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Formation of C–C Bonds via Iridium-Catalyzed Hydrogenation and Transfer Hydrogenation

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Abstract

The formation of C–C bonds via catalytic hydrogenation and transfer hydrogenation enables carbonyl and imine addition in the absence of stoichiometric organometallic reagents. In this review, iridium-catalyzed C–C bond-forming hydrogenations and transfer hydrogenations are surveyed. These processes encompass selective, atom-economic methods for the vinylation and allylation of carbonyl compounds and imines. Notably, under transfer hydrogenation conditions, alcohol dehydrogenation drives reductive generation of organoiridium nucleophiles, enabling carbonyl addition from the aldehyde or alcohol oxidation level. In the latter case, hydrogen exchange between alcohols and π-unsaturated reactants generates electrophile–nucleophile pairs en route to products of hydro-hydroxyalkylation, representing a direct method for the functionalization of carbinol C–H bonds.

Keywords

Iridium; Enantioselective; Hydrogenation; Transfer hydrogenation; Allylation; Vinylation

1 Introduction

The majority of chemical commodities (plastics, foams, pharmaceuticals, agrochemicals) are made from rapidly depleting petrochemical feedstocks. Consequently, there is a growing need to develop catalytic methods for the direct manufacture of chemical products from abundant renewable resources in the absence of stoichiometric byproducts [1]. In the specific case of carbonyl and imine addition, a departure from the use of premetallated nucleophiles represents a particularly important focus. Progress in this area will depend largely upon the discovery of new chemical reactivity.

Catalytic hydrogenation is the cleanest and most cost-effective method available for the reduction of organic molecules. Accordingly, chemical processes such as the Haber–Bosch reaction1 [2, 3], alkene hydroformylation2 [4–7], and enantioselective hydrogenation3 [8–

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[1]The catalytic hydrogenation of atmospheric nitrogen, accounts for the annual production of over 100,000,000 metric tons of ammonia, which is the limiting nutrient in terrestrial plant growth. The Haber–Bosch process is estimated to sustain one-third of the Earth's population. Approximately half the nitrogen in our bodies is nitrogen fixed through the Haber–Bosch reaction.

10], all of which provide materials essential to humanity, are practiced on a vast scale. The industrialization of these processes is assisted by the fact that such hydrogen-mediated transformations do not generate stoichiometric byproducts, which facilitate product purification and waste stream management. Interestingly, although catalytic hydrogenation and the Grignard reaction are both reductive transformations, a union between catalytic hydrogenation and carbonyl addition chemistry failed to materialize after the emergence of alkene hydroformylation, which may be viewed as the prototypical C–C bond-forming hydrogenation.

The collective studies from our laboratory establish metal-catalyzed hydrogenation and transfer hydrogenation as general methods for C–C bond formation.[4,5,6] These processes exploit π-unsaturated reactants as surrogates to moisture sensitive organometallic reagents, enabling carbonyl and imine addition under essentially neutral conditions in the absence of stoichiometric organometallic reagents and resulting metallic byproducts. Remarkably, under transfer hydrogenation conditions, hydrogen exchange between alcohols and π-unsaturated reactants generates electrophile–nucleophile pairs en route to products of hydro-hydroxyalkylation, representing a direct method for the functionalization of carbinol C–H bonds.[7,8,9] For such "carbonyl additions from the alcohol oxidation level," preactivation is not required as both the nucleophile and electrophile are generated catalytically from simple and stable precursors (Scheme 1). In this review, iridium-catalyzed C–C bond-forming hydrogenations and transfer hydrogenations are surveyed. Related hydrogen-mediated C–C couplings employing rhodium and ruthenium catalysts are not covered in this account but are described in several recent monographs (see footnote 4, [11–17]).

2 Iridium-Catalyzed Hydrogenation for C–C Bond Formation

2.1 Alkynes as Vinylmetal Surrogates via Iridium-Catalyzed Hydrogenation

Allylic alcohols and allylic amines are highly versatile building blocks for organic synthesis, and methods for their preparation in enantiomerically enriched form are the subject of intensive investigation.[10,11] The majority of established protocols rely upon metal-catalyzed allylic substitution employing *O*- and *N*-nucleophiles (For reviews on metal catalyzed allylic amination and alkoxylation, see: [37–43]). An alternative approach to allylic alcohols and allylic amines involves the catalytic enantioselective vinylation of aldehydes and imines. Based upon the seminal studies of Oguni [44] and Noyori [45] on the enantioselective addition of dialkylzinc reagents to aldehydes (For reviews encompassing catalytic enantioselective addition of organozinc reagents to carbonyl compounds, see: [46–51]), Oppolzer (see footnote 12, [52]) devised the first catalytic enantioselective aldehyde

[2]The prototypical C–C bond forming hydrogenation, hydroformylation combines basic feedstocks (α-olefins, carbon monoxide, and hydrogen) with perfect atom economy and accounts for the production of over 10 million metric tons of aldehyde annually, making it the largest volume application of homogeneous metal catalysis.

[3]The asymmetric hydrogenation of C=X π-bonds (X = O, NR) is estimated to account for over half the chiral drugs manufactured industrially, withstanding physical and enzymatic resolution.

[4]For selected reviews on C–C bond forming hydrogenation and transfer hydrogenation, see [11–17].

[5]Prior to our systematic studies, two isolated reports of hydrogen mediated C–C coupling were reported, see [18,19].

[6]Side products of reductive C–C bond formation have been observed in catalytic hydrogenation on rare occasions, see [20,21].

[7]The alcohol-unsaturate couplings developed in our laboratory provide products of carbonyl addition. In contrast, related hydrogen auto-transfer processes provide products of alcohol substitution via pathways involving oxidation–condensation–reduction and the use of preactivated nucleophiles. For recent reviews, see [22–25].

[8]Processes that enable direct catalytic C–C functionalization of carbinol C–H bonds are highly uncommon. Rh-catalyzed alcohol-vinylarene C–C coupling has been described. The requirement of BF_3 and trends in substrate scope suggest these processes involve alcohol dehydrogenation-reductive Prins addition: [26–29].

[9]For radical mediated C–C functionalization of carbinol C–H bonds, see [30,31].

[10]For reviews encompassing the synthesis of allylic alcohols, see [32,33].

[11]For reviews encompassing the synthesis of allylic amines, see [34–36].

[12]For enantioselective catalytic addition of vinylzinc reagents to aldehydes, see [52–70].

vinylations.[12,13] In this process, vinylzinc reagents are generated in situ by alkyne hydroboration followed by transmetallation from boron to zinc using $ZnMe_2$. A conceptually related approach was developed subsequently by Wipf, in which hydrozirconation-transmetallation is used to generate the vinylzinc reagent (see footnote 12, [55]). These studies, along with catalytic enantioselective alkyl- and aryl-zinc-mediated ketone additions described by Yus [73,74] and Fu [75], set the stage for catalytic enantioselective ketone vinylations, as described by Walsh (For catalytic enantioselective ketone vinylation using organozinc reagents, see: [76–78]). Catalytic methods for carbonyl vinylation continue to emerge, as demonstrated by recent reports on rhodium-catalyzed aldehyde additions employing vinylboron reagents [79].

Enantioselective vinylzinc-mediated imine additions reveal additional challenges (For reviews encompassing the catalytic enantioselective addition of organozinc reagents to imines, see: [80–84]). After the seminal report of Soai [85], several enantioselective catalysts for the addition of organozinc reagents to imines were developed. However, highly activated *N*-acyl and *N*-(diphenylphosphinoyl) imines are required (For enantioselective catalytic addition of organozinc reagents to imines, see: [85–96]). To address the issue of reactivity, Tomioka (see footnote 14, [97]) disclosed an enantioselective copper catalyst for organozinc-mediated imine addition.[14] In addition to late transition metals (Cu, Rh) (see footnote 14) [117, 118], early transition metal catalysts (Ti, Zr, Hf) (For enantioselective zirconium, titanium and hafnium catalyzed addition of organozinc reagents to imines, see: [119–124]) are found to promote the highly enantioselective addition of organozinc reagents to imines. The enantioselective addition of organolithium reagents to imines promoted or catalyzed by chiral chelating agents also has been described (For reviews encompassing catalytic enantioselective addition of organolithium reagents to carbonyl compounds and imines, see: [125–132]). Finally, under the conditions of rhodium catalysis, organotin, organotitanium, and organoboron reagents participate in catalytic asymmetric imine addition (For enantioselective rhodium catalyzed addition of organometallic reagents to imines, see: Organotin reagents [133–134], Organotitanium reagents [135] and Organoboron reagents [136]). Despite these efforts, highly enantioselective imine additions employing vinylmetal reagents remain elusive (Catalyzed addition of vinylzirconocenes to imines is known, but enantioselective variants have not been developed: [147, 148]).[15]

The direct metal-catalyzed reductive coupling of alkynes to carbonyl compounds or imines provides an alternative to the use of discrete vinylmetal reagents (For a compilation of reviews on the subject of metal catalyzed reductive C–C coupling, see: [150]).[16] Catalytic intramolecular carbonyl vinylation was first reported by Ojima (1994), who employed a rhodium catalyst in combination with a silane as the terminal reductant [159]. Related cyclizations using titanium or nickel catalysts later were reported by Crowe [160] (For an aligned study, see: [161]) and Montgomery [162–167], respectively. Finally, in an adaptation of Montgomery's cyclization protocol, intermolecular nickel-catalyzed alkyne–aldehyde reductive couplings were reported by Jamison [168–171]. Subsequently, improved nickel catalysts for this process were devised by Takai [172] and Montgomery [165]. However, while direct alkyne–carbonyl reductive couplings circumvent the use of discrete vinylmetal reagents, they nevertheless employ terminal reductants such as hydrosilanes, hydrostannanes, organozinc reagents, organoboron reagents or chromium(II) chloride, which generate stoichiometric quantities of byproduct.

[13]For reviews encompassing catalytic enantioselective aldehyde vinylation using organozinc reagents, see [71,72].
[14]For enantioselective copper catalyzed addition of organozinc reagents to imines, see [97–116].
[15]Enantioselective Ni-catalyzed alkyne, imine, triethylborane 3-component coupling has been reported, but modest selectivities (51–89% ee) are observed. For this method, vinylation is accompanied by ethyl transfer: [149]
[16]For selected reviews encompassing intra- and intermolecular direct reductive coupling of alkynes to carbonyl partners, see [151–158]

Under the conditions of iridium-catalyzed hydrogenation, alkyne–carbonyl and alkyne–imine reductive coupling occurs in the absence of stoichiometric byproducts. For example, iridium-catalyzed hydrogenation of nonconjugated alkynes in the presence of α-ketoesters delivers the corresponding α-hydroxy esters in excellent yield [173]. Notably, nonsymmetric alkynes engage in highly regioselective reductive coupling (Scheme 2).

Deuterium labeling studies are consistent with a mechanism involving alkyne–carbonyl oxidative coupling to furnish iridacycle A followed by Brønsted acid-assisted hydrogenolysis of this species to deliver the product. Deuterium at oxygen is removed through exchange in the course of chromatographic isolation but is observed via EI–MS analysis of reaction mixtures. Although mechanisms involving alkyne hydrometallation cannot be excluded on the basis of deuterium labeling studies alone, regioselectivity trends observed in response to variation of the steric features of both the alkyne and carbonyl partners strongly suggest that oxidative coupling pathways are operative (Scheme 3).

Cationic rhodium complexes also catalyze alkyne–carbonyl and alkyne–imine reductive coupling under hydrogenation conditions [174–178]. The rhodium-catalyzed processes are applicable to the reductive coupling of conjugated alkynes (1,3-enynes, 1,3-diynes) to activated ketones [174], aldehydes [175–177], or imines [178]. The rhodium-catalyzed reductive coupling of acetylene to carbonyl compounds or imines also is described [179–182]. For reactions of conjugated alkynes, the observed trends in substrate scope suggest π-backbonding at the stage of the metal–alkyne complex facilitates alkyne-C=X (X=O, NR) oxidative coupling [183–185]. As rhodium is a relatively weak π-donor, conjugated alkynes and activated carbonyl and imine partners, which embody lower lying LUMOs, are required for oxidative coupling. Due to relativistic effects, iridium is a stronger π-donor than rhodium [186–189] and, therefore, can promote oxidative coupling of nonconjugated alkynes, which have higher lying LUMOs (Scheme 4).17

Regarding the role of the Brønsted acid cocatalyst, computational studies by Musashi and Sakaki suggest that carboxylic acid additives accelerate coupling by circumventing highly energetic four-centered transition structures for hydrogenolysis of metallacyclic intermediates **A** [195]. In the presence of carboxylic acid, protonolysis of oxa-iridacyclic intermediates **A** provide iridium carboxylates, which engage in hydrogenolysis through lower energy six-centered transition structures **C**. Protonolysis itself may occur through six-centered transition structures **B**. This interpretation is consistent with recently reported ESI–MS and DFT studies on the rhodium-catalyzed reductive coupling of acetylene to carbonyl and imine partners under hydrogenation conditions (Fig. 1) [182].

Cationic iridium complexes modified by chiral phosphine ligands promote highly enantioselective alkyne–imine reductive coupling under hydrogenation conditions to furnish trisubstituted allylic amines as single geometrical isomers [196,197]. Carboxylic acid cocatalysts are required to enforce high levels of conversion. Additionally, Na_2SO_4 facilitates coupling by serving as a desiccant, thus mitigating imine hydrolysis by adventitious water. A remarkable feature of these transformations involves high levels of contrasteric regioselectivity observed in reductive couplings of nonsymmetric alkynes (Scheme 5).

As corroborated by deuterium labeling, the observed contrasteric regiocontrol appears to be a consequence of the oxidative coupling pathway. Specifically, formation of aza-iridacycle **A** via alkyne–imine oxidative coupling occurs such that nonbonded interactions between the

[17]Alkyne complexation by iridium(I) results in substantial deviation from linearity, as revealed by single crystal X-ray diffraction analysis: [190–194].

large alkyne substituent and the sterically demanding iridium center are minimized. Carboxylic acid-assisted hydrogenolysis (via **B** and **C**) delivers the allylic amine. Formation of the iridacyclic intermediate **A** is the enantiodetermining event. Here, square planar iridium(I) binds the alkyne and imine at adjacent coordination sites. In accordance with the Dewar–Chatt–Duncanson model [183–185], the bound alkyne exhibits iridacyclopropene character (Alkyne complexation by iridium(I) results in substantial deviation from linearity, as revealed by single crystal X-ray diffraction analysis: (see footnote 17) [190–194]). Bidentate coordination of the *N*-arylsulfonyl imine to the iridium center is anticipated18 [198]. Insertion of the imine into the iridium–carbon bond of the iridacyclopropene then delivers the indicated aza-iridacyclopentene **A**. Minimization of nonbonded interactions between the *N*-arylsulfonyl group and the phenylphosphino moieties accounts for the observed sense of stereoinduction (Scheme 6).

2.2 Allenes as Allylmetal Surrogates via Hydrogenation

Enantioselective carbonyl allylation is one of the most broadly utilized transformations in synthetic organic chemistry (For reviews on enantioselective carbonyl allylation, see: [199–204]). Shortly after the first reports of carbonyl allylation employing isolable allylboron and allylsilicon reagents by Mikhailov and Bubnov [205] and Hosomi and Sakurai [206], respectively, enantioselective carbonyl allylations were reported by Hoffmann (see footnote 19, [207]). While the design of increasingly effective chiral allylmetal reagents continues19 207–220], this approach only can be viewed as an interim solution as the use of stoichiometric chiral-inducing elements invariably leads to molar quantities of byproduct, diminishing prospects for large-volume applications (Fig. 2).

This limitation is addressed, in part, by the groundbreaking work of Yamamoto [221] and subsequent studies by Umani-Ronchi [222] and Keck [223] on chiral Lewis acid catalysts for enantioselective carbonyl allylation. Chiral Lewis base-catalyzed enantioselective carbonyl allylations soon followed, as reported by Denmark [224].20 Although these methods avoid the stoichiometric use of chiral modifiers, they employ molar quantities of allylmetal reagent and, consequently, generate stoichiometric quantities of metallic byproducts. Furthermore, preparation of the allylmetal reagent itself is often beset by excessive waste production. For example, allylstannanes employed in the Umani-Ronchi–Keck process are prepared from the corresponding organomagnesium reagents, which, in turn, are prepared from the allylic halides [222,223]. Thus, preactivation in the form of three stoichiometric operations is required in advance of C–C coupling (Scheme 7).

The reductive generation of transient allylmetal species from allylic alcohols, allylic carboxylates,21,22 or allylic halides23,24 represents an approach to carbonyl allylation that avoids discrete allylmetal reagents. However, with a few exceptions, (see footnote 21, [235–238]) such processes require stoichiometric quantities of metallic reductants, such as SmI_2, $SnCl_2$, and Et_2Zn. Finally, the carbonyl–ene reaction enables carbonyl allylation in the absence of stoichiometric byproducts by employing simple olefins as allyl donors; however, enantioselective variants are limited to highly activated electrophiles, and general protocols remain a distant goal.25,26

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[18]The bidentate κ2-mode of binding has been observed by single crystal X-ray diffraction analysis for a related palladium *N*-arylsulfonamidate complex.
[19]For selected examples of chirally modified allyl metal reagents, see [207–220].
[20]For selected examples of catalytic asymmetric carbonyl allylation employing allylmetal reagents, see [221–224].
[21]For selected examples of carbonyl allylations employing nucleophilic π-allyls derived from allylic acetates and carboxylates, see: *Palladium* [225–233], *Rhodium* [234,235], *Ruthenium* [236–238], *Iridium* [239–241].
[22]For selected reviews on carbonyl allylation via umpolung of π-allyls, see [242–247].
[23]For catalytic enantioselective carbonyl allylation and crotylation via Nozaki-Hiyama coupling, see [248–257].
[24]For recent reviews of catalytic Nozaki-Hiyama coupling, see [258–261].

Carbonyl allylation in the absence of metallic reagents is achieved under the conditions of iridium-catalyzed hydrogenation or transfer hydrogenation employing 1,2-dienes, 1,3-dienes, or allyl acetates as precursors to transient allylmetal species (see footnote 4, [16]). Here, hydrogen or isopropanol may serve as reductant. For transfer hydrogenative processes, isopropanol dehydrogenation drives reductive generation of allylmetal nucleophiles from unsaturates. Of greater significance is the fact that hydrogen exchange between reactant alcohols and π-unsaturated partners occurs to generate electrophile–nucleophile pairs en route to products of C–C coupling. In this way, carbonyl allylation is achieved directly from the alcohol oxidation level, availing a method for the hydro-hydroxyalkylation of unsaturates via functionalization of carbinol C–H bonds (Scheme 8) (see footnotes (7, 8, 9), [22–31]).

Hydrogen-mediated carbonyl allylation was first demonstrated under the conditions of iridium-catalyzed hydrogenation in studies of allene–carbonyl reductive coupling [269]. Using a cationic iridium catalyst, hydrogenation of commercially available 1,1-dimethylallene in the presence of carbonyl electrophiles delivers products of carbonyl *tert*-prenylation as single regioisomers in good to excellent yield. Note that functional groups typically considered “hydrogen-labile,” such as aryl halides, benzylic ethers, alkenes, and nitroarenes, are tolerated under these conditions. Unlike conventional allylation protocols, all reactant atoms, including hydrogen, are incorporated into the product and so no stoichiometric byproducts are generated (Scheme 9).

Reductive coupling of 1,1-dimethylallene and 5-nitro-2-furancarboxaldehyde under a deuterium atmosphere provides the product of *tert*-prenylation incorporating deuterium at the interior vinylic position (80% ^{2}H). This result is consistent with a mechanism involving allene–aldehyde oxidative coupling. However, alternate pathways involving allene hydrometallation to furnish allyliridium species cannot be excluded on the basis of these data (Scheme 10).

3 Iridium-Catalyzed Transfer Hydrogenation for C–C Bond Formation

3.1 Allenes as Allylmetal Surrogates via Transfer Hydrogenation

Although carbonyl *tert*-prenylation occurs efficiently upon iridium-catalyzed hydrogenation of 1,1-dimethylallene in the presence of aldehydes, attempted crotylations and allylations employing methylallene or allene gas, respectively, suffer from competing conventional hydrogenation of the olefinic C–C coupling product. Corresponding iridium-catalyzed transfer hydrogenations overcome this limitation [270]. Under nearly identical conditions, by simply substituting isopropanol (200 mol%) for hydrogen as the terminal reductant, 1,1-dimethylallene reductively couples to aldehydes to furnish products of *tert*-prenylation in good to excellent yield across a broad range of substrates. Remarkably, it was found that alcohol reactants serve dually as reductants and aldehyde precursors, enabling formation of identical products. Thus, carbonyl addition occurs with equal facility from the aldehyde or alcohol oxidation levels. This chemistry is also applicable to carbonyl crotylation and allylation employing methylallene or allene gas, respectively. However, the volatility of these reagents contributes to diminished efficiencies (Scheme 11).

The coupling of 1,1-dimethylallene to benzaldehyde employing d_8-isopropanol as reductant delivers the product of *tert*-prenylation, incorporating deuterium primarily at the internal vinylic position (85% ^{2}H). Similar results are obtained when the reaction is conducted from the alcohol oxidation level employing d_2-benzyl alcohol. Further mechanistic insight comes

[25] For reviews on carbonyl-ene reactions, see [262–265].
[26] For Nickel catalyzed carbonyl-ene reactions, see [266–268].

from crossover experiments in which 1,1-dimethylallene is exposed to equimolar quantities of *p*-nitrobenzyl alcohol and benzaldehyde. The *p*-nitrophenyl- and phenyl-containing adducts are obtained in a 4:1 ratio, respectively. An identical product distribution is obtained upon exposure of 1,1-dimethylallene to equimolar quantities of *p*-nitrobenzaldehyde and benzyl alcohol under otherwise identical conditions. These data are consistent with fast and reversible alcohol dehydrogenation to form nonmetal-bound aldehyde in advance of C–C coupling (Scheme 12).

Highly enantioselective variants of these processes employ a cyclometallated iridium *C,O*-benzoate derived from allyl acetate, *m*-nitrobenzoic acid, and (*S*)-SEGPHOS [271,272]. Using this complex as a precatalyst, transfer hydrogenation of 1,1-dimethylallene in the presence of diverse aldehydes mediated by isopropanol delivers products of *tert*-prenylation in good to excellent yield and with excellent levels of enantioselectivity. In the absence of isopropanol, enantioselective carbonyl reverse prenylation is achieved directly from the alcohol oxidation level to furnish an equivalent set of adducts. Notably, enantioselective *tert*-prenylation is achieved under mild conditions (30–50°C) in the absence of stoichiometric metallic reagents. Indeed, for reactions conducted from the alcohol oxidation level, stoichiometric byproducts are completely absent (Scheme 13).

Our collective mechanistic studies are consistent with the indicated catalytic cycle. Notably, the catalyst engages primary alcohols in rapid and reversible dehydrogenation, yet the coupling products, which are homoallylic alcohols, are not subject to oxidation as coordination of the homoallylic olefin to the catalyst provides a hexa-coordinate 18-electron complex lacking an open coordination site for β-hydride elimination (Scheme 14).

3.2 Dienes as Allylmetal Surrogates via Transfer Hydrogenation

Under the conditions of iridium-catalyzed transfer hydrogenation employing isopropanol as reductant, 1,3-cyclohexadiene couples to aryl aldehydes to provide products of carbonyl cyclohexenylation in good to excellent yield and with high levels of diastereocontrol. Under nearly identical conditions, but in the absence of isopropanol, corresponding alcohols couple directly to 1,3-cyclohexadiene to furnish identical products of carbonyl cyclohexenylation (Scheme 15) [273].

More recently, using the cyclometallated iridium *C,O*-benzoate derived from allyl acetate, 4-methoxy-3-nitrobenzoic acid and BIPHEP, catalytic carbonyl crotylation employing 1,3-butadiene from the aldehyde, or alcohol oxidation was achieved under transfer hydrogenation conditions [274]. Carbonyl addition occurs with roughly equal facility from the alcohol or aldehyde oxidation level. However, products are obtained as diastereomeric mixtures. Stereoselective variants of these processes are under development. It should be noted that under the conditions of ruthenium-catalyzed transfer hydrogenation, conjugated dienes, including butadiene, couple to alcohols or aldehydes to provide either products of carbonyl crotylation or β,γ-enones (Scheme 16) [275,276].

3.3 Alkynes as Allylmetal Surrogates via Transfer Hydrogenation

As demonstrated in recent work by Obora and Ishii, alkynes serve as allyl donors in carbonyl allylations from the alcohol oxidation level [277]. Specifically, upon exposure to an iridium catalyst generated in situ from $[Ir(OH)(cod)]_2$ and $P(n\text{-}Oct)_3$, 1-aryl-2-methylalkynes couple to primary alcohols to furnish homoallylic alcohols with complete branched regioselectivity and excellent levels of diastereoselectivity (Scheme 17).

For alkyne-mediated allylation, alcohol dehydrogenation generates an iridium hydride that hydrometallates the alkyne to form a vinylmetal species, which, in turn, isomerizes to generate the primary σ-allyliridium intermediate. Carbonyl addition through a closed six-

centered transition state accounts for the observed *anti*-diastereoselectivity (Scheme 18). Interestingly, under the conditions of ruthenium-catalyzed transfer hydrogenation, alkynes couple to alcohols or aldehydes to provide products of carbonyl vinylation [278]. Here, isomerization of the vinyl-ruthenium intermediate to the σ-allylruthenium intermediate is not observed.

3.4 Allylic Acetates as Allylmetal Surrogates via Transfer Hydrogenation

Using allyl acetate as the allyl donor, enantioselective variants of the parent carbonyl allylation process are achieved under the conditions of iridium-catalyzed transfer hydrogenation employing the cyclometallated iridium *C,O*-benzoate derived from allyl acetate, 3-nitrobenzoic acid, and a chiral *bis*-phosphine ligand, which is generated in situ [279,280]. Allyl acetate couples to diverse alcohols to furnish products of carbonyl allylation with exceptional levels of enantioselectivity. Identical products of carbonyl allylation are produced from the corresponding aldehydes upon use of isopropanol as terminal reductant. Thus, enantioselective carbonyl allylation is achieved from the alcohol or aldehyde oxidation level in the absence of metallic reagents or metallic reductants. The reactivity embodied by these processes is remarkable in light of the fact that iridium-catalyzed allylic substitution (*O*-allylation) employing alcohol nucleophiles is a well-established mode of reactivity (Scheme 19) [281–283].27

The results of deuterium labeling are consistent with intervention of a symmetric iridium π-allyl intermediate or rapid interconversion of σ-allyl haptomers through the agency of a symmetric π-allyl (Scheme 20) [280]. Competition experiments akin to those previously described (see Scheme 12) again demonstrate rapid and reversible dehydrogenation of the carbonyl partner in advance of C–C coupling.

The BINAP derivative of the *ortho*-cyclometallated iridium catalyst has been characterized by single crystal X-ray diffraction analysis [280]. Remarkably, although the reaction sequence depends upon oxidation of either the reactant alcohol or isopropanol, the enantiomeric purity of the homoallylic alcohol product is not subject to erosion through reversible dehydrogenation as the pendant alkene of the product prevents dehydrogenation by occupying the single remaining vacant coordination site on iridium, as required for β-hydride elimination (Scheme 21).

A model accounting for the observed sense of absolute stereoinduction is based upon the coordination mode revealed in the crystal structure of the cyclometallated *C,O*-benzoate complex [280]. It is postulated that aldehyde binding by the σ-allyl haptomer occurs such that the allyl moiety is placed between the naphthyl and phenyl moieties of the ligand, allowing the aldehyde to reside in a more open environment. In the favored mode of addition, the aldehyde C–H bond projects into the π-face of a phenyl moiety of the ligand, potentially resulting in a weakly attractive aldehyde C–H–π interaction. The disfavored mode of addition requires the aldehyde substituent to project into the π-face of the ligand phenyl moiety, resulting in a severe nonbonded interaction (Fig. 3).

Direct asymmetric carbonyl allylation from the alcohol oxidation level potentially streamlines synthesis by circumventing discrete alcohol oxidation as well as enabling carbonyl allylation processes that are unattainable using conventional allylmetal reagents. For example, two-directional chain elongation via double allylation of 1,3-dialdehydes has not been achieved due to the instability of the requisite 1,3-dicarbonyl precursors (For a review on two-directional chain synthesis, see: [285]). However, propane-1,3-diol and

[27]Under the conditions of ruthenium catalysis, alcohols and allylic acetates couple to form enones, see [284].

related glycols are highly tractable and participate in bidirectional allylation via sequential generation and capture of transient monoaldehydes to provide C_2-symmetric adducts in good yield [286]. In these processes, the minor enantiomer of the monoallylated intermediate is transformed to the *meso*-stereoisomer of the product, thus amplifying the level of enantiomeric enrichment (Scheme 22) (This mechanism for enantiomeric enrichment is documented by Eliel and Midland: [287,288]).

Iterative two-directional chain elongation enables rapid construction of 1,3-polyols (Scheme 23). For example, the polyol substructure that appears in the oxopolyene macrolide (+)-roxaticin is available in nine steps from propane-1,3-diol upon three iterations of double carbonyl allylation [286]. Notably, high levels of catalyst-directed stereoselectivity are observed (For selected examples of catalyst directed diastereoselectivity, see: [289–296]). Analogous 1,3-polyol syntheses via iterative homologation in one direction also are reported [297].

This carbonyl allylation strategy is extended to crotylation through the use of α-methyl allyl acetate as a crotylmetal surrogate [298]. Here, after screening several ortho-cyclometallated *C,O*-benzoates, the iridium complex derived from 4-cyano-3-nitrobenzoic acid and (*S*)-SEGPHOS [272] was found to provide good levels of *anti*-diastereoselectivity accompanied by uniformly high levels of enantioselectivity across a broad range of substrates. Notably, complete branch-regioselectivity is observed in all cases. The observed regio- and *anti*-diastereoselectivity suggest that aldehyde addition occurs from the primary (*E*)-σ-allyliridium haptomer. As before, carbonyl crotylation is achieved with equal facility from the aldehyde or alcohol oxidation level (Scheme 24).

Allylic *gem*-dibenzoates derived from acrolein serve as (alkoxy)allylmetal surrogates under the conditions of iridium-catalyzed transfer hydrogenation [299]. In this case, generation of the catalytic complex in situ failed to provide the desired products in good yield, requiring use of the isolated complex prepared from $[Ir(cod)\ Cl]_2$, 4-cyano-3-nitrobenzoic acid, allyl acetate, and the chiral phosphine ligand (*R*)-SEGPHOS [272]. To achieve high levels of *anti*-diastereoselectivity, efficient partitioning of transient (*E*)- and (*Z*)-σ-allyliridium intermediates is required. It was found that the allylic *gem*-dibenzoate derived from acrolein is unique in its ability to combine high levels of *anti*-diastereoselectivity and favorable reactivity. Under the reported conditions, iridium-catalyzed aldehyde *anti*-(hydroxy)allylation occurs under transfer hydrogenation conditions to provide *anti*-1-ene-3,4-diols with excellent relative and absolute stereocontrol. Corresponding carbonyl additions from the alcohol oxidation level are currently under development (Scheme 25).

New catalytic allylation methodologies continue to emerge. For example, iridium-catalyzed transfer hydrogenation of α-(trimethylsilyl)allyl acetate in the presence of aldehydes mediated by isopropanol and employing the iridium catalyst modified by (*R*)-SEGPHOS [272] delivers products of (trimethylsilyl)allylation in good isolated yields and with exceptional levels of *anti*-diastereo and enantiocontrol [300]. In the absence of isopropanol, carbonyl (trimethylsilyl)allylation is achieved directly from the alcohol oxidation level to furnish an equivalent set of adducts (Scheme 26, top). Similarly, using the enantiomeric iridium complex, the indicated cyclic carbonate engages in carbonyl (hydroxymethyl)allylation from the alcohol or aldehyde oxidation level with good *anti*-diastereoselectivities and exceptional levels of enantiocontrol [301]. Notably, stereoselective (hydroxymethyl) allylation protocols employing conventional allylmetal reagents are unknown (Scheme 26, bottom).[28,29,30]

[28]For (hydroxymethyl)allylation via palladium catalyzed reductive coupling of allylic carboxylates, see [302–304].
[29]For (hydroxymethyl)allylation via palladium catalyzed reductive coupling of vinyl epoxides, see [305,306].

Enantioselective ketone addition is one of the many challenging extensions in scope that remains. In a preliminary step toward this goal, the allylation, crotylation, and *tert*-prenylation of substituted isatins was examined using the cyclometallated iridium *C,O*-benzoate generated in situ from $[Ir(cod)Cl]_2$, 4-chloro-3-nitrobenzoic acid and CTH-(*R*)-P-PHOS [309]. Isopropanol-mediated transfer hydrogenation of allyl acetate, α-methyl allyl acetate or 1,1,-dimethylallene as allyl donors, in the presence of the substituted isatins delivered the anticipated products of allylation, crotylation, and *tert*-prenylation, respectively, in highly enantiomerically enriched form. Notably, highly enantioselective allylation, crotylation, and reverse prenylation of isatins employing conventional allylmetal reagents have not been reported (Scheme 27) (For enantioselective catalytic allylation of isatins, see: [310]).

4 Conclusion

Organic molecules are defined as compounds of carbon and hydrogen. Hence, the formation of C–C bonds under the conditions catalytic hydrogenation and transfer hydrogenation is a natural endpoint in the evolution of strategies for the synthesis of organic molecules. The use of unsaturates as surrogates to premetallated nucleophiles under hydrogenation conditions represents a departure from the use of stoichiometric organometallic reagents in carbonyl and imine addition that circumvents generation of stoichiometric byproducts. This concept is extended further via C–C bond-forming transfer hydrogenation – processes in which alcohol reactants serve dually as hydrogen donors and carbonyl precursors, enabling carbonyl addition directly from the alcohol oxidation level in the absence of stoichiometric byproducts and premetallated nucleophiles.

As highlighted in this review, iridium complexes are especially versatile catalysts for C–C bond-forming hydrogenation and transfer hydrogenation. And now, based on these studies, many aspirational transformations are placed within reach (Scheme 28). However, to fully realize the potential of hydrogen-mediated C–C coupling, alternate metal catalysts should be developed and applied to processes beyond those described herein. This challenge will ultimately evoke catalytic methods for the sustainable manufacture of pharmaceutical ingredients, bulk chemicals, and fuels from renewable feedstocks.

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References

1. Board on Chemical Sciences and Technology, National Research Council of the National Academies. Sustainability in the chemical industry: grand challenges and research needs. National Academies Press; Washington, DC: 2005.
2. Nobel Foundation. Nobel lectures, chemistry, 1901–1921. Elsevier; Amsterdam: 1966.
3. Smil, V. Enriching the earth: Fritz Haber, Carl Bosch, and the transformation of world food production. MIT; Cambridge, MA: 2004.
4. Roelen, O. Chemische Verwertungsgesellschaft mbH. German Patent. DE 849,548. 1938.
5. Roelen O. Chemische Verwertungsgesellschaft mbH. Chem Abstr. 1944; 38:5501.

[30]For catalytic enantioselective (hydroxymethyl)allylation, see [307,308].

6. Frohning, CD.; Kohlpaintner, CW. Applied homogeneous catalysis with organometallic compounds. Cornils, B.; Herrmann, WA., editors. Vol. vol 1. VCH; Weinheim: 1996. p. 29
7. van Leeuwen, PWNM. Homogeneous catalysis, understanding the art. Kluwer; Dordrecht: 2004.
8. Thommen M. Spec Chem Mag. 2005; 25(4):26.
9. Thayer A. Chem Eng News. 2005; 83(36):40.
10. Jäkel C, Paciello R. Chem Rev. 2006; 106:2912. [PubMed: 16836304]
11. Ngai M-Y, Kong JR, Krische MJ. J Org Chem. 2007; 72:1063. [PubMed: 17288361]
12. Skucas E, Ngai M-Y, Komanduri V, Krische MJ. Acc Chem Res. 2007; 40:1394. [PubMed: 17784728]
13. Iida H, Krische MJ. Top Curr Chem. 2007; 279:77.
14. Shibahara F, Krische MJ. Chem Lett. 2008; 37:1102.
15. Bower JF, Kim IS, Patman RL, Krische MJ. Angew Chem Int Ed. 2009; 48:34.
16. Han SB, Kim IS, Krische MJ. Chem Commun. 2009:7278.
17. Bower, JF.; Krische, MJ. Handbook of green chemistry. Anastas, P., editor. Vol. vol 1. VCH; Weinheim: 2009. p. 205
18. Molander GA, Hoberg JO. J Am Chem Soc. 1992; 114:3123.
19. Kokubo K, Miura M, Nomura M. Organometallics. 1995; 14:4521.
20. Moyes, RB.; Walker, DW.; Wells, PB.; Whan, DA.; Irvine, EA. Catalysis and surface characterisation (special publication). Dines, TJ.; Rochester, CH.; Thomson, J., editors. Vol. vol 114. Royal Society of Chemistry; London: 1992. p. 207
21. Bianchini C, Meli A, Peruzzini M, Vizza F, Zanobini F, Frediani P. Organometallics. 1989; 8:2080.
22. Guillena G, Ramón DJ, Yus M. Angew Chem Int Ed. 2007; 46:2358.
23. Hamid MHSA, Slatford PA, Williams JMJ. Adv Synth Catal. 2007; 349:1555.
24. Nixon TD, Whittlesey MK, Williams JMJ. Dalton Trans. 2009:753. [PubMed: 19156265]
25. Guillena G, Ramón DJ, Yus M. Chem Rev. 2010; 110:1611. [PubMed: 19928825]
26. Shi L, Tu Y-Q, Wang M, Zhang F-M, Fan C-A, Zhao Y-M, Xia WJ. J Am Chem Soc. 2005; 127:10836. [PubMed: 16076182]
27. Jiang Y-J, Tu Y-Q, Zhang E, Zhang S-Y, Cao K, Shi L. Adv Synth Catal. 2008; 350:552.
28. Zhang S-Y, Tu Y-Q, Fan C-A, Zhang F-M, Shi L. Angew Chem Int Ed. 2009; 48:8761.
29. Zhang S-Y, Tu Y-Q, Fan C-A, Jiang Y-J, Shi L, Cao K, Zhang E. Chem Eur J. 2008; 14:10201.
30. Kamitanaka T, Hikida T, Hayashi S, Kishida N, Matsuda T, Harada T. Tetrahedron Lett. 2007; 48:8460.
31. Liu Z-Q, Sun L, Wang J-G, Han J, Zhao YK, Zhou B. Org Lett. 2009; 11:1437. [PubMed: 19243113]
32. Seidel, A., editor. Kirk-Othmer's encyclopedia of chemical technology. 5th edn. Vol. vol 2. Wiley; Hoboken: 2004. p. 234
33. Banerjee AK, Poon PS, Laya MS, Vera WJ. Russ Chem Rev. 2004; 73:621.
34. Cheikh RB, Chaabouni R, Laurent A, Mison P, Nafti A. Synthesis. 1983:685.
35. Laurent A, Mison P, Nafti A, Cheikh RB, Chaabouni R. J Chem Res. 1984:354.
36. Johannsen M, Jørgensen KA. Chem Rev. 1998; 98:1689. [PubMed: 11848944]
37. Acemoglu, L.; Williams, JMJ. Handbook of organopalladium chemistry for organic synthesis. Negishi, E-i; de Meijere, A., editors. Vol. vol 2. Wiley; New York: 2002. p. 1689
38. Trost BM, Crawley ML. Chem Rev. 2003; 103:2921. [PubMed: 12914486]
39. Trost BM. J Org Chem. 2004; 69:5813. [PubMed: 15373468]
40. Miyabe H, Takemoto Y. Synlett. 2005:1641.
41. Takeuchi R, Kezuka S. Synthesis. 2006:3349.
42. Helmchen G, Dahnz A, Duebon P, Schelwies M, Weihofen R. Chem Commun. 2007:675.
43. Lu Z, Ma S. Angew Chem Int Ed. 2008; 47:258.
44. Oguni N, Omi T. Tetrahedron Lett. 1984; 25:2823.

45. Kitamura M, Suga S, Kawai K, Noyori R. J Am Chem Soc. 1986; 108:6071.
46. Pu L, Yu H-B. Chem Rev. 2001; 101:757. [PubMed: 11712502]
47. Betancort JM, Garcia C, Walsh PJ. Synlett. 2004:749.
48. Ramón DJ, Yus M. Angew Chem Int Ed. 2004; 43:284.
49. Garcia C, Martin VS. Curr Org Chem. 2006; 10:1849.
50. Ramón DJ, Yus M. Chem Rev. 2006; 106:2126. [PubMed: 16771446]
51. Hatano M, Ishihara K. Chem Rec. 2008; 8:143. [PubMed: 18563831]
52. Oppolzer W, Radinov R. Helv Chim Acta. 1992; 75:170.
53. Oppolzer W, Radinov R. J Am Chem Soc. 1993; 115:1593.
54. Soai K, Takahashi KJ. Chem Soc Perkin Trans. 1994; 1:1257.
55. Wipf P, Xu W. Tetrahedron Lett. 1994; 35:5197.
56. Oppolzer W, Radinov RN, De Brabander J. Tetrahedron Lett. 1995; 36:2607.
57. Wipf P, Ribe S. J Org Chem. 1998; 63:6454.
58. Oppolzer W, Radinov RN, El-Sayed E. J Org Chem. 2001; 66:4766. [PubMed: 11442401]
59. Dahmen S, Bräse S. Org Lett. 2001; 3:4119. [PubMed: 11735599]
60. Chen YK, Lurain AE, Walsh PJ. J Am Chem Soc. 2002; 124:12225. [PubMed: 12371863]
61. Ji J-X, Qiu L-Q, Yip CW, Chan ASC. J Org Chem. 2003; 68:1589. [PubMed: 12585911]
62. Lurain AE, Walsh PJ. J Am Chem Soc. 2003; 125:10677. [PubMed: 12940753]
63. Ko D-H, Kang S-W, Kim KH, Chung Y, Ha D-C. Bull Korean Chem Soc. 2004; 25:35.
64. Sprout CM, Richmond ML, Seto CT. J Org Chem. 2004; 69:6666. [PubMed: 15387588]
65. Jeon S-J, Chen YK, Walsh PJ. Org Lett. 2005; 7:1729. [PubMed: 15844892]
66. Lauterwasser F, Gall J, Hoefener S, Bräse S. Adv Synth Catal. 2006; 348:2068.
67. Jeon S-J, Fisher EL, Carroll PJ, Walsh PJ. J Am Chem Soc. 2006; 128:9618. [PubMed: 16866501]
68. Salvi L, Jeon S-J, Fisher EL, Carroll PJ, Walsh PJ. J Am Chem Soc. 2007; 129:16119. [PubMed: 18052173]
69. Wu H-L, Wu P-Y, Uang B-J. J Org Chem. 2007; 72:5935. [PubMed: 17595146]
70. Chai Z, Liu X-Y, Zhang J-K, Zhao G. Tetrahedron Asymmetry. 2007; 18:724.
71. Wipf P, Kendall C. Chem Eur J. 2002; 8:1778.
72. Wipf P, Nunes RL. Tetrahedron. 2004; 60:1269.
73. Ramón DJ, Yus M. Tetrahedron Lett. 1998; 39:1239.
74. Ramón DJ, Yus M. Tetrahedron. 1998; 54:5651.
75. Dosa PI, Fu GC. J Am Chem Soc. 1998; 120:445.
76. Li H, Walsh PJ. J Am Chem Soc. 2004; 126:6538. [PubMed: 15161266]
77. Li H, Walsh PJ. J Am Chem Soc. 2005; 127:8355. [PubMed: 15941269]
78. Jeon S-J, Li H, Garcia C, La Rochelle LK, Walsh PJ. J Org Chem. 2005; 70:448. [PubMed: 15651785]
79. Schmidt F, Rudolph J, Bolm C. Synthesis. 2006:3625.
80. Bloch R. Chem Rev. 1998; 98:1407. [PubMed: 11848938]
81. Kobayashi S, Ishitani H. Chem Rev. 1999; 99:1069. [PubMed: 11749440]
82. Vilaivan T, Bhanthumnavin W, Sritana-Anant Y. Curr Org Chem. 2005; 9:1315.
83. Schmidt F, Stemmler RT, Rudolph J, Bolm C. Chem Soc Rev. 2006; 35:454. [PubMed: 16636728]
84. K-i Y, Tomioka K. Chem Rev. 2008; 108:2874. [PubMed: 18652515]
85. Soai K, Hatanaka T, Miyazawa T. J Chem Soc Chem Commun. 1992:1097.
86. Katritsky AR, Harris PA. Tetrahedron Asymmetry. 1992; 3:437.
87. Andersson PG, Guijarro D, Tanner D. Synlett. 1996:727.
88. Andersson PG, Guijarro D, Tanner D. J Org Chem. 1997; 62:7364. [PubMed: 11671853]
89. Guijarro D, Pinho P, Andersson PG. J Org Chem. 1998; 63:2530. [PubMed: 11672115]
90. Brandt P, Hedberg C, Lawonn K, Pinho P, Andersson PG. Chem Eur J. 1999; 5:1692.

91. Jimeno C, Reddy S, Sola L, Moyano A, Pericas MA, Riera A. Org Lett. 2000; 2:3157. [PubMed: 11009370]
92. Sato I, Kodaka R, Soai K. J Chem Soc Perkin Trans 1. 2001; 22:2912.
93. Zhang X, Lin W, Gong L, Mi A, Cui X, Jiang Y, Choi MCK, Chan ASC. Tetrahedron Lett. 2002; 43:1535.
94. Sato I, Hosoi K, Kodaka R, Soai K. Eur J Org Chem. 2002; 18:3115.
95. Liu H, Zhang H-L, Wang S-J, Mi A-Q, Jiang Y-Z, Gong L-Z. Tetrahedron Asymmetry. 2005; 16:2901.
96. Almansa R, Guijarro D, Yus M. Tetrahedron Asymmetry. 2007; 18:2828.
97. Fujihara H, Nagai K, Tomioka K. J Am Chem Soc. 2000; 122:12055.
98. Nagai K, Fujihara H, Kuriyama M, Yamada K-I, Tomioka K. Chem Lett. 2002:8.
99. Shi M, Wang C-J. J Org Chem. 2003; 68:6229. [PubMed: 12895055]
100. Soeta T, Nagai K, Fujihara H, Kuriyama M, Tomioka K. J Org Chem. 2003; 68:9723. [PubMed: 14656099]
101. Shi M, Zhang W. Tetrahedron Asymmetry. 2003; 14:3407.
102. Shi M, Wang C-J. Adv Synth Catal. 2003; 345:971.
103. Boezio AA, Charette AB. J Am Chem Soc. 2003; 125:1692. [PubMed: 12580582]
104. Boezio AA, Pytkowicz J, Côté A, Charette AB. J Am Chem Soc. 2003; 125:14260. [PubMed: 14624558]
105. Côté A, Boezio AA, Charette AB. Proc Nat Acad Sci U S A. 2004; 101:5405.
106. Côté A, Boezio AA, Charette AB. Angew Chem Int Ed. 2004; 43:6525.
107. Wang M-C, Xu C-L, Zou Y-X, Liu H-M, Wang D-K. Tetrahedron Lett. 2005; 46:5413.
108. Desrosiers J-N, Côté A, Charette AB. Tetrahedron. 2005; 61:6186.
109. Wang M-C, Liu L-T, Hua Y-Z, Zhang J-S, Shi Y-Y, Wang D-K. Tetrahedron Asymmetry. 2005; 16:2531.
110. Kim B-S, Kang S-W, Kim KH, Ko D-H, Chung Y, Ha DC. Bull Korean Chem Soc. 2005; 26:1501.
111. Lauzon C, Charette AB. Org Lett. 2006; 8:2743. [PubMed: 16774246]
112. Wang M-C, Xu C-L, Cheng F, Ding X. Tetrahedron. 2006; 62:12220.
113. Shi M, Lei Z-Y, Xu Q. Adv Synth Catal. 2006; 348:2237.
114. Chen J, Li D, Ma H, Cun L, Zhu J, Deng J, Liao J. Tetrahedron Lett. 2008; 49:6921.
115. Perron Q, Alexakis A. Tetrahedron Asymmetry. 2008; 19:1871.
116. Pizzuti MG, Minnaard AJ, Feringa BL. J Org Chem. 2008; 73:940. [PubMed: 18171081]
117. Nishimura T, Yasuhara Y, Hayashi T. Org Lett. 2006; 8:979. [PubMed: 16494489]
118. Chen J, Li D, Ma H, Cun L, Zhu J, Deng J, Liao J. Tetrahedron Lett. 2008; 49:6921.
119. Porter JR, Traverse JF, Hoveyda AH, Snapper ML. J Am Chem Soc. 2001; 123:984. [PubMed: 11456637]
120. Porter JR, Traverse JF, Hoveyda AH, Snapper ML. J Am Chem Soc. 2001; 123:10409. [PubMed: 11604001]
121. Akullian LC, Snapper ML, Hoveyda AH. Angew Chem Int Ed. 2003; 42:4244.
122. Akullian LC, Porter JR, Traverse JF, Snapper ML, Hoveyda AH. Adv Synth Catal. 2005; 347:417.
123. Basra S, Fennie MW, Kozlowski MC. Org Lett. 2006; 8:2659. [PubMed: 16774225]
124. Fu P, Snapper ML, Hoveyda AH. J Am Chem Soc. 2008; 130:5530. [PubMed: 18376838]
125. Tomioka K. Synthesis. 1990:541.
126. Berrisford DJ. Angew Chem Int Ed. 1995; 34:178.
127. Denmark SE, Nicaise OJ-C. Chem Commun. 1996:999.
128. Enders D, Reinhold U. Tetrahedron Asymmetry. 1997; 8:1895.
129. Luderer MR, Bailey WF, Luderer MR, Fair JD, Dancer RJ, Sommer MB. Tetrahedron Asymmetry. 2009; 20:981.

130. Goldfuss B. Top Organomet Chem. 2003; 5:21.
131. Iguchi M, K-i Y, Tomioka K. Top Organomet Chem. 2003; 5:37.
132. Goldfuss B. Synthesis. 2005; 14:2271.
133. Hayashi T, Ishigedani M. J Am Chem Soc. 2000; 122:976.
134. Hayashi T, Ishigedani M. Tetrahedron. 2001; 57:2589.
135. Hayashi T, Kawai M, Tokunaga N. Angew Chem Int Ed. 2004; 43:6125.
136. Kuriyama M, Soeta T, Hao X, Chen Q, Tomioka K. J Am Chem Soc. 2004; 126:8128. [PubMed: 15225049]
137. Tokunaga N, Otomaru Y, Okamoto K, Ueyama K, Shintani R, Hayashi T. J Am Chem Soc. 2004; 126:13584. [PubMed: 15493893]
138. Weix DJ, Shi Y, Ellman JA. J Am Chem Soc. 2005; 127:1092. [PubMed: 15669835]
139. Otomaru Y, Tokunaga N, Shintani R, Hayashi T. Org Lett. 2005; 7:307. [PubMed: 15646984]
140. Duan H-F, Jia Y-X, Wang L-X, Zhou Q-L. Org Lett. 2006; 8:2567. [PubMed: 16737315]
141. Wang Z-Q, Feng C-G, Xu M-H, Lin G-Q. J Am Chem Soc. 2007; 129:5336. [PubMed: 17425322]
142. Marelli C, Monti C, Gennari C, Piarulli U. Synlett. 2007; 14:2213.
143. Nakagawa H, Rech JC, Sindelar RW, Ellman JA. Org Lett. 2007; 9:5155. [PubMed: 17988138]
144. Trincado M, Ellman JA. Angew Chem Int Ed. 2008; 47:5623.
145. Kurihara K, Yamamoto Y, Miyaura N. Adv Synth Catal. 2009; 351:260.
146. Okamoto K, Hayashi T, Rawal VH. Chem Commun. 2009:4815.
147. Kakuuchi A, Taguchi T, Hanzawa Y. Tetrahedron Lett. 2003; 44:923.
148. Wipf P, Kendall C, Stephenson CRJ. J Am Chem Soc. 2003; 125:761. [PubMed: 12526676]
149. Patel SJ, Jamison TF. Angew Chem Int Ed. 2004; 432:3941.
150. Top Curr Chem. 2007; 279:1.
151. Ojima I, Tzamarioudaki M, Li Z, Donovan RJ. Chem Rev. 1996; 96:635. [PubMed: 11848768]
152. Montgomery J. Acc Chem Res. 2000; 33:467. [PubMed: 10913235]
153. Montgomery J, Amarashinghe KKD, Chowdhury SK, Oblinger E, Seo J, Savchenko AV. Pure Appl Chem. 2002; 74:129.
154. Ikeda S-I. Angew Chem Int Ed. 2003; 42:5120.
155. Miller KM, Molinaro C, Jamison TF. Tetrahedron Asymmetry. 2003; 14:3619.
156. Montgomery J. Angew Chem Int Ed. 2004; 43:3890.
157. Montgomery J, Sormunen GJ. Top Curr Chem. 2007; 279:1.
158. Moslin RM, Miller-Moslin K, Jamison TF. Chem Commun. 2007:4441.
159. Ojima I, Tzamarioudaki M, Tsai C-Y. J Am Chem Soc. 1994; 116:3643.
160. Crowe WE, Rachita MJ. J Am Chem Soc. 1995; 117:6787.
161. Kablaoui NM, Buchwald SL. J Am Chem Soc. 1995; 117:6785.
162. Oblinger E, Montgomery J. J Am Chem Soc. 1997; 119:9065.
163. Tang X-Q, Montgomery J. J Am Chem Soc. 1999; 121:6098.
164. Tang X-Q, Montgomery J. J Am Chem Soc. 2000; 122:6950.
165. Mahandru GM, Liu G, Montgomery J. J Am Chem Soc. 2004; 126:3698. [PubMed: 15038707]
166. Knapp-Reed B, Mahandru GM, Montgomery J. J Am Chem Soc. 2005; 127:13156. [PubMed: 16173738]
167. Chaulagain MR, Sormunen GJ, Montgomery J. J Am Chem Soc. 2007; 129:9568. [PubMed: 17628066]
168. Huang W-S, Chan J, Jamison TF. Org Lett. 2000; 2:4221. [PubMed: 11150204]
169. Miller KM, Huang W-S, Jamison TF. J Am Chem Soc. 2003; 125:3442. [PubMed: 12643701]
170. Miller KM, Jamison TF. Org Lett. 2005; 7:3077. [PubMed: 15987209]
171. Liu P, McCarren P, Cheong PH-Y, Jamison TF, Houk KN. J Am Chem Soc. 2010; 132:2050. [PubMed: 20095609]
172. Takai K, Sakamoto S, Isshiki T. Org Lett. 2003; 5:653. [PubMed: 12605482]

173. Ngai M-Y, Barchuk A, Krische MJ. J Am Chem Soc. 2007; 129:280. [PubMed: 17212400]
174. Kong J-R, Ngai M-Y, Krische MJ. J Am Chem Soc. 2006; 128:718. [PubMed: 16417351]
175. Cho C-W, Krische MJ. Org Lett. 2006; 8:3873. [PubMed: 16898839]
176. Hong Y-T, Cho C-W, Skucas E, Krische MJ. Org Lett. 2007; 9:3745. [PubMed: 17705502]
177. Komanduri V, Krische MJ. J Am Chem Soc. 2006; 128:16448. [PubMed: 17177363]
178. Komanduri V, Grant CD, Krische MJ. J Am Chem Soc. 2008; 130:12592. [PubMed: 18759388]
179. Kong J-R, Krische MJ. J Am Chem Soc. 2006; 128:16040. [PubMed: 17165749]
180. Skucas E, Kong J-R, Krische MJ. J Am Chem Soc. 2007; 129:7242. [PubMed: 17511459]
181. Han SB, Kong J-R, Krische MJ. Org Lett. 2008; 10:4133. [PubMed: 18729371]
182. Williams VM, Kong J-R, Ko B-J, Mantri Y, Brodbelt JS, Baik M-H, Krische MJ. J Am Chem Soc. 2009; 131:16054. [PubMed: 19845357]
183. Dewar MJS. Bull Soc Chim Fr. 1951:C71.
184. Chatt J, Duncanson LA. J Chem Soc. 1953:2939.
185. Dewar MJS, Ford GP. J Am Chem Soc. 1979; 101:783.
186. Li J, Schreckenbach G, Ziegler T. J Am Chem Soc. 1995; 117:486.
187. Vaska L, Peone J Jr. Chem Commun. 1971:418.
188. Haynes A, McNish J, Pearson JMJ. Organomet Chem. 1998; 551:339.
189. Grotjohn DB, Collins LSB, Wolpert M, Bikzhanova GA, Lo HC, Combs D, Hubbard JL. J Am Chem Soc. 2001; 123:8260. [PubMed: 11516277]
190. Kirchner RM, Ibers JA. J Am Chem Soc. 1973; 95:1095.
191. Calabrese JC, Roe DC, Thorn DL, Tulip TH. Organometallics. 1984; 3:1223.
192. Rappoli BJ, Churchill MR, Janik TS, Rees WM, Atwood JD. J Am Chem Soc. 1987; 109:5145.
193. Rees WM, Churchill MR, Fettinger JC, Atwood JD. J Organomet Chem. 1987; 319:411.
194. Marinelli G, Streib WE, Huffman JC, Caulton KG, Gagne MR, Takats J, Dartiguenave M, Chardon C, Jackson SA, Eisenstein O. Polyhedron. 1990; 9:1867.
195. Musashi Y, Sakaki S. J Am Chem Soc. 2002; 124:7588. [PubMed: 12071769]
196. Barchuk A, Ngai M-Y, Krische MJ. J Am Chem Soc. 2007; 129:8432. [PubMed: 17571894]
197. Ngai M-Y, Barchuk A, Krische MJ. J Am Chem Soc. 2007; 129:12644. [PubMed: 17914825]
198. Fujita, K-i; Yamashita, M.; Puschmann, F.; Alvarez-Flacon, MM.; Incarvito, CD.; Hartwig, JF. J Am Chem Soc. 2006; 128:9044. [PubMed: 16834372]
199. Ramachandran PV. Aldrichim Acta. 2002; 35:23.
200. Kennedy JWJ, Hall DG. Angew Chem Int Ed. 2003; 42:4732.
201. Denmark SE, Fu J. Chem Rev. 2003; 103:2763. [PubMed: 12914480]
202. Yu C-M, Youn J, Jung H-K. Bull Korean Chem Soc. 2006; 27:463.
203. Marek I, Sklute G. Chem Commun. 2007:1683.
204. Hall DG. Synlett. 2007:1644.
205. Mikhailov BM, Bubnov YN. Izv Akad Nauk SSSR, Ser Khim. 1964:1874.
206. Hosomi A, Sakurai H. Tetrahedron Lett. 1976; 17:1295.
207. Herold T, Hoffmann RW. Angew Chem Int Ed Engl. 1978; 17:768.
208. Hoffmann RW, Herold T. Chem Ber. 1981; 114:375.
209. Hayashi T, Konishi M, Kumada M. J Am Chem Soc. 1982; 104:4963.
210. Brown HC, Jadhav PK. J Am Chem Soc. 1983; 105:2092.
211. Roush WR, Walts AE, Hoong LK. J Am Chem Soc. 1985; 107:8186.
212. Reetz M. Pure Appl Chem. 1988; 60:1607.
213. Short RP, Masamune S. J Am Chem Soc. 1989; 111:1892.
214. Corey EJ, Yu C-M, Kim SS. J Am Chem Soc. 1989; 111:5495.
215. Seebach D, Beck AK, Imwinkeiried R, Roggo S, Wonnacott A. Helv Chim Acta. 1987; 70:954.
216. Riediker M, Duthaler RO. Angew Chem Int Ed Engl. 1998; 28:494.
217. Panek JS, Yang M. J Am Chem Soc. 1991; 113:6594.

218. Kinnaird JWA, Ng PY, Kubota K, Wang X, Leighton JL. J Am Chem Soc. 2002; 124:7920. [PubMed: 12095334]
219. Hackman BM, Lombardi PJ, Leighton JL. Org Lett. 2004; 6:4375. [PubMed: 15524487]
220. Burgos CH, Canales E, Matos K, Soderquist JA. J Am Chem Soc. 2005; 127:8044. [PubMed: 15926828]
221. Furuta K, Mouri M, Yamamoto H. Synlett. 1991:561.
222. Costa AL, Piazza MG, Tagliavini E, Trombini C, Umani-Ronchi A. J Am Chem Soc. 1993; 115:7001.
223. Keck GE, Tarbet KH, Geraci LS. J Am Chem Soc. 1993; 115:8467.
224. Denmark SE, Coe DM, Pratt NE, Griedel BD. J Org Chem. 1994; 59:6161.
225. Tabuchi T, Inanaga J, Yamaguchi M. Tetrahedron Lett. 1986; 27:1195.
226. Takahara JP, Masuyama Y, Kurusu Y. J Am Chem Soc. 1992; 114:2577.
227. Kimura M, Ogawa Y, Shimizu M, Sueishi M, Tanaka S, Tamaru Y. Tetrahedron Lett. 1998; 39:6903.
228. Kimura M, Tomizawa T, Horino Y, Tanaka S, Tamaru Y. Tetrahedron Lett. 2000; 41:3627.
229. Kimura M, Shimizu M, Shibata K, Tazoe M, Tamaru Y. Angew Chem Int Ed. 2003; 42:3392.
230. Zanoni G, Gladiali S, Marchetti A, Piccinini P, Tredici I, Vidari G. Angew Chem Int Ed. 2004; 43:846.
231. Kimura M, Shimizu M, Tanaka S, Tamaru Y. Tetrahedron. 2005; 61:3709.
232. Howell GP, Minnaard AJ, Feringa BL. Org Biomol Chem. 2006; 4:1278.
233. Barczak NT, Grote RE, Jarvo ER. Organometallics. 2007; 26:4863.
234. Masuyama Y, Kaneko Y, Kurusu Y. Tetrahedron Lett. 2004; 45:8969.
235. Vasylyev M, Alper H. J Org Chem. 2010 doi:10.1021/jo902706p.
236. Tsuji Y, Mukai T, Kondo T, Watanabe Y. J Organomet Chem. 1989; 369:C51.
237. Kondo T, Ono H, Satake N, Mitsudo T-a, Watanabe Y. Organometallics. 1945; 1995:14.
238. Denmark SE, Nguyen ST. Org Lett. 2009; 11:781. [PubMed: 19175354]
239. Masuyama Y, Chiyo T, Kurusu Y. Synlett. 2005; 14:2251.
240. Banerjee M, Roy S. J Mol Catal A. 2006; 246:231.
241. Masuyama Y, Marukawa M. Tetrahedron Lett. 2007; 48:5963.
242. Masuyama, Y. Advances in metal-organic chemistry. Liebeskind, LS., editor. Vol. vol 3. JAI; Greenwich: 1994. p. 255
243. Tamaru, Y. Handbook of organopalladium chemistry for organic synthesis. Negishi, E-i; de Meijere, A., editors. Vol. vol 2. Wiley; New York: 2002. p. 1917
244. Tamaru, Y. Perspectives in organopalladium chemistry for the XXI century. Tsuji, J., editor. Elsevier; Amsterdam: 1999. p. 215
245. Kondo T, Mitsudo T-A. Curr Org Chem. 2002; 6:1163.
246. Tamaru Y. Eur J Org Chem. 2005:2647.
247. Zanoni G, Pontiroli A, Marchetti A, Vidari G. Eur J Org Chem. 2007:3599.
248. Bandini M, Cozzi PG, Umani-Ronchi A. Polyhedron. 2000; 19:537.
249. Bandini M, Cozzi PG, Umani-Ronchi A. Tetrahedron. 2001; 57:835.
250. Bandini M, Cozzi PG, Umani-Ronchi A. Angew Chem Int Ed. 2000; 39:2327.
251. Inoue M, Suzuki T, Nakada M. J Am Chem Soc. 2003; 125:1140. [PubMed: 12553795]
252. Lee J-Y, Miller JJ, Hamilton SS, Sigman MS. Org Lett. 2005; 7:1837. [PubMed: 15844919]
253. McManus HA, Cozzi PG, Guiry PJ. Adv Synth Catal. 2006; 348:551.
254. Xia G, Yamamoto H. J Am Chem Soc. 2006; 128:2554. [PubMed: 16492037]
255. Hargaden GC, Müuller-Bunz H, Guiry PJ. Eur J Org Chem. 2007:4235.
256. Hargaden GC, O'Sullivan TP, Guiry PJ. Org Biomol Chem. 2008; 6:562. [PubMed: 18219428]
257. Liu X, Henderson JA, Sasaki T, Kishi Y. J Am Chem Soc. 2009; 131:16678. [PubMed: 19874019]
258. Avalos M, Babiano R, Cintas P, Jiménez JL, Palacios JC. Chem Soc Rev. 1999; 28:169.

259. Bandini M, Cozzi PG, Umani-Ronchi A. Chem Commun. 2002:919.
260. Hargaden GC, Guiry PJ. Adv Synth Catal. 2007; 349:2407.
261. Inoue M, Suzuki T, Kinoshita A, Nakada M. Chem Rec. 2008; 8:169. [PubMed: 18563811]
262. Mikami K, Shimizu M. Chem Rev. 1992; 92:1021.
263. Berrisford DJ, Bolm C. Angew Chem Int Ed. 1995; 34:1717.
264. Johnson JS, Evans DA. Acc Chem Reds. 2000; 33:325.
265. Clarke ML, France MB. Tetrahedron. 2008; 64:9003.
266. Ho C-Y, Ng S-S, Jamison TF. J Am Chem Soc. 2006; 128:5362. [PubMed: 16620106]
267. Ng S-S, Ho C-Y, Jamison TF. J Am Chem Soc. 2006; 128:11513. [PubMed: 16939275]
268. Ho C-Y, Schleicher KD, Chan C-W, Jamison TF. Synlett. 2009:2565.
269. Skucas E, Bower JF, Krische MJ. J Am Chem Soc. 2007; 129:12678. [PubMed: 17900123]
270. Bower JF, Skucas E, Patman RL, Krische MJ. J Am Chem Soc. 2007; 129:15134. [PubMed: 18020342]
271. Han SB, Kim I-S, Han H, Krische MJ. J Am Chem Soc. 2009; 131:6916. [PubMed: 19453190]
272. Saito T, Yokozawa T, Ishizaki T, Moroi T, Sayo N, Miura T, Kumobayashi H. Adv Synth Catal. 2001; 343:264.
273. Bower JF, Patman RL, Krische MJ. Org Lett. 2008; 10:1033. [PubMed: 18254642]
274. Zbieg JR, Fukuzumi T. Adv Synth Catal. 2010; 352 (In Press).
275. Shibahara F, Bower JF, Krische MJ. J Am Chem Soc. 2008; 130:6338. [PubMed: 18444617]
276. Shibahara F, Bower JF, Krische MJ. J Am Chem Soc. 2008; 130:14120. [PubMed: 18841895]
277. Obora Y, Hatanaka S, Ishii Y. Org Lett. 2009; 11:3510. [PubMed: 19719194]
278. Patman RL, Chaulagain MR, Williams VM, Krische MJ. J Am Chem Soc. 2009; 131:2066. [PubMed: 19173651]
279. Kim IS, Ngai M-Y, Krische MJ. J Am Chem Soc. 2008; 130:6340. [PubMed: 18444616]
280. Kim IS, Ngai M-Y, Krische MJ. J Am Chem Soc. 2008; 130:14891. [PubMed: 18841896]
281. Lopez F, Ohmura T, Hartwig JF. J Am Chem Soc. 2003; 125:3426. [PubMed: 12643693]
282. Shu C, Hartwig JF. Angew Chem Int Ed. 2004; 43:4794.
283. Ueno S, Hartwig JF. Angew Chem Int Ed. 2008; 47:1928.
284. Kondo T, Mukai T, Watanabe Y. J Org Chem. 1991; 56:487.
285. Poss CS, Schreiber SL. Acc Chem Res. 1994; 27:9.
286. Lu Y, Kim I-S, Hassan A, Del Valle DJ, Krische MJ. Angew Chem Int Ed. 2009; 48:5018.
287. Kogure T, Eliel ELJ. Org Chem. 1984; 49:576.
288. Midland MM, Gabriel J. J Org Chem. 1985; 50:1144.
289. Minami N, Ko SS, Kishi Y. J Am Chem Soc. 1982; 104:1109.
290. Ko SY, Lee AWM, Masamune S, Reed LA III, Sharpless KB, Walker FJ. Science. 1983; 220:949. [PubMed: 17816019]
291. Kobayashi S, Ohtsubo A, Mukaiyama T. Chem Lett. 1991:831.
292. Hammadi A, Nuzillard JM, Poulin JC, Kagan HB. Tetrahedron Asymmetry. 1992; 3:1247–1262.
293. Doyle MP, Kalinin AV, Ene DG. J Am Chem Soc. 1996; 118:8837.
294. Trost BM, Calkins TL, Oertelt C, Zambrano J. Tetrahedron Lett. 1998; 39:1713.
295. Balskus EP, Jacobsen EN. Science. 2007; 317:1736. [PubMed: 17885133]
296. Han SB, Kong JR, Krische MJ. Org Lett. 2008; 10:4133. [PubMed: 18729371]
297. Hassan A, Lu Y, Krische MJ. Org Lett. 2009; 11:3112. [PubMed: 19586067]
298. Kim IS, Han SB, Krische MJ. J Am Chem Soc. 2009; 131:2514. [PubMed: 19191498]
299. Han SB, Han H, Krische MJ. J Am Chem Soc. 2010; 132:1760. [PubMed: 20099821]
300. Han SB, Gao X, Krische MJ. J Am Chem Soc. 2010; 132:9153. [PubMed: 20540509]
301. Zhang YJ, Yang JH, Kim SH, Krische MJ. J Am Chem Soc. 2010; 132:4562. [PubMed: 20225853]
302. Masuyama Y, Takahara JP, Kurusu Y. J Am Chem Soc. 1988; 110:4473.

303. Masuyama Y, Otake K, Kurusu Y. Tetrahedron Lett. 1988; 29:3563.
304. Takahara JP, Masuyama Y, Kurusu Y. J Am Chem Soc. 1992; 114:2577.
305. Araki S, Kameda K, Tanaka J, Hirashita T, Yamamura H, Kawai M. J Org Chem. 2010; 66:7919. [PubMed: 11701061]
306. Gagliardo M, Selander N, Mehendale NC, van Koten G, Gebbink RJM Klein, Szabó KJ. Chem Eur J. 2008; 14:4800.
307. Bandini M, Cozzi PG, Licciulli S, Umani-Ronchi A. Synthesis. 2004:409.
308. Nakajima M, Saito M, Hashimoto S. Chem Pharm Bull. 2000; 48:306. [PubMed: 10705529]
309. Itoh J, Han SB, Krische MJ. Angew Chem Int Ed. 2009; 48:6313.
310. Kitajima M, Mori I, Arai K, Kogure N, Takayama H. Tetrahedron Lett. 2006; 47:3199.

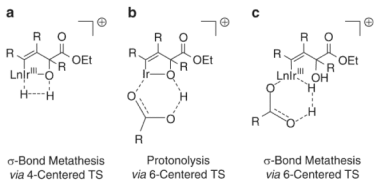


Fig. 1.
Carboxylic acid-assisted hydrogenolysis of oxa-iridacyclic intermediates that arise via alkyne–carbonyl oxidative coupling

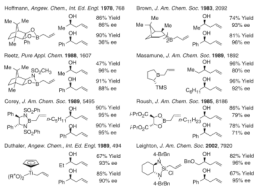


Fig. 2.
Selected examples of chiral allylmetal reagents for enantioselective carbonyl allylation

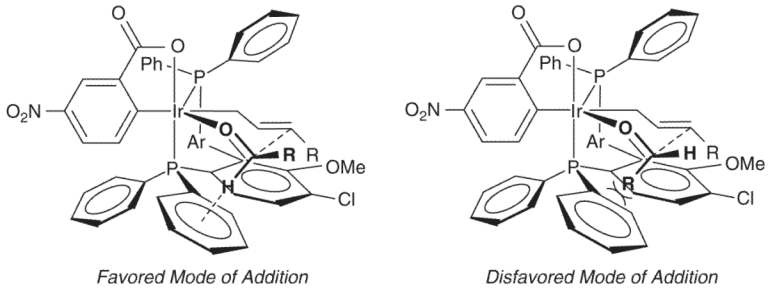
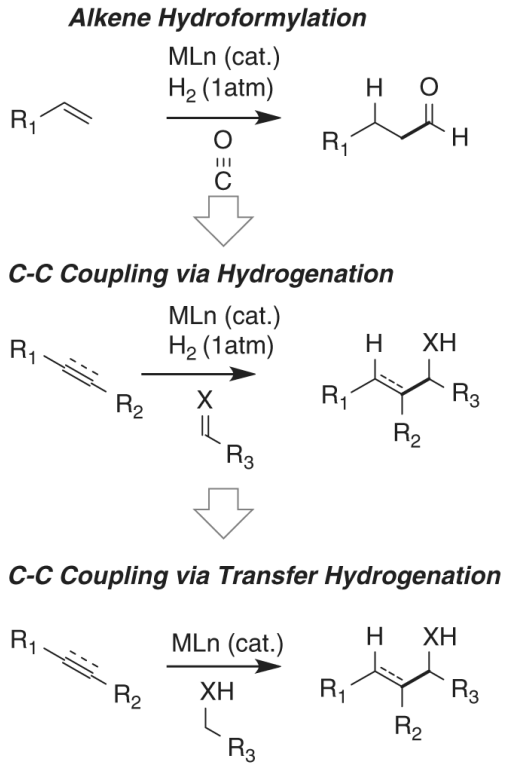
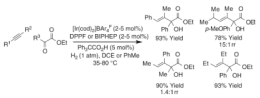


Fig. 3.
Proposed stereochemical model accounting for the observed sense of absolute stereoinduction (chiral ligand = (*S*)-Cl,MeO-BIPHEP)

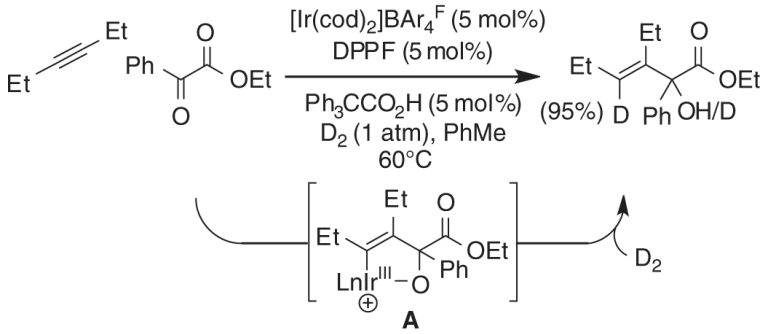


Scheme 1.
Catalytic C–C coupling via hydrogenation and transfer hydrogenation (X=O, NR_2)



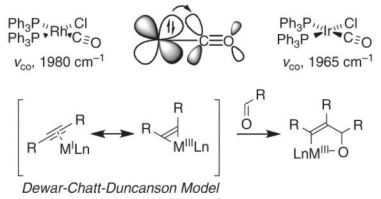
Scheme 2.

Iridium-catalyzed hydrogenation of alkynes in the presence of α-ketoesters to furnish α-hydroxy esters

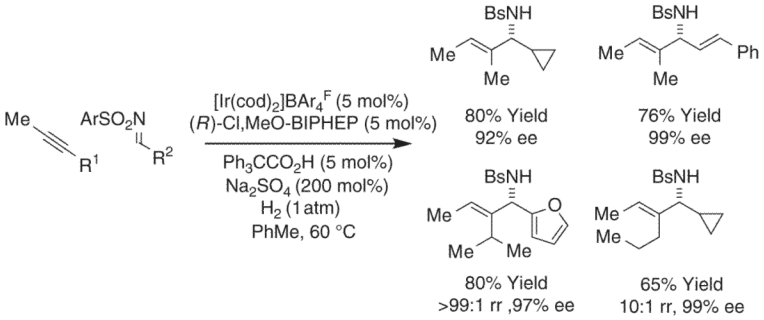


Scheme 3.

Alkyne-carbonyl reductive coupling via iridium-catalyzed hydrogenation under a deuterium atmosphere

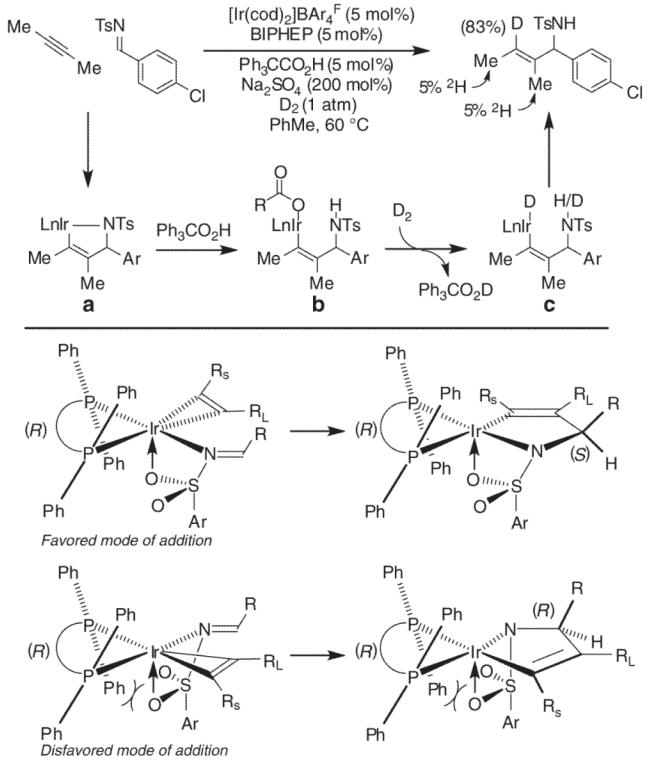


Scheme 4.
Significance of π-backbonding at the stage of the alkyne–metal complex



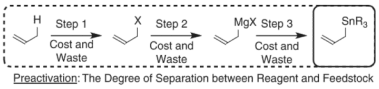
Scheme 5.

Enantioselective iridium-catalyzed hydrogenation of alkynes in the presence of *N*-arylsulfonyl imines to furnish trisubstituted allylic amines

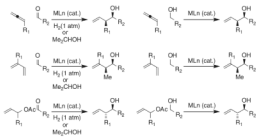


Scheme 6.

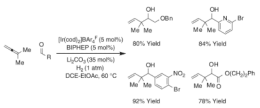
Proposed mechanism for hydrogenative imine vinylation and proposed enantiodetermining transition states



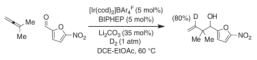
Scheme 7.
Preactivation often accompanies the use of stoichiometric organometallic reagents



Scheme 8.
Carbonyl allylation via hydrogenation and transfer hydrogenation

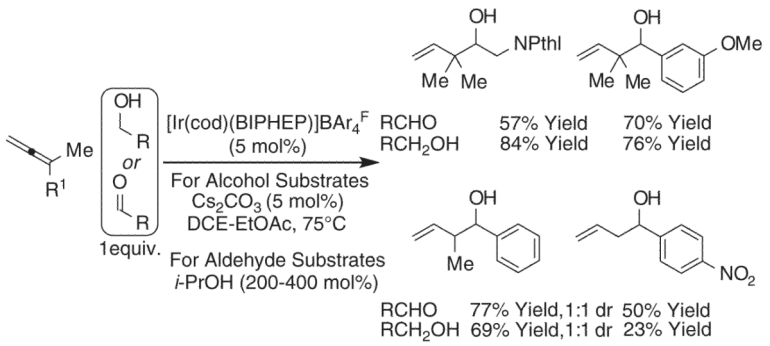


Scheme 9.
Catalytic carbonyl addition via iridium-catalyzed hydrogenative coupling of dimethylallene



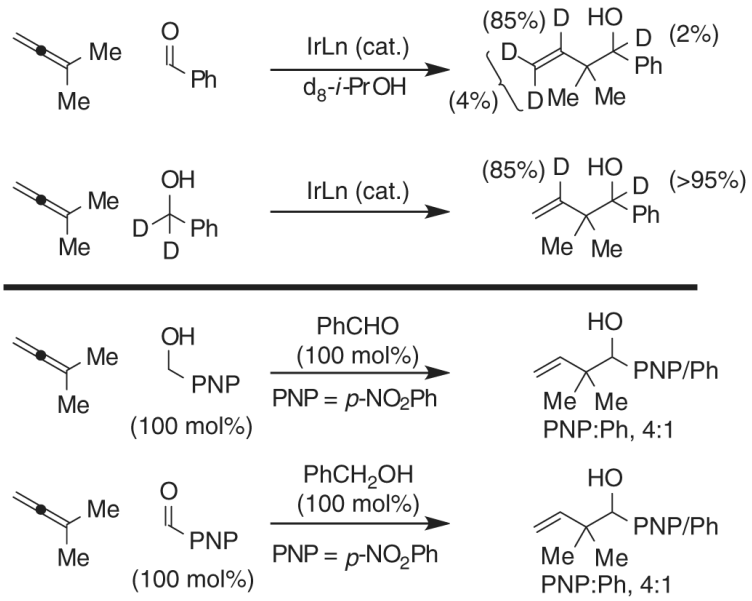
Scheme 10.

Iridium-catalyzed reductive coupling of 1,1-dimethylallene to an aldehyde under an atmosphere of deuterium



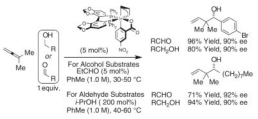
Scheme 11.

Carbonyl *tert*-prenylation, crotylation, and allylation from the aldehyde or alcohol oxidation level under the conditions or iridium-catalyzed transfer hydrogenation



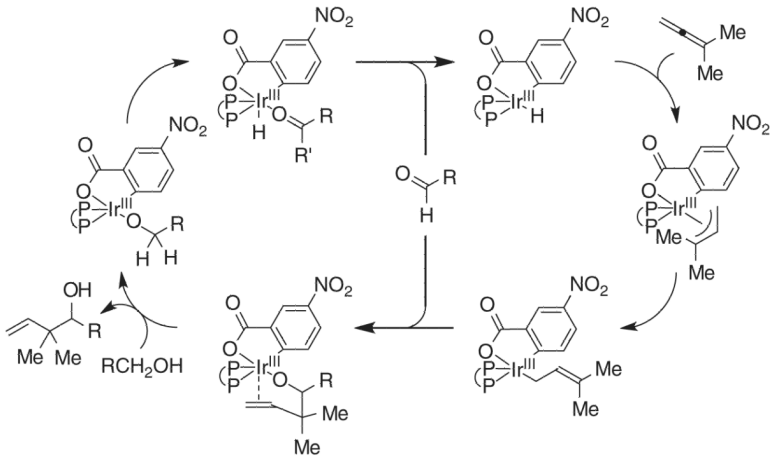
Scheme 12.

Isotopic labeling and crossover experiments in iridium-catalyzed couplings of 1,1-dimethylallene under transfer hydrogenation conditions



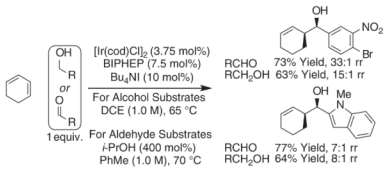
Scheme 13.

Enantioselective carbonyl *tert*-prenylation from the alcohol or aldehyde oxidation level via iridium-catalyzed C–C bond-forming transfer hydrogenation



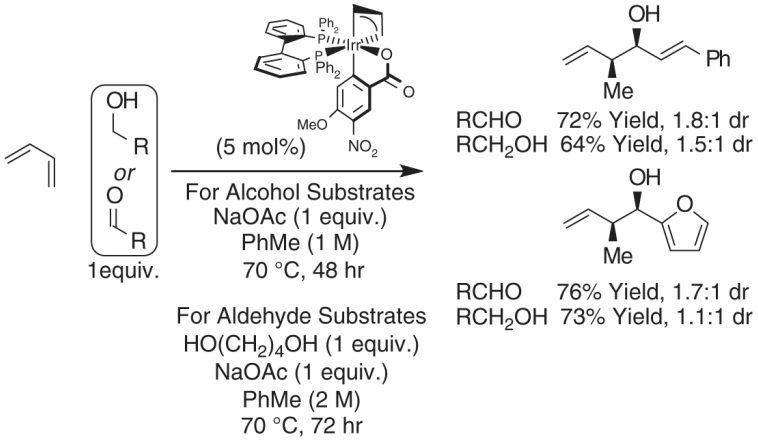
Scheme 14.

Proposed catalytic mechanism for carbonyl *tert*-prenylation from the alcohol oxidation level via iridium-catalyzed C-C bond-forming transfer hydrogenation

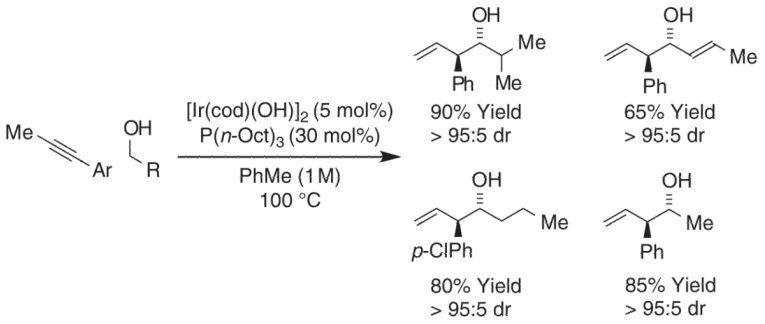


Scheme 15.

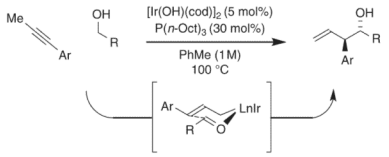
Iridium-catalyzed couplings of 1,3-cyclohexadiene under transfer hydrogenation conditions (ratio refers to 1,4-olefinic versus 1,5-olefinic alcohols)



Scheme 16.
Iridium-catalyzed C–C couplings of 1,3-butadiene under transfer hydrogenation conditions

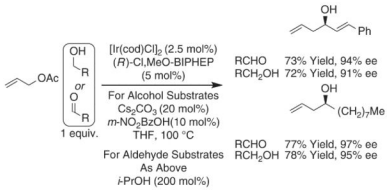


Scheme 17.
Carbonyl arylallylation from the alcohol oxidation level via iridium-catalyzed transfer hydrogenation employing alkynes as allyl donors



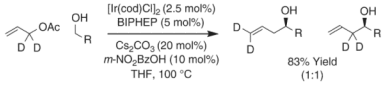
Scheme 18.

Plausible stereochemical model for *anti*-diastereoselective iridium-catalyzed allylation of alcohols employing alkynes as allyl donors



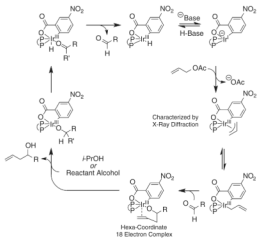
Scheme 19.

Enantioselective carbonyl allylation from the alcohol or aldehyde oxidation level via iridium-catalyzed C–C bond-forming transfer hydrogenation



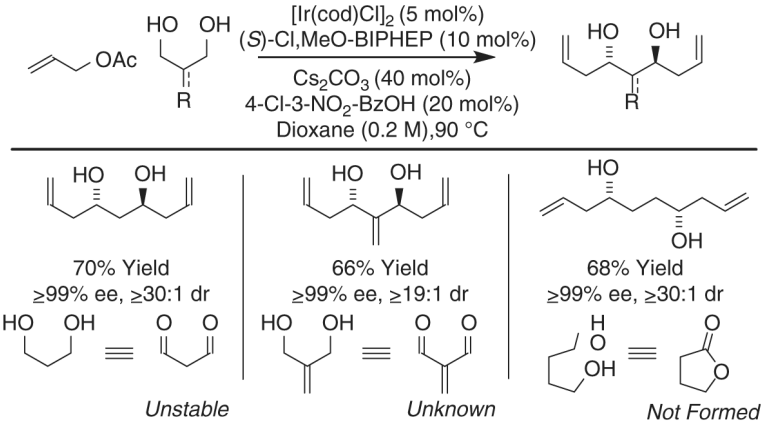
Scheme 20.

Carbonyl allylation from the alcohol oxidation level employing isotopically labeled allyl acetate [R = *p*-(CO_2Me)C_6H_4]



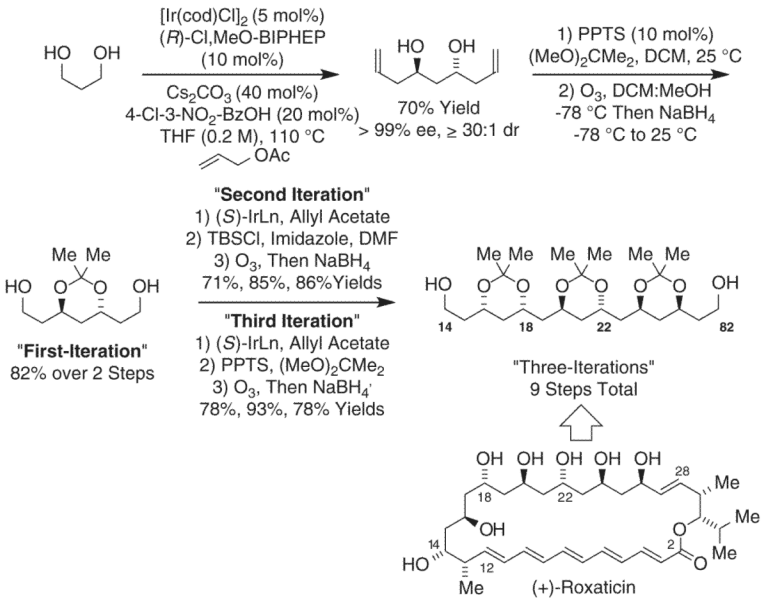
Scheme 21.

Proposed catalytic mechanism for carbonyl allylation from the alcohol oxidation level via iridium-catalyzed C–C bond-forming transfer hydrogenation

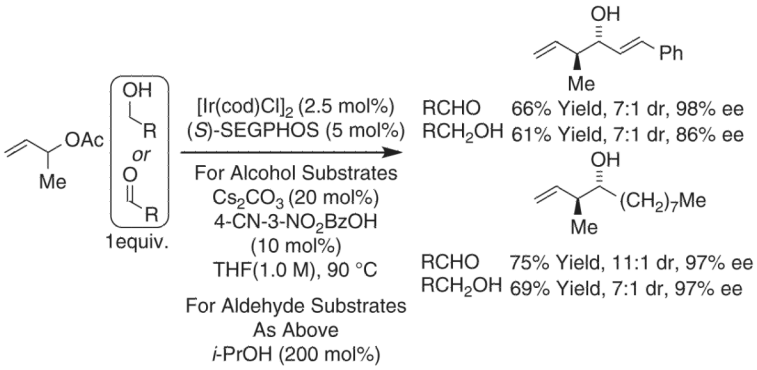


Scheme 22.

1,n-Glycols as dialdehyde equivalents in iridium-catalyzed enantioselective carbonyl allylation from the alcohol oxidation level

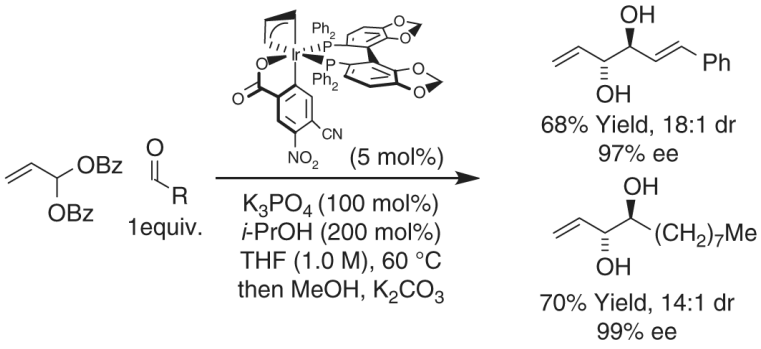


Scheme 23.
Synthesis of the 1,3-polyol substructure of the polyene macrolide (+)-roxaticin



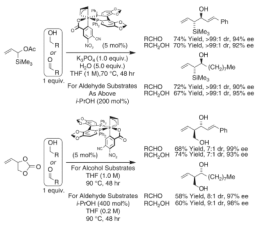
Scheme 24.

Enantioselective carbonyl crotylation from the alcohol or aldehyde oxidation level via iridium-catalyzed C–C bond-forming transfer hydrogenation



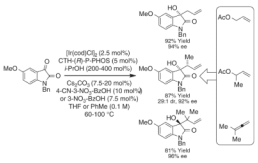
Scheme 25.

Diastereo- and enantioselective *anti*-(hydroxy)allylation employing allylic *gem*-dicarboxylates as allyl donors via iridium-catalyzed transfer hydrogenation

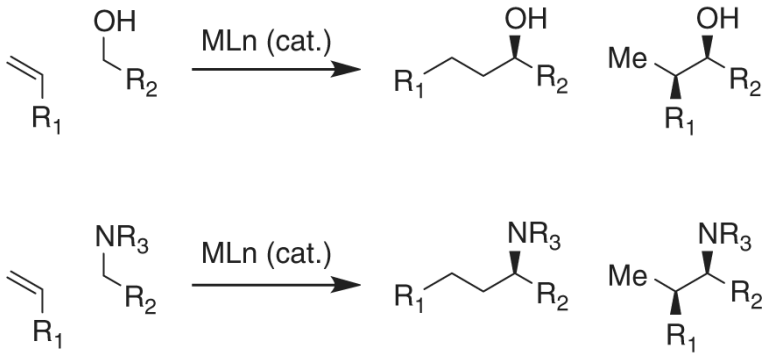


Scheme 26.

Enantioselective carbonyl (trimethylsilyl)allylation and (hydroxymethyl)allylation from the alcohol or aldehyde oxidation level via iridium-catalyzed C–C bond-forming transfer hydrogenation



Scheme 27.
Enantioselective allylation, crotylation, and *tert*-prenylation of substituted isatins via iridium-catalyzed transfer hydrogenation



Scheme 28.

Examples of two aspirational processes: byproduct-free couplings of α-olefins to (renewable) alcohols and amines with linear or branch regiocontrol