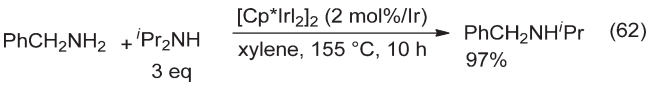
(Scheme 32).[119] In the bimetallic catalyst system, the author suggests that oxidation of the alcohol to aldehyde is catalyzed by iridium and reduction of nitroarene to amine is catalyzed by palladium.

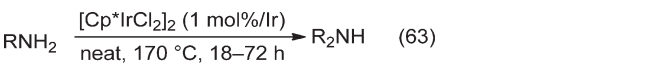
Peris reported the *N*-alkylation of aromatic amines by primary alkylamines using the [Cp*IrCl$_2$(NHC)] and AgOTf catalyst system (Scheme 33).[113a] The reaction proceeds without additional base, and secondary amines are produced selectively.

Williams employed secondary and tertiary amines in addition to primary amines as an alkyl source (eq 61).[120] Alkyl exchange reactions between tertiary amines with $Ir_4(CO)_{12}$ have been known since 1980.[121] A wide range of aliphatic primary amines can be converted to the isopropylated secondary amines using ^{i}Pr$_2$NH (eq 62). Madsen reported the dimerizations of primary amines to secondary amines are catalyzed by [Cp*IrCl$_2$]$_2$ (eq 63).[122] The neat conditions allow the straightforward isolation of the product by direct distillation.



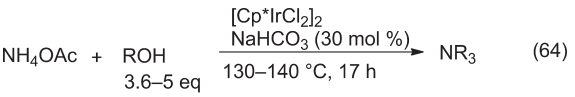
X	amine	yield(%
OMe	^{n}Pr$_2$NH	50
OMe	^{n}Pr$_3$N	90
OMe	^{i}PrNH$_2$	88
OMe	^{i}Pr$_2$NH	99
H	^{i}Pr$_2$NH	98



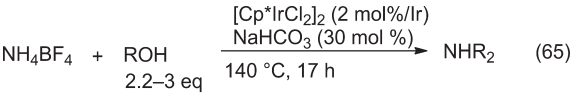


R = Bn: 70%; R = ^{n}C$_6$H$_{13}$: 72%; R = ^{c}C$_6$H$_{11}$: 73%

Ammonium salts can be used for iridium-catalyzed selective *N*-alkylations without solvent.[123] NH_4OAc, with weak acidity, affords tertiary amines by reaction of primary alcohols (eq 64). NH_4BF_4, with stronger acidity, can be used for the synthesis of secondary amines (eq 65). Current conditions have been shown to be ineffective for the selective synthesis of primary amines, however.

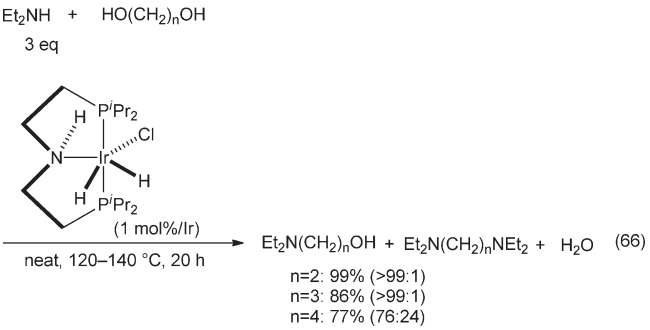


R	catalyst	yield
PhCH$_2$	1 mol%/Ir	83%
^{n}C$_6$H$_{13}$	5	60

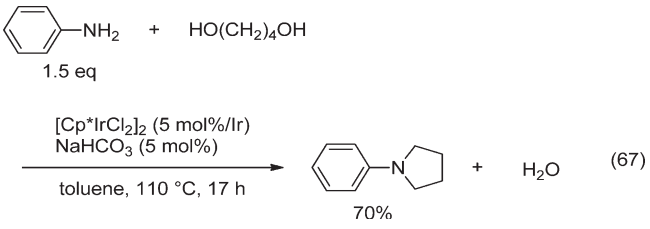


R = ^{n}C$_6$H$_{13}$: 75%; R = ^{c}C$_6$H$_{13}$: 84%

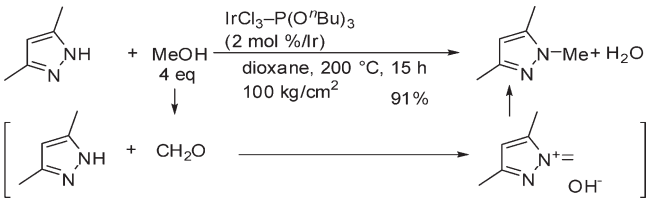
Andrushko and Börner reported the reaction of secondary amine and alcohols and diols with an Ir pincer catalyst.[124] The reaction of primary or secondary amine with methanol gave the corresponding methylated tertiary amine in high yield. Reaction of (*S*)-1-phenylethylamine led to selectively (*S*)-*N*,*N*-dimethyl-1-phenylethylamine without racemization in quantitative yield. The reaction of diols with secondary amine affords the corresponding aminoalcohols selectively (eq 66).



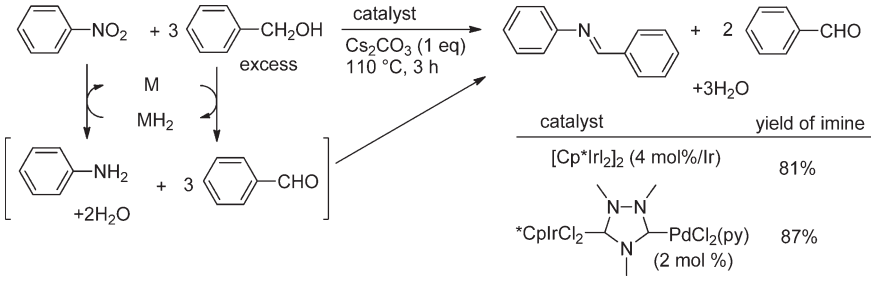
N-Alkylation with diols using [Cp*IrCl$_2$]$_2$ affords a variety of five-, six-, and seven-membered cyclic amines in good yields (eqs 67−69).[125] The two-step asymmetric synthesis of (*S*)-2-phenylpiperidine was also attained by use of (*R*)-1-phenylethylamine as a starting primary amine.



Scheme 31

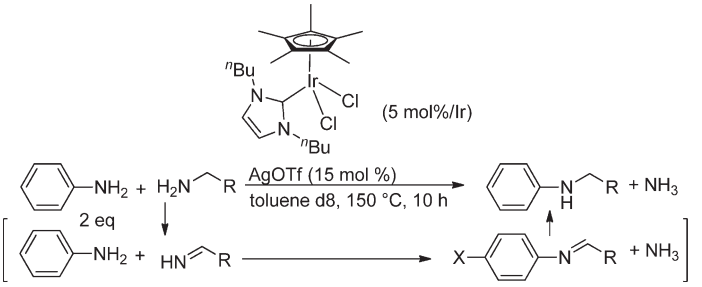


Scheme 32



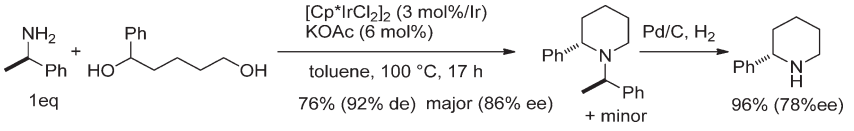
dx.doi.org/10.1021/cr100378r |*Chem. Rev.* 2011, 111, 1825–1845

Scheme 33

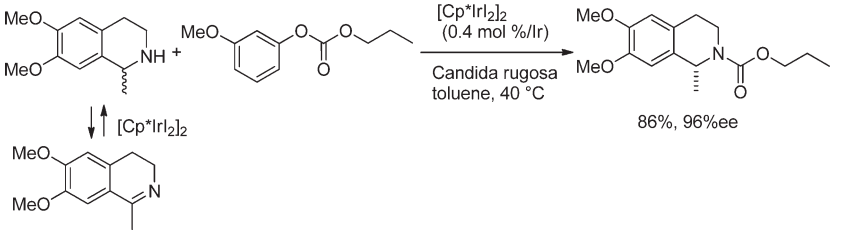


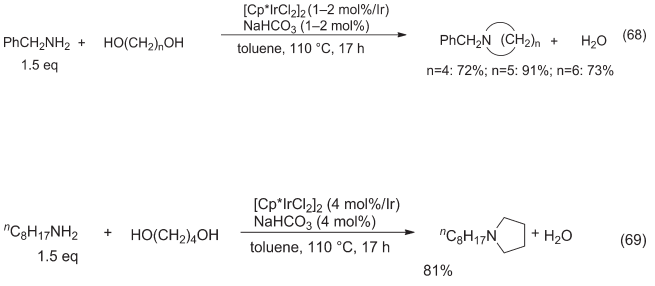
amine	yield(%)
n-$C_6H_{13}NH_2$	>95
c-$C_6H_{11}NH_2$	>95
$PhCH_2NH_2$	94

Scheme 34



Scheme 35

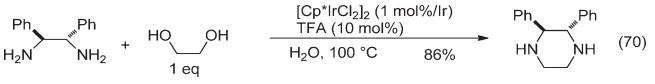




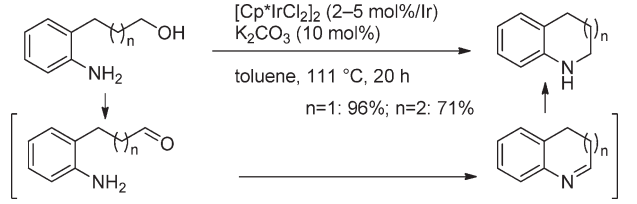
The coupling reaction of racemic diols with (*R*)-phenethylamine gave a diasetereomixture of 2-phenylpiperidines with a small extent of racemization. Hydrogenolysis of the diastereomixture afforded 2-phenylpiperidine of 78% ee (Scheme 34).[125] This approach was applied by Trudell to the synthesis of both the *R* and the *S* enantiomers of the amphibian alkaloid noranabasamine with 80% ee.[126]

The synthesis of piperazines has been reported by Madsen using the reaction of 1,2-diols and 1,2-diamines or primaryamines in aqueous media.[127] The reaction with an optically pure diamine affords the corresponding product without racemization (eq 70). Piperadine derivatives can be synthesized by homocoupling of ethanolamines using $[Cp^*IrCl_2]$–$NaHCO_3$.[128]

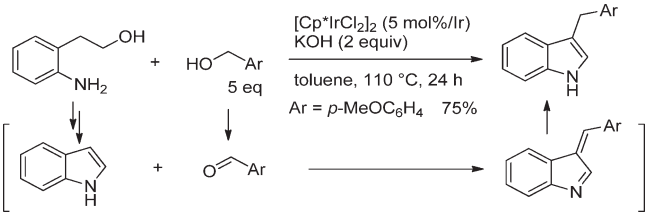
Chemoenzymatic dynamic kinetic resolution of secondary amines was reported by Page and Blacker (Scheme 35).[129a,b]



Scheme 36



Scheme 37

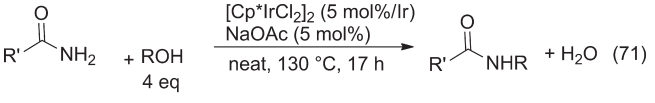


$[Cp^*IrI_2]$ racemizes the amine with a 120-fold rate increase compared to $[Cp^*IrCl_2]$. The reaction was performed at 10 g scale, and the product carbamate was isolated in 82% yield with 96% ee. Chemenzymatic dynamic kinetic resolution of secondary alcohols were reported for the synthesis of chiral esters or epoxides using Ir NHC complex or iridacyclic complex, respectively.[129c,d]

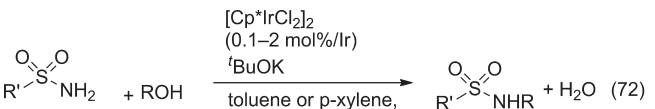
N-Alkylations of carbamates and amides with alcohols have been developed by Fujita and Yamaguchi (eq 71).[130] These

dx.doi.org/10.1021/cr100378r |*Chem. Rev.* 2011, 111, 1825–1845

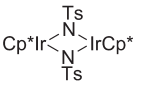
compounds are benzylated or alkylated by [Cp*IrCl$_2$]−NaOAc without solvent. *N*-Alkylation of TsNH$_2$ with benzyl alcohol also proceeds with [Cp*IrCl$_2$]−K$_2$CO$_3$.[110] Fujita and Yamaguchi found the reactions are promoted with a low catalyst loading of [Cp*IrCl$_2$]−^{t}BuOK (eq 72).[131] Mechanistic investigations revealed the key catalytic species is a sulfonylimido-bridged unsaturated diiridium complex [(Cp*Ir)$_2$-(μ-NTs)$_2$].



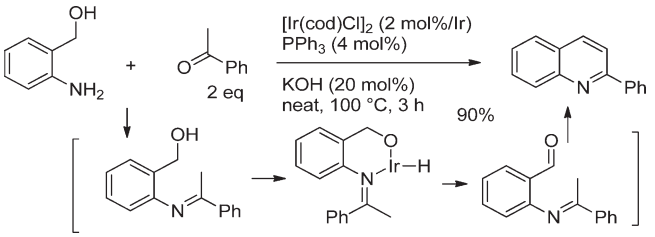
R'	R	yield (%)
O^{n}Bu	PhCH$_2$	87
O^{n}Bu	^{n}Bu	65
Ph	PhCH$_2$	81
Ph	^{n}Bu	82



R'	R	yield (%)
p-Tol	PhCH$_2$	95
p-Tol	^{n}C$_8$H$_{17}$	92
p-Tol	^{c}C$_6$H$_{11}$	93
Me	PhCH$_2$	90

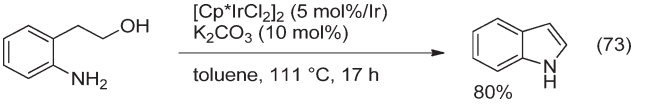


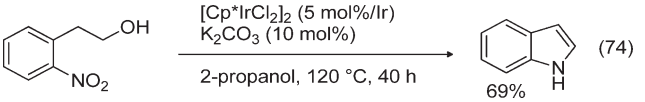
Scheme 38



6.6. Synthesis of Heteroaromatic Compounds

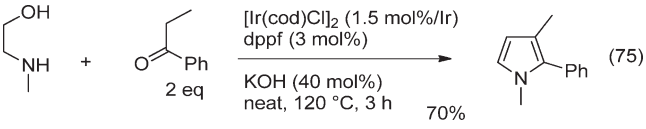
In 2002, Fujita and Yamaguchi reported the synthesis of indoles from 2-aminophenethyl alcohols using the [Cp*IrCl$_2$]$_2$/K$_2$CO$_3$ catalyst system (eq 73).[132] 2-Nitrophenethyl alcohols have also been used for the synthesis of indoles (eq 74). This catalyst system is also effective for the synthesis of 1,2,3,4-tetrahydroquinolines from 3-(2-aminophenyl)propanols and 2,3,4,5-tetrahydro-1-benzazepines from 4-(2-aminophenyl)butanols (Scheme 36). Eary reported the synthesis of tetrahydroquinoxalines and tetrahydrobenzodiazepines from the corresponding aniline alcohols using the [Cp*IrCl$_2$]$_2$/K$_2$CO$_3$ catalyst system.[133]



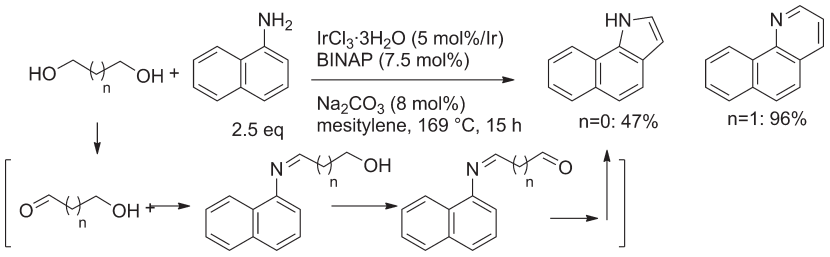


Grigg extended the strategy to the synthesis of 3-substituted indoles (Scheme 37).[134] Aromatic, heteroaromatic, and aliphatic alcohols can be used as the alkyl substituent.

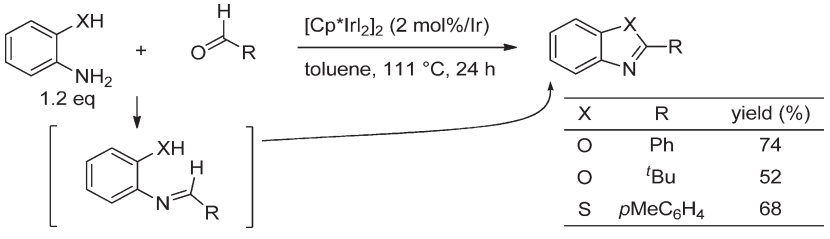
Ishii reported the synthesis of quinolines and pyroles from aminoalcohols and ketones in the presence of several iridium catalyst systems and KOH without any solvent (Scheme 38, eq 75).[135] The reaction is even catalyzed by IrCl$_3$, which does not promote the α-alkylation of ketones. His group proposed the formation of a six-membered iridium hydride complex stabilized by a ketimine group as the driving force in the reaction.



Scheme 39



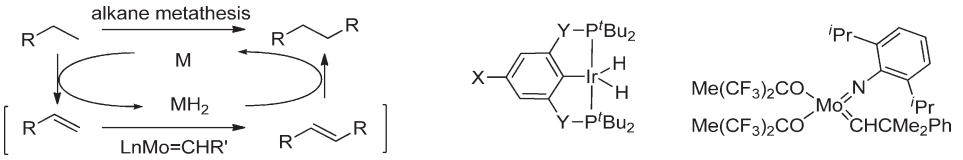
Scheme 40



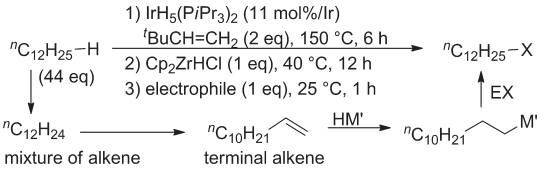
X	R	yield (%)
O	Ph	74
O	^{t}Bu	52
S	*p*MeC$_6$H$_4$	68

dx.doi.org/10.1021/cr100378r |*Chem. Rev.* 2011, 111, 1825–1845

Scheme 41



Scheme 42



EX	X	NMR yield
I_2	I	80%
^{t}BuOOH	OH	70
CH_2=$CHCH_2Br$	CH_2=$CHCH_2$	57
CO	CHO	55

Benzoindoles and benzoquinolines were synthesized from naphthylamine and 1,2- and 1,3-diols. The *N*-heterocyclization was influenced by the ligand employed. The $IrCl_3$/BINAP catalyst system gave the best results (Scheme 39).[136]

Blacker, Marsden, and Williams reported the synthesis of benzazoles and benzothiazoles from *o*-aminophenol or *o*-aminothiophenol and aldehydes in the presence of $[Cp^*IrI_2]_2$ (Scheme 40).[137] No reaction took place between benzyl alcohol and *o*-aminophenol, however. The reaction proceeds without an added hydrogen acceptor, and $[Cp^*IrI_2]$ shows higher activity than $[Cp^*IrCl_2]_2$.

6.7. Synthesis of Alkanes

Alkane metathesis was reported by Goldman and Brookhart (Scheme 41).[138] The reaction proceeds with alkane dehydrogenation using an Ir(PCP) complex followed by Schrock Mo-based alkene metathesis and hydrogenation of the resulting alkene. Schrock evaluated various Mo and W metathesis catalysts for this reaction.[139] Goldman and Scott also carried out metathesis−polymerization of cycloalkanes.[140]

The alkenes generated by the alkane dehydrogenation reaction are a mixture of terminal and internal alkenes, resulting in a complex product distribution. Takai developed the regioselective one-pot functionalization of alkanes utilizing a hydrozirconation step (Scheme 42).[141]

7. CONCLUSION

The foregoing sections clearly demonstrate the impressive progress made in the area of iridium-catalyzed oxidation. The methodologies described, such as the hydrogen autotransfer process, present new synthetic strategies for modern organic synthesis. These tandem methodologies depend on the reversibility and the functional group compatibility of iridium-catalyzed oxidation. These green processes have just been born, however, and further improvements in catalyst activities for milder conditions are strongly expected in the near future. Further development of enantioselective hydrogen autotransfer processes might also become part of mainstream synthetic organic chemistry.

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BIOGRAPHY

Takeyuki Suzuki was born in 1966 in Sapporo, Japan, and received his B.Sc. (1989) and M.Sc (1991) degrees from Hokkaido University and Ph.D. degree from the University of Tokyo in 1994 under the direction of Professor Masakatsu Shibasaki. He joined Nagoya University as an assistant professor in 1994 and has worked with Professor Ryoji Noyori; then he moved to the University of Tokyo in 2000, became Lecturer of Tohoku Pharamaceutical University in 2001, and worked with Professsor Kunio Hiroi and Professor Tadashi Katoh. From 2003 to 2004 he worked at ETH with Professor Erick M. Carreira; then he became an associate professor of Osaka University in 2005. His research interests are in synthetic organic chemistry and asymmetric catalysis.

REFERENCES

(1) In *Modern Oxidation Methods*; Bäckvall, J.-E., Ed.; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, 2004.

(2) (a) Sheldon, R. A.; Arends, I. W. C. E.; ten Brink, G.-J.; Dijksman, A. *Acc. Chem. Res.* **2002**, *35*, 774. (b) Piera, J.; Bäckvall, J. E. *Angew. Chem., Int. Ed.* **2008**, *47*, 3506.

(3) (a) Crabtree, R. *Acc. Chem. Res.* **1979**, *12*, 331. (b) In *Iridium Complexes in Organic Synthesis*; Oro, L. A., Claver, C., Eds.; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, 2009. (c) Takeuchi, R. *Synlett* **2002**, 1954. (d) Ishii, Y.; Sakaguchi, S. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 909. (e) Takeuchi, R.; Kezuka, S. *Synthesis* **2006**, 3349. (f) Liu, J.; Wu, X.; Iggo, J. A.; Xiao, J. *Coord. Chem. Rev.* **2008**, *252*, 782. (g) In *Iridium Catalysis*; Anderson, P. G., Ed.; Springer: Heidelberg, 2011.

(4) Tejel, C.; Ciriano, M. A. *Top. Organomet. Chem.* **2007**, *22*, 97.
(5) (a) Haddad, Y. M. Y.; Henbest, H. B.; Husbands, J.; Mitchell, T. R. B. *Proc. Chem. Soc.* **1964**, 361. (b) Trocha-Grimshaw, J.; Henbest, H. B. *Chem. Commun.* **1967**, 544.
(6) Camus, A.; Mestroni, G.; Zassinovich, G. *J. Mol. Catal.* **1979**, *6*, 231.
(7) (a) Nait Ajjou, A. *Tetrahedron Lett.* **2001**, *42*, 13. (b) Nait Ajjou, A.; Pinet, J. L. *Can. J. Chem.* **2005**, *83*, 702.
(8) (a) Fujita, K.; Furukawa, S.; Yamaguchi, R. *J. Organomet. Chem.* **2002**, *649*, 289. (b) Hanasaka, F.; Fujita, K.; Yamaguchi, R. *Organometallics* **2004**, *23*, 1490. (c) Hanasaka, F.; Fujita, K.; Yamaguchi, R. *Organometallics* **2005**, *24*, 3422. (d) Hanasaka, F.; Fujita, K.; Yamaguchi, R. *Organometallics* **2006**, *25*, 4643. (e) Fujita, K.; Yamaguchi, R. *Synlett* **2005**, 560.
(9) Levy, R.; Azerraf, C.; Gelman, D.; Rueck-Braun, K.; Kapoor, P. N. *Catal. Commun.* **2009**, *11*, 298.
(10) (a) Farnetti, E.; Kašpar, J.; Crotti, C. *Green Chem.* **2009**, *11*, 704. (b) Crotti, C.; Kašpar, J.; Farnetti, E. *Green Chem.* **2010**, *12*, 1295.
(11) Morales-Morales, D.; Redón, R.; Wang, Z. H.; Lee, D. W.; Yung, C.; Magnuson, K.; Jensen, C. M. *Can. J. Chem.* **2001** *79*, 823.
(12) Arita, S.; Koike, T.; Kayaki, Y.; Ikariya, T. *Chem.—Asian J.* **2008**, *3*, 1479.
(13) Jiang, B.; Feng, Y.; Ison, E. A. *J. Am. Chem. Soc.* **2008**, *130*, 14462.
(14) Lin, Y.; Ma, D.; Lu, X. *Tetrahedron Lett.* **1987**, *28*, 3115.
(15) Fujita, K.; Tanino, N.; Yamaguchi, R. *Org. Lett.* **2007**, *9*, 109.
(16) Royer, A. M.; Rauchfuss, T. B.; Wilson, S. R. *Inorg. Chem.* **2008**, *47*, 395.
(17) Li, Y. Y.; Zhang, X. Q.; Dong, Z. R.; Shen, W. Y.; Chen, G.; Gao, J. X. *Org. Lett.* **2006**, *8*, 5565.
(18) Arita, S.; Koike, T.; Kayaki, Y.; Ikariya, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 2447.
(19) Heiden, Z. M.; Rauchfuss, T. B. *J. Am. Chem. Soc.* **2007**, *129*, 14303.
(20) (a) Suzuki, T.; Ghozati, K.; Katoh, T.; Sasai, H. *Org. Lett.* **2009**, *11*, 4286. (b) Suzuki, T.; Ghozati, K.; Zhou, D.-Y.; Katoh, T.; Sasai, H. *Tetrahedron* **2010**, *66*, 7562.
(21) Suzuki, T.; Morita, K.; Tsuchida, M.; Hiroi, K. *J. Org. Chem.* **2003**, *68*, 1601.
(22) (a) Donati, N.; Königsmann, M.; Stein, D.; Udino, L.; Grützmacher, H. *C. R. Chim.* **2007**, *10*, 721. (b) Königsmann, M.; Donati, N.; Stein, D.; Schönberg, H.; Harmer, J.; Sreekanth, A.; Grützmacher, H. *Angew. Chem., Int. Ed.* **2007**, *46*, 3567.
(23) Gabrielsson, A.; van Leeuwen, P.; Kaim, W. *Chem. Commun.* **2006**, 4926.
(24) Suzuki, T.; Matsuo, T.; Watanabe, K.; Katoh, T. *Synlett* **2005**, 1453.
(25) Izumi, A.; Obora, Y.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **2006**, *47*, 9199.
(26) Kiyooka, S.-i.; Wada, Y.; Ueno, M.; Yokoyama, T.; Yokoyama, R. *Tetrahedron* **2007**, *63*, 12695.
(27) Yamamoto, N.; Obora, Y.; Ishii, Y. *Chem. Lett.* **2009**, *38*, 1106.
(28) Lin, Y.; Zhu, X.; Zhou, Y. *J. Organomet. Chem.* **1992**, *429*, 269.
(29) (a) Suzuki, T.; Morita, K.; Tsuchida, M.; Hiroi, K. *Org. Lett.* **2002**, *4*, 2361. (b) Suzuki, T.; Yamada, T.; Watanabe, K.; Katoh, T. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2583. (c) Suzuki, T.; Morita, K.; Ikemiyagi, H.; Watanabe, K.; Hiroi, K.; Katoh, T. *Heterocycles* **2006**, *69*, 457.
(30) Oger, C.; Brinkmann, Y.; Bouazzaoui, S.; Durand, T.; Galano, J.-M. *Org. Lett.* **2008**, *10*, 5087.
(31) Kosaka, M.; Sekiguchi, S.; Naito, J.; Uemura, M.; Kuwahara, S.; Watanabe, M.; Harada, N.; Hiroi, K. *Chirality* **2005**, *17*, 218.
(32) Suzuki, T.; Morita, K.; Matsuo, Y.; Hiroi, K. *Tetrahedron Lett.* **2003**, *44*, 2003.
(33) (a) Tandon, P. K.; Sahgal, S.; Singh, A. K.; Gayatri; Purwar, M. *J. Mol. Catal. A: Chem.* **2005**, *232*, 83. (b) Tandon, P. K.; Sahgal, S.; Gayatri; Purwar, M.; Dhusia, M. *J. Mol. Catal. A: Chem.* **2006**, *250*, 203. (c) Tandon, P. K.; Sahgal, S.; Singh, A. K.; Kumar, S.; Dhusia, M. *J. Mol. Catal. A: Chem.* **2006**, *258*, 320. (d) Tandon, P. K.; Purwar, M.; Singh, S.; Srivastava, N.; Srivastava, M. *J. Mol. Catal. A: Chem.* **2008**, *293*, 39. (e) Tandon, P. K.; Singh, A. K.; Sahgal, S.; Kumar, S. *J. Mol. Catal. A: Chem.* **2008**, *282*, 136. (f) Tandon, P. K.; Dwivedi, P. B.; Singh, S. *Synth. Commun.* **2009**, *39*, 1920.
(34) (a) Goel, A.; Verma, G. R.; Singh, H. S. *J. Indian Chem. Soc.* **2002**, *79*, 665. (b) Singh, A. K.; Srivastava, S.; Srivastava, J.; Singh, R. *Carbohydr. Res.* **2007**, *342*, 1078. (c) Singh, S. P.; Singh, A. K. *J. Mol. Catal. A: Chem.* **2008**, *293*, 97.
(35) (a) Barbaro, P.; Bianchini, C.; Frediani, P.; Meli, A.; Vizza, F. *Inorg. Chem.* **1992**, *31*, 1523. (b) Barbaro, P.; Bianchini, C.; Linn, K.; Mealli, C.; Meli, A.; Vizza, F.; Laschi, F.; Zanello, P. *Inorg. Chim. Acta* **1992**, *198*, 31.
(36) Iwasa, S.; Fakhruddin, A.; Widagdo, H. S.; Nishiyama, H. *Adv. Synth. Catal.* **2005**, *347*, 517.
(37) Shi, M. *J. Chem. Res. Synop.* **1998**, 592.
(38) Gu, X.-Q.; Chen, W.; Morales-Morales, D.; Jensen, C. M. *J. Mol. Catal. A: Chem.* **2002**, *189*, 119.
(39) Zhang, X.; Fried, A.; Knapp, S.; Goldman, A. S. *Chem. Commun.* **2003**, 2060.
(40) Bernskoetter, W. H.; Brookhart, M. *Organometallics* **2008**, *27*, 2036.
(41) Yamaguchi, R.; Ikeda, C.; Takahashi, Y.; Fujita, K. *J. Am. Chem. Soc.* **2009**, *131*, 8410.
(42) (a) La Placa, S. J.; Ibers, J. A. *J. Am. Chem. Soc.* **1965**, *87*, 2581. (b) McGinnety, J. A.; Doedens, R. J.; Ibers, J. A. *Inorg. Chem.* **1967**, *6*, 2243.
(43) Jacobi, B. G.; Laitar, D. S.; Pu, L.; Wargocki, M. F.; DiPasquale, A. G.; Fortner, K. C.; Schuck, S. M.; Brown, S. N. *Inorg. Chem.* **2002**, *41*, 4815.
(44) Crabtree, R. H.; Mihelcic, J. M.; Quirk, J. M. *J. Am. Chem. Soc.* **1979**, *101*, 7738.
(45) (a) Crabtree, R. H.; Mellea, M. F.; Mihelcic, J. M.; Quirk, J. M. *J. Am. Chem. Soc.* **1982**, *104*, 107. (b) Burk, M. J.; Crabtree, R. H.; McGrath, D. V. *J. Chem. Soc., Chem. Commun.* **1985**, 1829. (c) Burk, M. J.; Crabtree, R. H. *J. Am. Chem. Soc.* **1987**, *109*, 8025. (d) Aoki, T.; Crabtree, R. H. *Organometallics* **1993**, *12*, 294. (e) Belli, J.; Jensen, C. M. *Organometallics* **1996**, *15*, 1532.
(46) Gupta, M.; Hagen, C.; Flesher, R. J.; Kaska, W. C.; Jensen, C. M. *Chem. Commun.* **1996**, 2083.
(47) Gupta, M.; C. Kaska, W.; M. Jensen, C. *Chem. Commun.* **1997**, 461.
(48) Liu, F.; Pak, E. B.; Singh, B.; Jensen, C. M.; Goldman, A. S. *J. Am. Chem. Soc.* **1999**, *121*, 4086.
(49) Ray, A.; Zhu, K.; Kissin, Y. V.; Cherian, A. E.; Coates, G. W.; Goldman, A. S. *Chem. Commun.* **2005**, 3388.
(50) Gupta, M.; Hagen, C.; Kaska, W. C.; Cramer, R. E.; Jensen, C. M. *J. Am. Chem. Soc.* **1997**, *119*, 840.
(51) Göttker-Schnetmann, I.; White, P.; Brookhart, M. *J. Am. Chem. Soc.* **2004**, *126*, 1804.
(52) Kuklin, S. A.; Sheloumov, A. M.; Dolgushin, F. M.; Ezernitskaya, M. G.; Peregudov, A. S.; Petrovskii, P. V.; Koridze, A. A. *Organometallics* **2006**, *25*, 5466.
(53) Xu, W.-w.; Rosini, G. P.; Krogh-Jespersen, K.; Goldman, A. S.; Gupta, M.; Jensen, C. M.; Kaska, W. C. *Chem. Commun.* **1997**, 2273.
(54) (a) Liu, F.; Goldman, A. S. *Chem. Commun.* **1999**, 655. (b) Haenel, M. W.; Oevers, S.; Angermund, K.; Kaska, W. C.; Fan, H. J.; Hall, M. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 3596. (c) Zhu, K.; Achord, P. D.; Zhang, X.; Krogh-Jespersen, K.; Goldman, A. S. *J. Am. Chem. Soc.* **2004**, *126*, 13044. (d) Kundu, S.; Choliy, Y.; Zhuo, G.; Ahuja, R.; Emge, T. J.; Warmuth, R.; Brookhart, M.; Krogh-Jespersen, K.; Goldman, A. S. *Organometallics* **2009**, *28*, 5432.
(55) Chianese, A. R.; Mo, A.; Lampland, N. L.; Swartz, R. L.; Bremer, P. T. *Organometallics* **2010**, *29*, 3019.
(56) Tandon, P. K.; Srivastava, M.; Singh, S. B.; Srivastava, N. *Synth. Commun.* **2008**, *38*, 3183.

(57) Yamanaka, I.; Furukawa, T.; Otsuka, K. *Chem. Commun.* **2000**, 2209.
(58) Collman, J. P.; Kubota, M.; Hosking, J. W. *J. Am. Chem. Soc.* **1967**, *89*, 4809.
(59) Fusi, A.; Ugo, R.; Fox, F.; Pasini, A.; Cenini, S. *J. Organomet. Chem.* **1971**, *26*, 417.
(60) (a) Quijije, L. A.; Mediavilla, M.; Pardey, A. J.; de Pardey, C. L.; Baricelli, P.; Moya, S. A. *React. Kinet. Catal. Lett.* **1997**, *62*, 251. (b) Baricelli, P. J.; Sánchez, V. J.; Pardey, A. J.; Moya, S. A. *J. Mol. Catal. A: Chem.* **2000**, *164*, 77.
(61) (a) Weiner, H.; Trovarelli, A.; Finke, R. G. *J. Mol. Catal. A: Chem.* **2003**, *191*, 217. (b) Weiner, H.; Trovarelli, A.; Finke, R. G. *J. Mol. Catal. A: Chem.* **2003**, *191*, 253.
(62) Takao, K.; Fujiwara, Y.; Imanaka, T.; Teranishi, S. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 1153.
(63) Lyons, J. E.; Turner, J. O. *J. Org. Chem.* **1972**, *37*, 2881.
(64) Atlay, M. T.; Preece, M.; Strukul, G.; James, B. R. *J. Chem. Soc., Chem. Commun.* **1982**, 406.
(65) Lyons, J. E.; Turner, J. O. *Tetrahedron Lett.* **1972**, 2903.
(66) Müller, P.; Bobillier, C. *Tetrahedron Lett.* **1981**, *22*, 5157.
(67) Tandon, P. K.; Srivastava, M.; Singh, S. B.; Singh, S. *Synth. Commun.* **2008**, *38*, 2125.
(68) (a) Black, P. J.; Edwards, M. G.; Williams, J. M. J. *Eur. J. Org. Chem.* **2006**, *2006*, 4367. (b) Hamid, M. H. S. A.; Slatford, P. A.; Williams, J. M. J. *Adv. Synth. Catal.* **2007**, *349*, 1555. (c) Nixon, T. D.; Whittlesey, M. K.; Williams, J. M. J. *Dalton Trans.* **2009**, 753. (d) Watson, A. J. A.; Williams, J. M. J. *Science* **2010**, *329*, 635.
(69) (a) Guillena, G.; Ramón, D. J.; Yus, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 2358. (b) Guillena, G.; Ramón, D. J.; Yus, M. *Chem. Rev.* **2010**, *110*, 1611.
(70) Dobereiner, G. E.; Crabtree, R. H. *Chem. Rev.* **2010**, *110*, 681.
(71) (a) Edwards, M. G.; Williams, J. M. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 4740. (b) Shermer, D. J.; Slatford, P. A.; Edney, D. D.; Williams, J. M. J. *Tetrahedron: Asymmetry* **2007**, *18*, 2845.
(72) Black, P. J.; Cami-Kobeci, G.; Edwards, M. G.; Slatford, P. A.; Whittlesey, M. K.; Williams, J. M. J. *Org. Biomol. Chem.* **2006**, *4*, 116.
(73) Pridmore, S. J.; Williams, J. M. J. *Tetrahedron Lett.* **2008**, *49*, 7413.
(74) Suzuki, T.; Yamada, T.; Matsuo, T.; Watanabe, K.; Katoh, T. *Synlett* **2005**, 1450.
(75) Owston, N. A.; Parker, A. J.; Williams, J. M. J. *Org. Lett.* **2007**, *9*, 73.
(76) Taguchi, K.; Nakagawa, H.; Hirabayashi, T.; Sakaguchi, S.; Ishii, Y. *J. Am. Chem. Soc.* **2004**, *126*, 72.
(77) Maeda, K.; Obora, Y.; Sakaguchi, S.; Ishii, Y. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 689.
(78) Onodera, G.; Nishibayashi, Y.; Uemura, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 3819.
(79) Löfberg, C.; Grigg, R.; Whittaker, M. A.; Keep, A.; Derrick, A. *J. Org. Chem.* **2006**, *71*, 8023.
(80) Löfberg, C.; Grigg, R.; Keep, A.; Derrick, A.; Sridharan, V.; Kilner, C. *Chem. Commun.* **2006**, 5000.
(81) Grigg, R.; Whitney, S.; Sridharan, V.; Keep, A.; Derrick, A. *Tetrahedron* **2009**, *65*, 4375.
(82) Grigg, R.; Whitney, S.; Sridharan, V.; Keep, A.; Derrick, A. *Tetrahedron* **2009**, *65*, 7468.
(83) Morita, M.; Obora, Y.; Ishii, Y. *Chem. Commun.* **2007**, 2850.
(84) Grigg, R.; Löfberg, C.; Whitney, S.; Sridharan, V.; Keep, A.; Derrick, A. *Tetrahedron* **2009**, *65*, 849.
(85) Iuchi, Y.; Obora, Y.; Ishii, Y. *J. Am. Chem. Soc.* **2010**, *132*, 2536.
(86) Fujita, K.; Asai, C.; Yamaguchi, T.; Hanasaka, F.; Yamaguchi, R. *Org. Lett.* **2005**, *7*, 4017.
(87) Pontes da Costa, A.; Viciano, M.; Sanaú, M.; Merino, S.; Tejeda, J.; Peris, E.; Royo, B. *Organometallics* **2008**, *27*, 1305.
(88) Gnanamgari, D.; Sauer, E. L. O.; Schley, N. D.; Butler, C.; Incarvito, C. D.; Crabtree, R. H. *Organometallics* **2009**, *28*, 321.
(89) Gnanamgari, D.; Leung, C. H.; Schley, N. D.; Hilton, S. T.; Crabtree, R. H. *Org. Biomol. Chem.* **2008**, *6*, 4442.
(90) Matsu-ura, T.; Sakaguchi, S.; Obora, Y.; Ishii, Y. *J. Org. Chem.* **2006**, *71*, 8306.
(91) Koda, K.; Matsu-ura, T.; Obora, Y.; Ishii, Y. *Chem. Lett.* **2009**, *38*, 838.
(92) (a) Bower, J. F.; Kim, I. S.; Patman, R. L.; Krische, M. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 34. (b) Han, S. B.; Kim, I. S.; Krische, M. J. *Chem. Commun.* **2009**, 7278.
(93) Bower, J. F.; Skucas, E.; Patman, R. L.; Krische, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 15134.
(94) Han, S. B.; Kim, I. S.; Han, H.; Krische, M. J. *J. Am. Chem. Soc.* **2009**, *131*, 6916.
(95) Bower, J. F.; Patman, R. L.; Krische, M. J. *Org. Lett.* **2008**, *10*, 1033.
(96) Kim, I. S.; Ngai, M.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 6340.
(97) Kim, I. S.; Ngai, M.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 14891.
(98) Harsh, P.; O'Doherty, G. A. *Tetrahedron* **2009**, *65*, 5051.
(99) Bechem, B.; Patman, R. L.; Hashmi, A. S. K.; Krische, M. J. *J. Org. Chem.* **2010**, *75*, 1795.
(100) Lu, Y.; Kim, I. S.; Hassan, A.; Del Valle, D. J.; Krische, M. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 5018.
(101) (a) Lu, Y.; Krische, M. J. *Org. Lett.* **2009**, *11*, 3108. (b) Hassan, A.; Lu, Y.; Krische, M. J. *Org. Lett.* **2009**, *11*, 3112.
(102) Kim, I. S.; Han, S. B.; Krische, M. J. *J. Am. Chem. Soc.* **2009**, *131*, 2514.
(103) Han, S. B.; Gao, X.; Krische, M. J. *J. Am. Chem. Soc.* **2010**, *132*, 9153.
(104) Zhang, Y. J.; Yang, J. H.; Kim, S. H.; Krische, M. J. *J. Am. Chem. Soc.* **2010**, *132*, 4562.
(105) Obora, Y.; Hatanaka, S.; Ishii, Y. *Org. Lett.* **2009**, *11*, 3510.
(106) Hatanaka, S.; Obora, Y.; Ishii, Y. *Chem.—Eur. J.* **2010**, *16*, 1883.
(107) Grigg, R.; Mitchell, T. R. B.; Sutthivaiyakit, S.; Tongpenyai, N. *J. Chem. Soc., Chem. Commun.* **1981**, 611.
(108) Tanaka, N.; Hatanaka, M.; Watanabe, Y. *Chem. Lett.* **1992**, *21*, 575.
(109) (a) Fujita, K.; Li, Z.; Ozeki, N.; Yamaguchi, R. *Tetrahedron Lett.* **2003**, *44*, 2687. (b) Fujita, K.; Enoki, Y.; Yamaguchi, R. *Tetrahedron* **2008**, *64*, 1943.
(110) Balcells, D.; Nova, A.; Clot, E.; Gnanamgari, D.; Crabtree, R. H.; Eisenstein, O. *Organometallics* **2008**, *27*, 2529.
(111) Saidi, O.; Blacker, A. J.; Farah, M. M.; Marsden, S. P.; Williams, J. M. J. *Chem. Commun.* **2010**, *46*, 1541.
(112) Saidi, O.; Blacker, A. J.; Lamb, G. W.; Marsden, S. P.; Taylor, J. E.; Williams, J. M. J. *Org. Process Res. Dev.* **2010**, *14*, 1046.
(113) (a) Prades, A.; Corberán, R.; Poyatos, M.; Peris, E. *Chem.—Eur. J.* **2008**, *14*, 11474. (b) Liu, S.; Rebros, M.; Stephens, G.; Marr, A. C. *Chem. Commun.* **2009**, 2308.
(114) Cami-Kobeci, G.; Slatford, P. A.; Whittlesey, M. K.; Williams, J. M. J. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 535.
(115) Cami-Kobeci, G.; Williams, J. M. J. *Chem. Commun.* **2004**, 1072.
(116) (a) Blank, B.; Madalska, M.; Kempe, R. *Adv. Synth. Catal.* **2008**, *350*, 749. (b) Blank, B.; Michlik, S.; Kempe, R. *Chem.—Eur. J.* **2009**, *15*, 3790. (c) Blank, B.; Michlik, S.; Kempe, R. *Adv. Synth. Catal.* **2009**, *351*, 2903.
(117) Michlik, S.; Kempe, R. *Chem.—Eur. J.* **2010**, *16*, 13193.
(118) Blank, B.; Kempe, R. *J. Am. Chem. Soc.* **2010**, *132*, 924.
(119) Zanardi, A.; Mata, J. A.; Peris, E. *Chem.—Eur. J.* **2010**, *16*, 10502.
(120) Saidi, O.; Blacker, A. J.; Farah, M. M.; Marsden, S. P.; Williams, J. M. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 7375.
(121) Shvo, Y.; Laine, R. M. *J. Chem. Soc., Chem. Commun.* **1980**, 753.
(122) Lorentz-Petersen, L. L. R.; Jensen, P.; Madsen, R. *Synthesis* **2009**, 4110.
(123) (a) Yamaguchi, R.; Kawagoe, S.; Asai, C.; Fujita, K. *Org. Lett.* **2008**, *10*, 181. (b) Yamaguchi, R.; Mingwen, Z.; Kawagoe, S.; Asai, C.; Fujita, K. *Synthesis* **2009**, 1220.

(124) Andrushko, N.; Andrushko, V.; Roose, P.; Moonen, K.; Börner, A. *ChemCatChem* **2010**, *2*, 640.
(125) Fujita, K.; Fujii, T.; Yamaguchi, R. *Org. Lett.* **2004**, *6*, 3525.
(126) Miao, L.; DiMaggio, S. C.; Shu, H.; Trudell, M. L. *Org. Lett.* **2009**, *11*, 1579.
(127) Nordstrom, L. U.; Madsen, R. *Chem. Commun.* **2007**, 5034.
(128) Fujita, K.; Kida, Y.; Yamaguchi, R. *Heterocycles* **2009**, *77*, 1371.
(129) (a) Blacker, A. J.; Stirling, M. J.; Page, M. I. *Org. Process Res. Dev.* **2007**, *11*, 642. (b) Stirling, M.; Blacker, J.; Page, M. I. *Tetrahedron Lett.* **2007**, *48*, 1247. (c) Marr, A. C.; Pollock, C. L.; Saunders, G. C. *Organometallics* **2007**, *26*, 3283. (d) Haak, R. M.; Berthiol, F.; Jerphagnon, T.; Gayet, A. J. A.; Tarabiono, C.; Postema, C. P.; Ritleng, V.; Pfeffer, M.; Janssen, D. B.; Minnaard, A. J.; Feringa, B. L.; de Vries, J. G. *J. Am. Chem. Soc.* **2008**, *130*, 13508.
(130) Fujita, K.; Komatsubara, A.; Yamaguchi, R. *Tetrahedron* **2009**, *65*, 3624.
(131) Zhu, M.; Fujita, K.; Yamaguchi, R. *Org. Lett.* **2010**, *12*, 1336.
(132) Fujita, K.; Yamamoto, K.; Yamaguchi, R. *Org. Lett.* **2002**, *4*, 2691.
(133) Eary, C. T.; Clausen, D. *Tetrahedron Lett.* **2006**, *47*, 6899.
(134) Whitney, S.; Grigg, R.; Derrick, A.; Keep, A. *Org. Lett.* **2007**, *9*, 3299.
(135) Taguchi, K.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **2005**, *46*, 4539.
(136) Aramoto, H.; Obora, Y.; Ishii, Y. *J. Org. Chem.* **2009**, *74*, 628.
(137) Blacker, A. J.; Farah, M. M.; Hall, M. I.; Marsden, S. P.; Saidi, O.; Williams, J. M. J. *Org. Lett.* **2009**, *11*, 2039.
(138) Goldman, A. S.; Roy, A. H.; Huang, Z.; Ahuja, R.; Schinski, W.; Brookhart, M. *Science* **2006**, *312*, 257.
(139) Bailey, B. C.; Schrock, R. R.; Kundu, S.; Goldman, A. S.; Huang, Z.; Brookhart, M. *Organometallics* **2009**, *28*, 355.
(140) Ahuja, R.; Kundu, S.; Goldman, A. S.; Brookhart, M.; Vicente, B. C.; Scott, S. L. *Chem. Commun.* **2008**, 253.
(141) Kuninobu, Y.; Ureshino, T.; Yamamoto, S.; Takai, K. *Chem. Commun.* **2010**, *46*, 5310.