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Formation of C-C Bonds via Catalytic Hydrogenation and Transfer Hydrogenation: Vinylation, Allylation, and Enolate Addition of Carbonyl Compounds and Imines

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1. Introduction

A fundamental challenge in organic chemistry resides in the development of increasingly efficient protocols for carbon–carbon-bond formation. The ideal C–C-bond forming processes should be applicable to both petrochemical and renewable feedstocks and should be aligned with the economic and aesthetic ideals of atom-economy,[1] step-economy,[2] and Green Chemistry.[3] Ultimately, chemical production should be sustainable, that is, it should not compromise human health, the environment, or the economy.

Hydrogen is vastly abundant, constituting roughly 90% of the atoms present in the Universe. Catalytic additions of elemental hydrogen, termed “hydrogenations,” rank among the most significant catalytic transformations in existence in terms of social and economic impact. For example, the catalytic hydrogenation of atmospheric nitrogen to produce ammonia, the Haber-Bosch process,[4] is used to produce over 10^7 metric tons of ammonia annually. Nitrogenous fertilizer obtained from the Haber-Bosch process is estimated to sustain one-third of the Earth’s population.[5] 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.[6]

The Fischer-Tropsch reaction[7] and alkene hydroformylation[8] may be viewed as the prototypical C-C-bond forming hydrogenations. Hydroformylation combines basic feedstocks (α-olefins, carbon monoxide, and hydrogen) with perfect atom-economy, and accounts for the production of over 7 million metric tons of aldehyde annually, making it the largest-volume application of homogeneous metal catalysis.[9] Given the impact of hydroformylation, it is surprising that the field of “hydrogenative C-C bond formation” lay fallow for over 70 years.[10,11]

As described in this account, we find that hydrogenation and transfer hydrogenation may be used to couple diverse π-unsaturated reactants to carbonyl compounds and imines.[12] Such hydrogenative C-C couplings define a departure from the use of preformed organometallic reagents in classical C=X (X = O, NR) addition reactions, in many cases enabling completely byproduct-free C=X addition processes. Further, under transfer-hydrogenative coupling conditions, carbonyl addition can be attained from the alcohol or aldehyde oxidation level, thereby circumventing redox manipulations often required to adjust the oxidation level (Scheme 1).

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2. Vinylation of Carbonyl Compounds and Imines

Numerous methods exist for the preparation of allylic alcohols and allylic amines.[13,14] For example, the metal-catalyzed allylic substitution employing oxygen and nitrogen nucleophiles is a powerful protocol for the synthesis of chiral nonracemic allylic alcohols and allylic amines.[15] Another approach, though less developed, involves a catalytic enantioselective aldehyde vinylation.[16-19 16,17,18,19] Catalytic enantioselective vinyl transfer to imines had not been achieved prior to our work (vide infra).[20,21]

Limitations associated with the use of preformed vinyl metal reagents are potentially overcome through direct metal-catalyzed alkyne-carbonyl reductive couplings. The first catalytic process of this type, a rhodium-catalyzed reductive cyclization of acetylenic aldehydes mediated by silane, was reported in 1994 by Ojima et al.[22] In 1995, Crowe and Rachita disclosed related silane-mediated titanocene-catalyzed cyclizations.[23] The corresponding nickel-catalyzed cyclizations were first reported in 1997 by Montgomery and co-workers.[24a-c,e] Based on Montgomery's finding, the nickel-catalyzed intermolecular alkyne-aldehyde reductive coupling was achieved by Jamison in 2000.[25] Improved nickel-based catalysts were developed later by Takai[26] and Montgomery.[24d] While reductive couplings of this type signal a departure from the use of preformed organometallic reagents, these methods employ terminal reductants such as hydrosilanes, hydrostannanes, organozinc reagents, organoboron reagents or chromium(II) chloride and, hence, produce molar equivalents of byproducts.

Under hydrogenation conditions, alkynes engage in completely byproduct-free reductive couplings to both carbonyl compounds and imines.[12d] First-generation catalytic systems based on rhodium promote the highly enantioselective coupling of conjugated alkynes to activated aldehydes and ketones in the form of vicinal dicarbonyl compounds.[27a-c 27a,b,c] Heterocyclic aromatic aldehydes and ketones couple to conjugated alkynes under closely related conditions, providing access to heteroaryl-substituted carbinols.[27d] Notably, the diene- and enyne-containing products are not subject to over-reduction under the hydrogenative coupling conditions. Presumably, upon consumption of the electrophile (the limiting reagent) excess alkyne unproductively coordinates rhodium and so impedes the rate of further conventional hydrogenation (Scheme 2).[27?]

The coupling of conjugated enynes or diynes to ethyl (*N*-sulfinyl)iminoacetates proceeds efficiently under the conditions of rhodium-catalyzed hydrogenation.[28] Using appropriately substituted (*N*-sulfinyl)iminoacetates, one generates the corresponding β,γ-unsaturated α-amino acid esters as single diastereomers. A second hydrogenation of the unsaturated side chain of the coupling product provides access to β-substituted α-amino acids (Scheme 3).

Gaseous acetylene couples to aldehydes and imines under hydrogenation conditions to furnish products of (*Z*)-butadienylation.[29] Using chirally modified rhodium catalysts, allylic alcohols and allylic amines are formed in highly optically enriched form.[29,30] These byproduct-free couplings combine acetylene, an abundant feedstock,[31] with carbonyl compounds or imines to furnish chiral adducts in the absence of any preformed vinyl metal reagents (Scheme 4).

Using second-generation catalysts based on iridium, the highly enantioselective hydrogenative coupling of 1,2-dialkyl-substituted alkynes to *N*-arylsulfonyl imines is achieved (Scheme 5).[32] The trisubstituted allylic amine products are formed with complete levels of *E*:*Z* selectivity (≥95:5), and excellent regiocontrol is observed using unsymmetrical alkynes. This byproduct-free coupling provides trisubstituted allylic amines that are not accessible via metal-catalyzed asymmetric allylic alkylation.[15]

Finally, intramolecular coupling of alkynes to tethered aldehydes occurs readily in the rhodium-catalyzed hydrogenation. Using chirally modified catalysts, products of reductive carbocyclization are formed with uniformly high levels of optical enrichment.[33] Using an achiral rhodium catalyst, chiral racemic acetylenic aldehydes engage in highly *syn*-diastereoselective reductive cyclizations to furnish cyclic allylic alcohols (Scheme 6).

3. Allylation and Propargylation of Carbonyl Compounds

Carbonyl allylation is employed routinely in synthetic organic chemistry.[34] Asymmetric allylation has been achieved using chirally modified allyl metal reagents,[35] chiral Lewis acid catalysts or chiral Lewis base catalysts.[36] These methods invariably employ preformed allyl metal reagents, such as allyl stannanes or trichlorosilanes, which generate stoichiometric quantities of metallic byproducts. Other methods for catalytic carbonyl allylation include the reduction of metallo-π-allyls derived from allylic alcohols and allylic carboxylates,[37] which require stoichiometric quantities of metal-based terminal reductants for catalytic turnover.[38]

We find that allyl metal species arising transiently in the course of allene hydrogenation may be captured by exogenous carbonyl electrophiles, thus enabling byproduct-free carbonyl allylation. For example, iridium-catalyzed hydrogenation of dimethylallene in the presence of activated aldehydes or ketones delivers products of reverse prenylation.[39a] In the iridium-catalyzed transfer hydrogenation employing isopropanol as the terminal reductant, dimethylallene also couples to aldehydes.[39b] Finally, hydrogen embedded within an alcohol substrate can be redistributed among reactants to generate nucleophile-electrophile pairs, enabling byproduct-free carbonyl reverse prenylation from the alcohol oxidation level (Scheme 7).[39b]

These results prompted efforts toward general catalytic protocols for alcohol-unsaturate transfer-hydrogenative coupling.[40] Under iridium-catalyzed transfer-hydrogenation conditions, 1,3-cyclohexadiene couples readily to aldehydes employing isopropanol as terminal reductant. An identical set of products may be prepared from the corresponding alcohols under nearly identical conditions (Scheme 8).[41] In the ruthenium-catalyzed transfer hydrogenation employing $RuHCl(CO)(PPh_3)_3$ as precatalyst, simple acyclic dienes (butadiene, isoprene, and 2,3-dimethylbutadiene) couple to diverse alcohols.[42] Again, coupling is possible from the alcohol or aldehyde oxidation level. In the latter case, isopropanol or formic acid may be employed as terminal reductants (Scheme 9).

Under the ruthenium-catalyzed auto-transfer hydrogenation conditions, conjugated enynes couple to benzylic, allylic, and aliphatic alcohols to furnish products of carbonyl propargylation.[43-45] [43,44,45] Under related transfer-hydrogenation conditions employing isopropanol as terminal reductant, enyne coupling to aldehydes provides identical products of carbonyl propargylation. In this way, carbonyl propargylation is achieved from the alcohol or the aldehyde oxidation level in the absence of preformed allenyl metal reagents. Stereocontrolled variants of these newly developed allene, diene, and enyne couplings are currently under investigation (Scheme 10).

An especially powerful application of transfer hydrogenative C-C coupling involves iridium-catalyzed carbonyl allylation from the aldehyde or alcohol oxidation level employing allyl acetate as the allyl donor.[46a] Exposure of allyl acetate to benzylic alcohols in the presence of commercially available $[Ir(cod)Cl]_2$ and (*R*)-BINAP delivers products of *C*-allylation in good-to-excellent yields and with high levels of asymmetric induction. Allylation from the carbonyl oxidation level is achieved by employing isopropyl alcohol as the terminal reductant. In this case, (-)-TMBTP is used as the chiral phosphine ligand to generate identical allylation adducts with high degrees of enantioselectivity. As such, asymmetric allylation can be achieved from the alcohol or aldehyde oxidation levels with

equal facility. More recently, this asymmetric allylation protocol has been extended to allylic alcohols and aliphatic alcohols (Scheme 11).[46b]

4. Hydrogenative Aldol and Mannich Additions

For well over a century, the aldol reaction has served as a core method in organic synthesis.[47] Intensive efforts have led to the realization of aldol addition protocols that enable excellent levels of diastereo- and enantiocontrol.[48] A particularly significant advance involves the refinement of methods for the direct asymmetric aldol additions of unmodified ketones employing metallic[49] or organic[50] catalysts. These byproduct-free processes herald a departure from the use of chiral auxiliaries and preformed enol(ate) derivatives. A significant limitation of these nascent technologies resides in the issue of regiocontrolled enolization. For example, direct catalytic asymmetric aldol additions of unsymmetrical ketones, such as 2-butanone, typically result in coupling at the less substituted enolizable position to furnish linear aldol adducts.[51]

The challenge of regiocontrolled enolization is overcome via enone reduction. Pioneering work by Stork demonstrates that dissolving metal reduction of enones enables regiospecific generation and capture of enolate isomers that cannot be prepared exclusively under standard conditions for base-mediated deprotonation.[52] Subsequently, catalytic reductive couplings of enones to aldehydes emerged.[53] To date, myriad metallic catalysts for "reductive aldol coupling" have been devised, including those based on rhodium,[54] cobalt,[55] iridium,[56] ruthenium,[57] palladium,[58] copper,[59,60] nickel,[61] and indium.[62,63] These protocols invariably employ metallic terminal reductants, such as stannanes, silanes, and organozinc reagents, which mandates the generation of stoichiometric byproducts. Inspired by the prospect of developing completely byproduct-free processes, catalytic reductive aldol additions employing elemental hydrogen as the terminal reductant were investigated.[64]

Our initial efforts centered on developing intramolecular reductive aldol couplings of tethered enone-aldehydes under hydrogenative conditions (Scheme 12).[64a] It was found that upon exposure to catalytic quantities of phosphine-modified cationic rhodium complexes under ambient pressures of hydrogen, a range of enone-aldehydes engage in highly diastereoselective cyclization to deliver five- and six-membered-ring products. In a similar fashion, enone-ketones cyclize under nearly identical conditions to furnish *syn*-aldol adducts as single diastereomers.[64b] However, in these cases, the diminished electrophilicity of the ketone leads to substantial quantities of simple enone reduction product. Extension of this method to enone-diketone substrates provides a powerful desymmetrization strategy for the stereocontrolled generation of bicyclic frameworks bearing three contiguous stereocenters. The addition of aldehyde enolates to ketones, for which a single stoichiometric variant is known,[65] represents a highly challenging class of aldol addition. Under hydrogenative conditions, enal-ketones cyclize with a high degree of efficiency to provide products of aldehyde enolate-ketone addition, although competitive 1,4 reduction is also observed. Specifically, cationic rhodium complexes, in conjunction with catalytic quantities of base, are essential in suppressing conventional reduction of the starting material and enabling the desired coupling (Scheme 13).[64c]

Intermolecular hydrogenative aldol couplings also are possible. Under an atmosphere of hydrogen, cationic rhodium complexes catalyze the coupling of vinyl ketones to diverse aldehydes.[64a] Whereas the catalyst derived from $Rh(cod)_2OTf$ and triphenylphosphine provided aldol adducts as diastereomeric mixtures, high *syn*-diastereoselectivity may be realized using tri(2-furyl)phosphine as ligand.[64e,66] Under these modified conditions, a wide range of aldehydes couple to methyl or ethyl vinyl ketone with exceptional levels of *syn*-diastereoselectivity. Of note is the wide range of potentially "hydrogen-labile" functionality

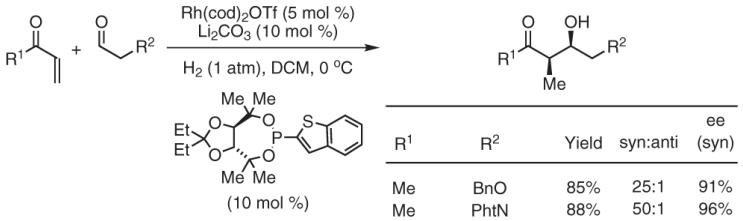
tolerated, enabling the use of substrates containing alkynes, alkenes, benzylic ethers, nitroarenes, and aryl bromides. Furthermore, functionalized enones also are tolerated, as demonstrated by the employment of crotyl vinyl ketone.[64f] Remarkably, the mild reaction conditions permit aldol coupling of configurationally sensitive *N*-Boc-α-aminoaldehydes without racemization. Here, high levels of *anti*-Felkin-Anh control are achieved by taking advantage of hydrogen-bonded chelates, which arise in reaction media with low dielectric constants (Scheme 14).[64g]

The ability to access *syn*-aldol adducts relevant to polyketide synthesis inspired further efforts toward enantioselective variants. π-Acidic monodentate phosphine ligands are required to enforce high levels of diastereoselectivity and catalytic turnover. However, commercially available phosphines of this type (e.g., phosphoramidites and BINOL-derived phosphites) give rise to inactive rhodium complexes, suggesting a very narrow window in terms of ligand π acidity. Consequently, the design of an effective, chiral, monodentate, phosphorus-based ligand was undertaken. The versatility of TADDOL-like phosphonites enabled the determination of key structure-selectivity trends, ultimately leading to the design of an effective ligand. Thus, by simply exposing methyl or ethyl vinyl ketone to aldehydes under an atmosphere of gaseous hydrogen in the presence of the rhodium phosphonite complex, aldol addition occurs with high levels of relative and absolute stereocontrol. This method generates optically enriched polyketide substructures and circumvents the stoichiometric generation of byproducts (**eq 1**).[64h]

Based on the preceding results, reductive Mannich couplings of vinyl ketones were explored.[67] Previously, reductive Mannich couplings had been accomplished using silane,[68] the Hantzsch ester,[69] or diethylzinc[70] as the terminal reductant. Under hydrogenative conditions employing a tri(2-furyl)phosphine-ligated rhodium catalyst, vinyl ketones couple to *N*-(*o*-nitrophenyl)sulfonyl aldimines to furnish the desired Mannich addition products with good levels of *syn*-diastereoselectivity.[67] These preliminary studies suggest the feasibility of developing asymmetric variants of this transformation (**eq 2**).

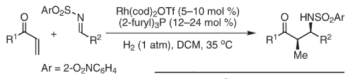
5. Future Directions

The stereoselective vinylation, allylation, and enolate addition of carbonyl compounds rank among the most broadly utilized methods in organic synthesis. Traditional protocols have relied upon the use of organometallic reagents, which are often basic, moisture sensitive, and give rise to stoichiometric quantities of metallic byproducts. Inspired by alkene hydroformylation and the parent Fischer-Tropsch reaction, hydrogenative variants of these classical carbonyl addition processes are aimed at meeting the environmental, economic, and health and safety ideals set by Green Chemistry. For the hydrogenative protocols, carbonyl and imine addition occurs under essentially neutral conditions simply upon exposure of an unsaturate-electrophile pair to gaseous hydrogen in the presence of a metal catalyst. Accordingly, vinylation, allylation, and enolate addition are achieved without stoichiometric byproduct generation and with stereoselectivities often surpassing traditional methods. The discovery of related transfer-hydrogenative couplings not only evades the stoichiometric generation of metallic byproducts, but also the requirement for substrate oxidation level adjustment. The ability to perform carbonyl addition from either the aldehyde or alcohol oxidation level has broad implications for the field of organic synthesis. These nascent reactivity modes should serve as the basis for innumerable byproduct-free alcohol-unsaturate and amine-unsaturate coupling processes.



R^1	R^2	Yield	syn:anti	ee (syn)
Me	BnO	85%	25:1	91%
Me	PhtN	88%	50:1	96%
Et	1-Me-indol-3-yl	97%	25:1	90%
Et	Ph	76%	22:1	90%

eq 1



R^1	R^2	Yield	syn:anti
Et	4-$O_2NC_6H_4$	80%	7:1
Me	3,4-$Cl_2C_6H_3$	67%	9:1
Et	5-O_2N-furan-2-yl	83%	4:1
Me	4-$F_3CC_6H_4$	71%	6:1

eq 2

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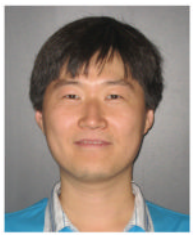
Biographies

Ryan L. Patman was born in 1982 in Elk City, Oklahoma. In 2006, he received a B.S. degree in chemistry from Oklahoma State University, where he conducted undergraduate research under the supervision of Professor Richard A. Bunce. He is currently a doctoral candidate in the research group of Professor Michael J. Krische at The University of Texas at Austin.

John F. Bower was born in 1980 in Chester, England. In 2003, he obtained an M.Sci. degree in chemistry from the University of Bristol, U.K., where he conducted research under the supervision of Professor Guy C. Lloyd-Jones. He continued doctoral studies at Bristol under the supervision of Professor Timothy Gallagher and, in 2007, received his Ph.D. degree. In May 2007, he joined the research group of Professor Michael J. Krische at The University of Texas at Austin as a postdoctoral research associate.



In Su Kim was born in 1975 in Gapyeong, Republic of Korea. In 2001, he received a B.S. degree from the College of Pharmacy, Sungkyunkwan University, Republic of Korea. He obtained an M.S. degree in 2003 and a Ph.D. degree in 2006, working under the guidance of Professor Young Hoon Jung. In September 2007, he joined the group of Professor Michael J. Krische at the University of Texas at Austin as a postdoctoral fellow of the Korea Research Foundation (KRF).

Michael J. Krische obtained a B.S. degree in chemistry from the University of California at Berkeley, where he performed research under the guidance of Professor Henry Rapoport as a President's Undergraduate Fellow. After one year of study abroad as a Fulbright Fellow, he initiated graduate research at Stanford University under the mentorship of Professor Barry Trost as a Veatch Graduate Fellow. Following receipt of his Ph.D. degree, he worked with Jean-Marie Lehn at the Université Louis Pasteur as an NIH Post-Doctoral Fellow. In the fall of 1999, he was appointed Assistant Professor at the University of Texas at Austin. He was promoted directly to Full Professor in 2004 and in 2007 he received the Robert A. Welch Chair in Science. Professor Krische's research program is focused on the development of C-C-bond-forming hydrogenations and transfer hydrogenations. Research from his laboratory demonstrates that hydrogenation and transfer hydrogenation may be used to couple diverse π-unsaturated reactants to carbonyl compounds, imines, and even alcohols offering a byproduct-free alternative to stoichiometrically preformed organometallics in a range of classical C=X (X = O, NR) addition processes. These studies represent the first systematic efforts to exploit hydrogenation in C-C couplings beyond hydroformylation, and define a departure from the use of preformed organometallic reagents in carbonyl and imine additions. His research accomplishments led to the receipt of numerous awards and honors: Novartis Chemistry Lectureship (2008), Presidential Green Chemistry Award (2007), Dowpharma Prize (2007), ACS Elias J. Corey Award (2007), Solvias Ligand Prize (2006), Society of Synthetic Chemistry Japan Lectureship (2005), Johnson & Johnson Focused Giving Award (2005), Dreyfus Teacher Scholar Award (2003), Alfred P. Sloan Research Fellowship (2003), Cottrell Scholar Award (2002), Frasch

Foundation Award in Chemistry (2002), Lilly Grantee Award (2002), National Science Foundation-CAREER Award (2000), Maître de Conference, Collége de France (1999), NIH Post-Doctoral Fellow (1997), Veatch Graduate Fellow (1995), Sigma Xi Grantee (1991), and Fulbright Fellow (1990).

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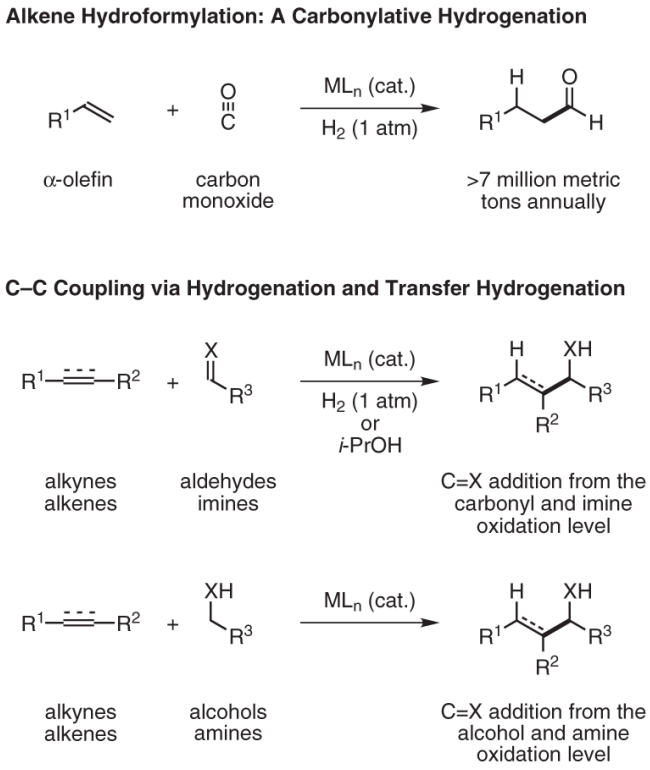
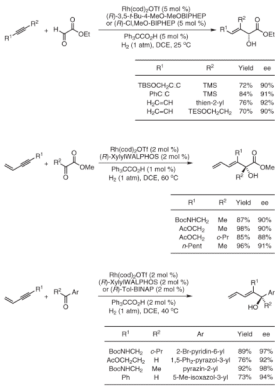
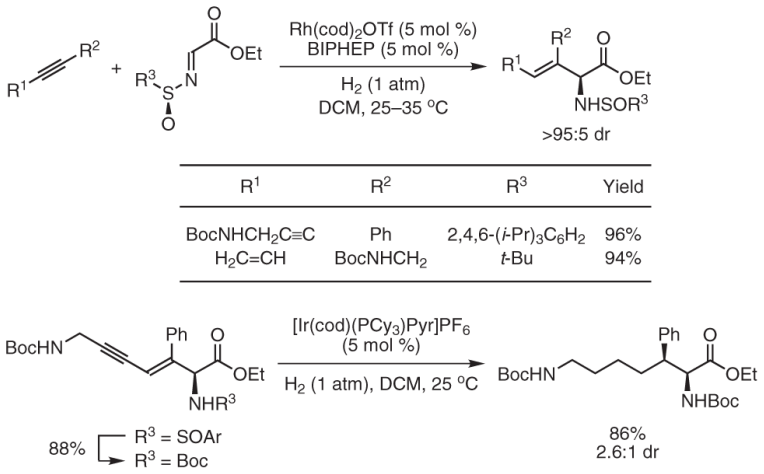


Scheme 1.
Catalytic C-C Coupling via Hydrogenation and Transfer Hydrogenation.

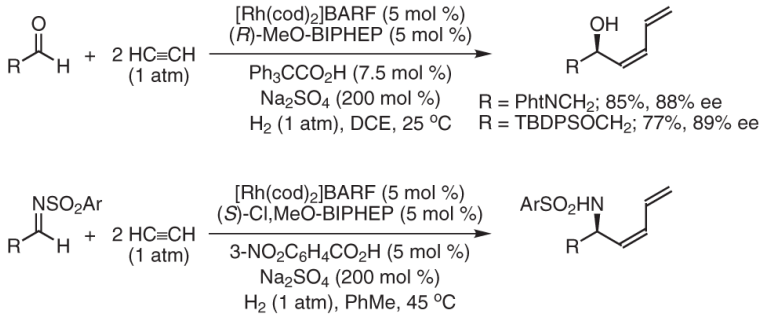


Scheme 2.

Direct, Byproduct-Free Hydrogenative Coupling of Conjugated Alkynes to Activated Carbonyl Compounds and Imines Employing Cationic Rhodium Catalysts. (Ref. 27)



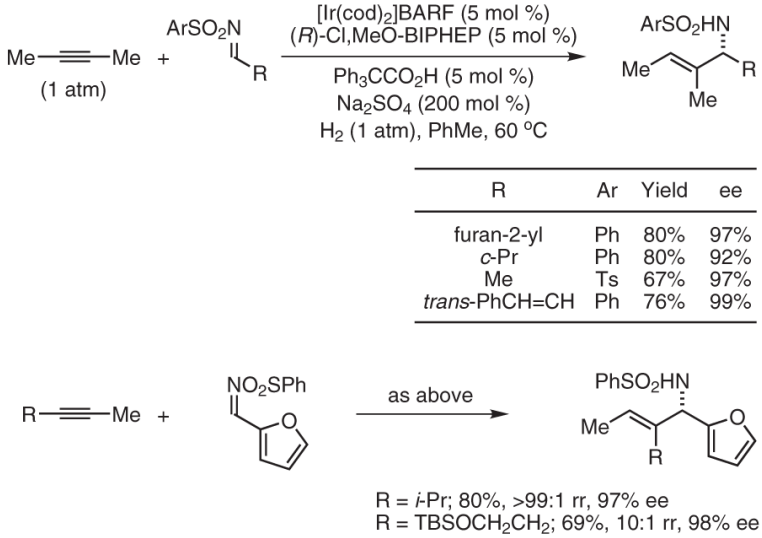
Scheme 3.
Unnatural α-Amino Acids via C-C-Bond-Forming Hydrogenation. (Ref. 28)



R	Ar	Yield	ee
Ph	Ns	86%	93%
3-Br-4-FC$_6$H$_3$	Ns	70%	97%
i-Pr	Ts	70%	98%
c-Pr	Ts	65%	97%

Scheme 4.

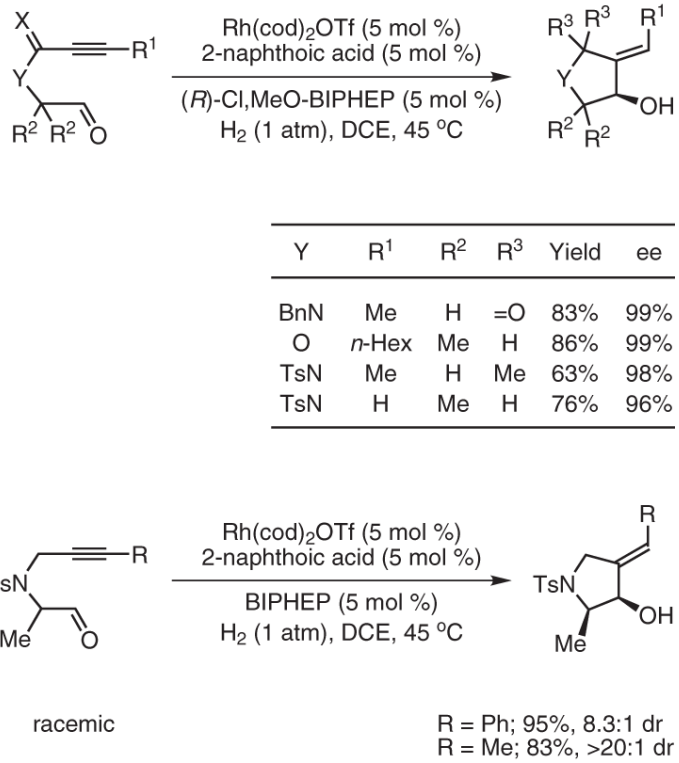
Enantioselective Carbonyl and Imine (*Z*)-Butadienylation via Rhodium-Catalyzed Hydrogenative Coupling of Acetylene. (Ref. 29,30)



R	Ar	Yield	ee
furan-2-yl	Ph	80%	97%
c-Pr	Ph	80%	92%
Me	Ts	67%	97%
trans-PhCH=CH	Ph	76%	99%

R = *i*-Pr; 80%, >99:1 rr, 97% ee
R = $TBSOCH_2CH_2$; 69%, 10:1 rr, 98% ee

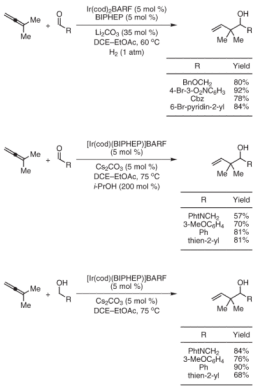
Scheme 5.
Enantioselective Imine Vinylation via Iridium-Catalyzed Hydrogenative Coupling of Unconjugated Alkynes. (Ref. 32)



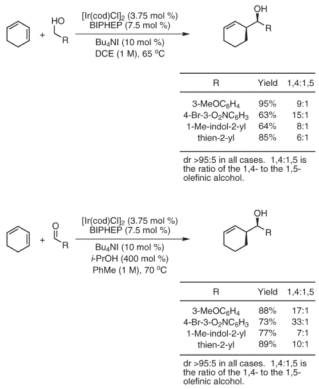
Y	R^1	R^2	R^3	Yield	ee
BnN	Me	H	=O	83%	99%
O	*n*-Hex	Me	H	86%	99%
TsN	Me	H	Me	63%	98%
TsN	H	Me	H	76%	96%

Scheme 6.

Enantio- and Diastereoselective Carbocyclizations of Acetylenic Aldehydes by the Rhodium-Catalyzed Asymmetric Hydrogenation. (Ref. 33)



Scheme 7.
Catalytic Carbonyl Addition via Iridium-Catalyzed Hydrogenative Coupling of Dimethylallene. (Ref. 39)



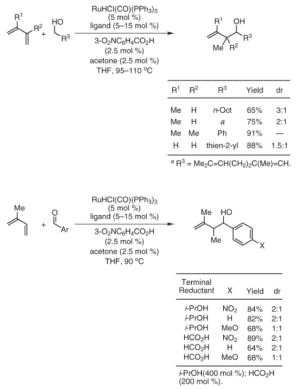
R	Yield	1,4:1,5
3-MeOC$_6$H$_4$	95%	9:1
4-Br-3-O$_2$NC$_6$H$_3$	63%	15:1
1-Me-indol-2-yl	64%	8:1
thien-2-yl	85%	6:1

dr >95:5 in all cases. 1,4:1,5 is the ratio of the 1,4- to the 1,5-olefinic alcohol.

R	Yield	1,4:1,5
3-MeOC$_6$H$_4$	88%	17:1
4-Br-3-O$_2$NC$_6$H$_3$	73%	33:1
1-Me-indol-2-yl	77%	7:1
thien-2-yl	89%	10:1

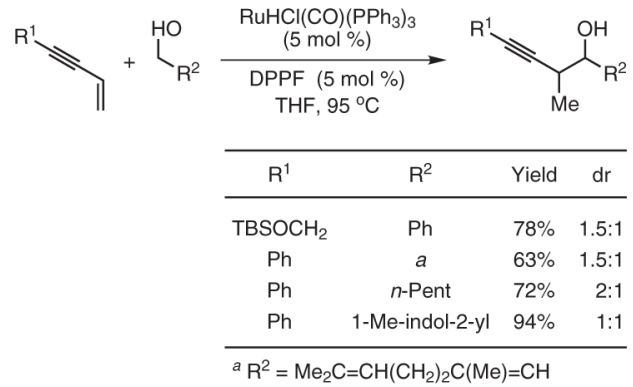
dr >95:5 in all cases. 1,4:1,5 is the ratio of the 1,4- to the 1,5-olefinic alcohol.

Scheme 8.
Coupling of Dienes to Alcohols or Aldehydes by the Iridium-Catalyzed Transfer Hydrogenation. (Ref. 41)



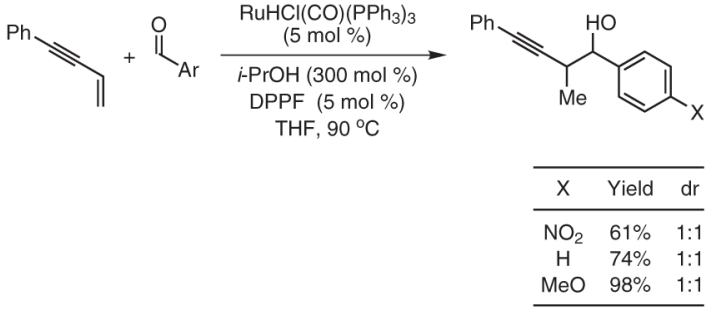
Scheme 9.

Coupling of Dienes to Alcohols or Aldehydes by the Ruthenium-Catalyzed Transfer Hydrogenation. (Ref. 42)



R^1	R^2	Yield	dr
$TBSOCH_2$	Ph	78%	1.5:1
Ph	*a*	63%	1.5:1
Ph	*n*-Pent	72%	2:1
Ph	1-Me-indol-2-yl	94%	1:1

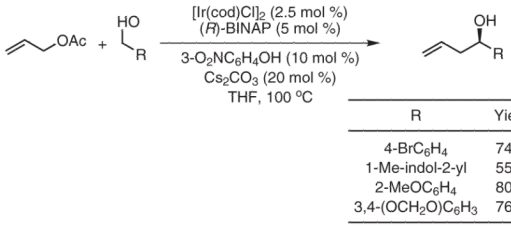
[a] $R^2 = Me_2C{=}CH(CH_2)_2C(Me){=}CH$



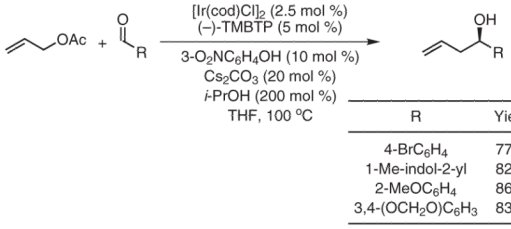
X	Yield	dr
NO_2	61%	1:1
H	74%	1:1
MeO	98%	1:1

Scheme 10.

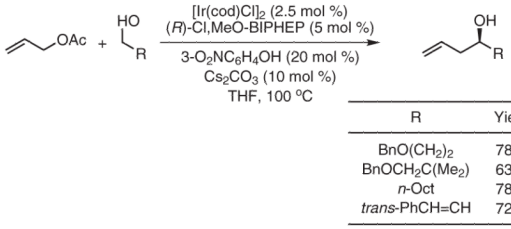
Carbonyl Propargylation from the Alcohol or Aldehyde Oxidation Level via Ruthenium-Catalyzed Transfer-Hydrogenative Coupling of 1,3-Enynes. (Ref. 43-45)



R	Yield	ee
4-BrC_6H_4	74%	93%
1-Me-indol-2-yl	55%	90%
2-$MeOC_6H_4$	80%	92%
3,4-$(OCH_2O)C_6H_3$	76%	91%

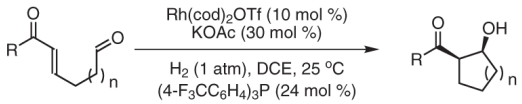


R	Yield	ee
4-BrC_6H_4	77%	97%
1-Me-indol-2-yl	82%	94%
2-$MeOC_6H_4$	86%	95%
3,4-$(OCH_2O)C_6H_3$	83%	94%



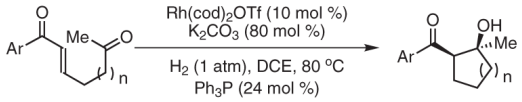
R	Yield	ee
$BnO(CH_2)_2$	78%	95%
$BnOCH_2C(Me_2)$	63%	93%
n-Oct	78%	95%
trans-PhCH=CH	72%	91%

Scheme 11.
Enantioselective Carbonyl Allylation from the Alcohol or Aldehyde Oxidation Level via Iridium-Catalyzed Transfer-Hydrogenative Coupling of Allyl Acetate. (Ref. 46)



R	n	Yield	syn:anti	1,4[a]
Ph	1	71%	24:1	1%
Ph	2	89%	10:1	0.1%
Me	2	65%	1:5	—
thien-2-yl	2	76%	19:1	2%

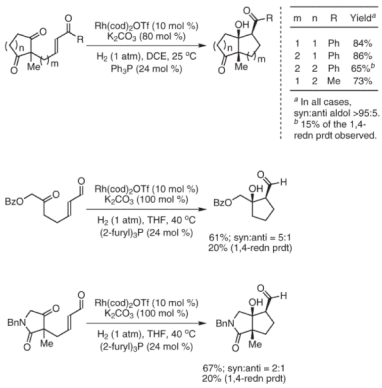
[a] Yield of the 1,4-reduction product.



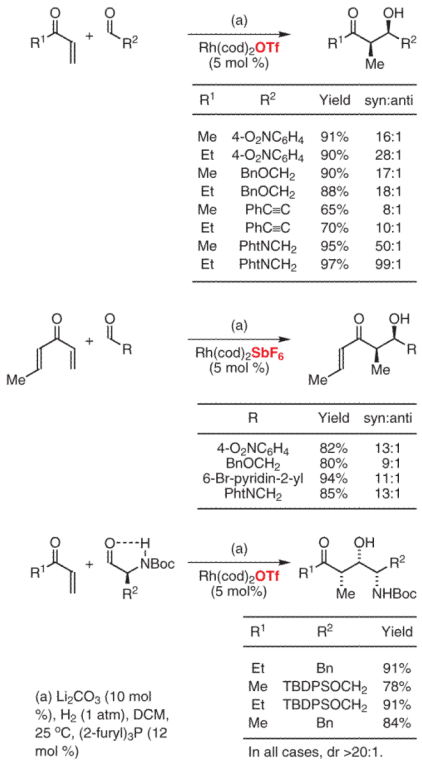
Ar	n	Yield[a]	1,4[b]
2-Np	1	74%	18%
2-Np	2	78%	18%
thien-2-yl	1	66%	24%
thien-2-yl	2	78%	8%

[a] In all cases, syn:anti >95:5. [b] Yield of the 1,4-reduction product.

Scheme 12.
Reductive Aldol Cyclization via Catalytic Hydrogenation. (Ref. 64a,b)



Scheme 13.
Reductive Aldol Cyclization via Catalytic Hydrogenation. (Ref. 64b,c)



Scheme 14.

syn-Diastereoselective Hydrogen-Mediated Aldol Coupling Employing Cationic Rhodium Catalysts Ligated By Tri(2-furyl)phosphine. (Ref. 64e-g)