Highlight Review

Formation of C–C Bonds via Ruthenium-catalyzed Transfer Hydrogenation: Carbonyl Addition from the Alcohol or Aldehyde Oxidation Level

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Abstract

Under the conditions of ruthenium-catalyzed transfer hydrogenation employing isopropyl alcohol as terminal reductant, π-unsaturated compounds (1,3-dienes, allenes, 1,3-enynes, and alkynes) reductively couple to aldehydes to furnish products of carbonyl addition. In the absence of isopropyl alcohol, π-unsaturated compounds couple directly from the alcohol oxidation level to form identical products of carbonyl addition. Such "*alcohol-unsaturate C–C couplings*" enable carbonyl allylation, propargylation and vinylation from the alcohol oxidation level in the absence of stoichiometric organometallic reagents or metallic reductants. Thus, direct catalytic C–H functionalization of alcohols at the carbinol carbon is achieved.

♦ Introduction

We have found that hydrogenation of unsaturates in the presence of carbonyl compounds and imines enables reductive C–C bond formation.[1–5,6a] More recently, under the conditions of iridium[4b,6b,7] or ruthenium-catalyzed[8] transfer hydrogenation, C–C coupling between unsaturates and carbonyl partners was observed. In such "*transfer hydrogenative C–C couplings*," hydrogen embedded within a donor alcohol, typically isopropyl alcohol, mediates unsaturate-carbonyl reductive coupling. Of greater significance, an alcoholic reactant may serve a dual role: as hydrogen donor and precursor to the carbonyl electrophile. *Thus, by exploiting alcohols and unsaturates as redox partners, carbonyl addition may be conducted from the alcohol oxidation level.*

Transfer hydrogenative carbonyl addition adds significantly to the evolution of carbonyl addition chemistry. First, C–C bond formation from the alcohol oxidation level enhances step economy by avoiding the redox manipulations typically required to convert alcohols to aldehydes. Secondly, the use of unsaturates as nonstabilized carbanion equivalents circumvents the use of preformed organometallic reagents and, hence, the generation of stoichiometric metallic by-products. In this account, the formation of C–C bonds under the conditions of ruthenium-catalyzed transfer hydrogenation is reviewed (Scheme 1).
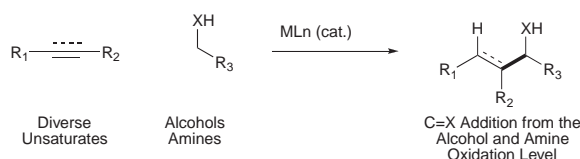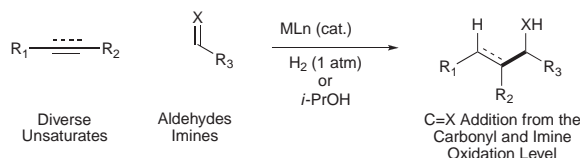
♦ Diene–Carbonyl Coupling from the Alcohol or Aldehyde Oxidation Level

Under the conditions of ruthenium-catalyzed transfer hydrogenation employing RuHCl(CO)(PPh₃)₃ as the precatalyst, di-
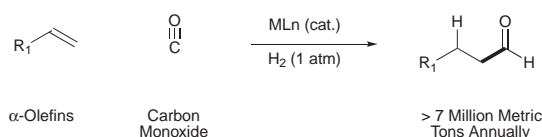
Scheme 1. Catalytic C–C bond formation under the conditions of hydrogenation and transfer hydrogenation.

rect coupling of acyclic dienes to carbonyl partners is achieved with complete regiocontrol from the alcohol or aldehyde oxidation level.[8a] Butadiene, isoprene, and 2,3-dimethylbutadiene couple to benzylic alcohols to provide products of carbonyl crotylation, isoprenylation, and reverse 2-methyl-prenylation, respectively. The presence of an acid cocatalyst (m-NO₂BzOH) is essential as only trace quantities of product are observed otherwise. Additionally, added acetone (2.5 mol %) and phosphine ligand have a beneficial effect upon the reaction efficiency. Using this first generation catalytic system, simple unactivated aliphatic alcohols engage in C–C coupling, as demonstrated by the union of isoprene and 1-nonanol (Scheme 2). For diene–aldehyde coupling, m-NO₂BzOH and acetone are not needed, though larger loadings of diene are required. Isopropyl alcohol or formic acid may serve as terminal reductant. The observed branched regioselectivity complements the linear regioselectivity observed in related Ni-catalyzed diene–aldehyde reductive couplings.[9,10] A limitation of this first-generation catalytic system involves control of relative and absolute stereochemistry (Table 1).

The coupling of isoprene to d_2-benzyl alcohol results in

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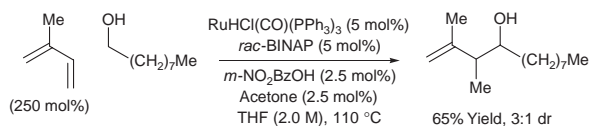
Scheme 2. Ruthenium-catalyzed transfer hydrogenative coupling of isoprene to an unactivated aliphatic alcohol.
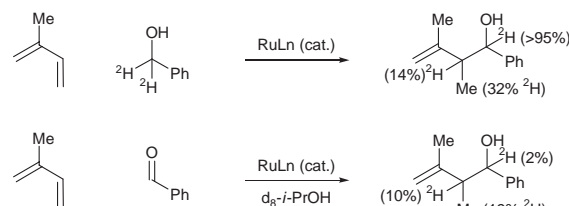
Table 1. Ruthenium-catalyzed transfer hydrogenative coupling of conjugated dienes to alcohols and aldehydes to furnish homoallylic alcohols[a]

[a]Conditions A employ no added ligand: Conditions B employ (p-MeOPh)$_3$P (15 mol %) as ligand; Conditions C employ rac-BINAP (5 mol %) as ligand.

Scheme 3. Isotopic labeling experiments in ruthenium-catalyzed transfer hydrogenative couplings of isoprene to benzyl alcohol and benzaldehyde.
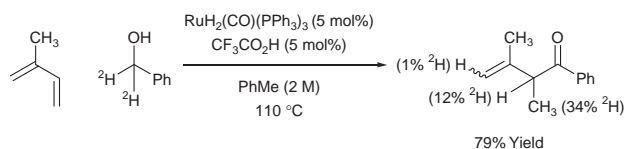
Table 2. Ruthenium-catalyzed transfer hydrogenative coupling of conjugated dienes to alcohols and aldehydes to furnish β,γ-unsaturated ketones[a]

[a]Butadiene (800 mol %), isoprene (250 mol %), 2,3-dimethylbutadiene (300 mol %), myrcene (300 mol %). [b]The reaction product was contaminated with approximately 10% of the α,β-unsaturated ketone.

transfer of a benzylic deuteride to the allylic methyl (19% ^{2}H) and allylic methine (32% ^{2}H). These data are consistent with reversible hydrometallation of the less substituted olefin to form a secondary σ-allyl. Conversion to the more stable primary σ-allyl haptomer occurs in advance of carbonyl addition, which proceeds through a closed six-centered transition state with allylic inversion to deliver the branched product of carbonyl allylation. In related aldehyde couplings employing d_8-isopropyl alcohol as the terminal reductant, incorporation of deuterium is observed at the allylic methyl (19% ^{2}H) and allylic methine (10% ^{2}H) (Scheme 3).

Based on the hypothesis that coordinative unsaturation should promote oxidation of the initially formed homoallylic alcohol, a ruthenium complex possessing a counter ion less strongly coordinating than chloride was sought. Exposure of RuH$_2$(CO)(PPh$_3$)$_3$ to acids HX is known to generate RuHX(CO)(PPh$_3$)$_3$ or RuX$_2$(CO)(PPh$_3$)$_2$.[11] Through an assay of acidic additives, it was found that diene–alcohol couplings performed using a catalyst generated in situ from RuH$_2$(CO)(PPh$_3$)$_3$ (5 mol %) and trifluoroacetic acid (TFA) (5 mol %) produce the

β,γ-unsaturated ketones in good to excellent isolated yields.[8d] Butadiene, isoprene, 2,3-dimethylbutadiene, and myrcene may serve as nucleophilic partners. In each case, complete branch regioselectivity is observed. Under identical conditions, isoprene couples to aldehydes to provide β,γ-unsaturated ketones in good to excellent isolated yields (Table 2).[8d,12]

Coupling of isoprene to d_2-benzyl alcohol under standard conditions employing the catalyst generated in situ from RuH$_2$(CO)(PPh$_3$)$_3$ (5 mol %) and trifluoroacetic acid (TFA) (5 mol %) provides the indicated β,γ-unsaturated ketone, which incorporates deuterium primarily at the allylic methyl (34%), and the allylic methine (12%). This pattern of deuterium incor-

Scheme 4. Ruthenium-catalyzed transfer hydrogenative coupling of isoprene to d_2-benzyl alcohol under oxidative conditions.
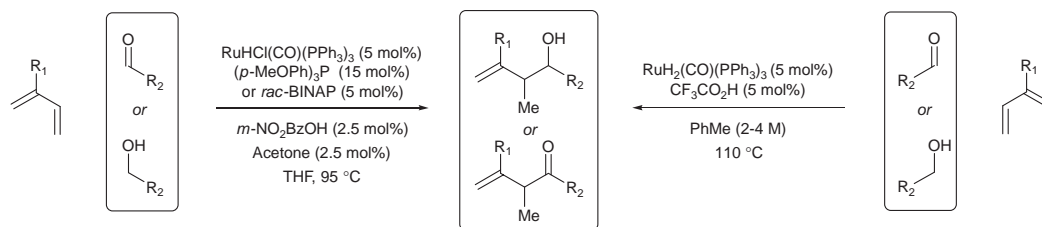
poration closely matches that obtained in the analogous coupling reaction of isoprene to d_2-benzyl alcohol to provide the homoallylic alcohol. Hence, a similar mechanism appears operative: hydrometallation of the less substituted olefin of isoprene to deliver the secondary σ-allyl metal haptomer, followed by carbonyl addition from the more stable primary σ-allyl haptomer through a six-centered transition structure with β-hydride elimination of the resulting alkoxide to deliver the ketone (Scheme 4).

Our collective studies of ruthenium-catalyzed diene–alcohol and diene–aldehyde transfer hydrogenative C–C coupling demonstrate that carbonyl addition may be achieved from the alcohol or aldehyde oxidation level to deliver either the homoallylic alcohol or the β,γ-unsaturated ketone. Thus, all oxidations levels of substrate (alcohol or aldehyde) and product (homoallyl alcohol or β,γ-unsaturated ketone) are accessible (Scheme 5).

Just as diene hydrometallation enables generation of transient allyl metal species, so should allene hydrometallation. Consequently, allenes were explored as nucleophilic partners in ruthenium-catalyzed transfer hydrogenative carbonyl addition. To our delight, upon exposure of 1,1-disubstituted allenes to paraformaldehyde and higher aldehydes in the presence of [RuBr(CO)$_3$(η^3-C$_3$H$_5$)] (5 mol %), t-BuPPh$_2$ (15 mol %), and isopropyl alcohol (400 mol %), branched products of carbonyl allylation bearing all-carbon quaternary centers are formed as single regioisomers.[8c] Related ruthenium-catalyzed allene–alcohol transfer hydrogenative couplings are currently under investigation. Again, a limitation of this first-generation catalytic system involves control of relative and absolute stereochemistry (Table 3).

♦ *Enyne–Carbonyl Coupling from the Alcohol or Aldehyde Oxidation Level*

Carbonyl propargylation based on C–C bond forming transfer hydrogenation is potentially achieved using conjugated enynes as surrogates to preformed allenyl metal reagents. The

Table 3. Ruthenium-catalyzed transfer hydrogenative coupling of allenes to paraformaldehyde and higher aldehydes to furnish homoallylic alcohols[a]

Allene	Product	Isolated Yield
Ph, Me	OH, R$_3$, Me, Ph	R$_3$ = H, 86% Yield; R$_3$ = p-NO$_2$Ph, 87% Yield, 2:1 dr; R$_3$ = CH$_2$OBn, 71% Yield, 1:1 dr
p-MeOPh, MeO	OH, R$_3$, p-MeOPh, OMe	R$_3$ = H, 74% Yield; R$_3$ = p-NO$_2$Ph, 76% Yield, 1:1 dr; R$_3$ = CH$_2$OBn, 72% Yield, 2:1 dr
n-Bu, Et	OH, R$_3$, n-Bu, Et	R$_3$ = H, 77% Yield; R$_3$ = p-NO$_2$Ph, 82% Yield, 1:1 dr; R$_3$ = CH$_2$OBn, 70% Yield, 1:1 dr

[a]For couplings to paraformaldehyde: allene (100 mol %), paraformaldehyde (400 mol %). For couplings to higher aldehydes: allene (200 mol %), paraformaldehyde (200 mol %).

outcome of such couplings was uncertain, as enynes engage in C–C bond formation at the acetylenic terminus under the conditions of rhodium[2a,2b,2e,2g] and nickel[13] catalysis. Nevertheless, it was found that exposure of 1,3-enynes to alcohols in the presence of catalyst prepared in situ from RuHCl(CO)(PPh$_3$)$_3$ and DPPF provides the desired products of carbonyl propargylation as single regioisomers.[8b] Iridium complexes also catalyze enyne-mediated propargylation, but ruthenium catalysts were found to be superior.

This carbonyl propargylation protocol exhibits remarkably broad substrate scope. Benzylic alcohols, allylic alcohols and unactivated aliphatic alcohols participate in enyne-mediated carbonyl propargylation in good to excellent yield and with exceptional regiocontrol. Additionally, a variety of 1,3-enynes are tolerated (Table 4, top). Under related transfer hydrogenation conditions employing isopropyl alcohol as the terminal reductant, carbonyl propargylation is achieved from the aldehyde oxidation level, although in certain cases the coupling product is contaminated by small quantities ($\leq$10%) of alkyne reduction to form the *cis*-alkene (Table 4, bottom). Thus, through ruthenium-catalyzed transfer hydrogenative coupling, carbonyl propargylation can be achieved in the absence of preformed allenyl metal reagents from the alcohol or aldehyde oxidation level.

All Oxidation Levels of Substrate and Product are Accessible

Scheme 5. Transcending oxidation level via ruthenium-catalyzed diene–alcohol and diene–aldehyde transfer hydrogenative C–C coupling.
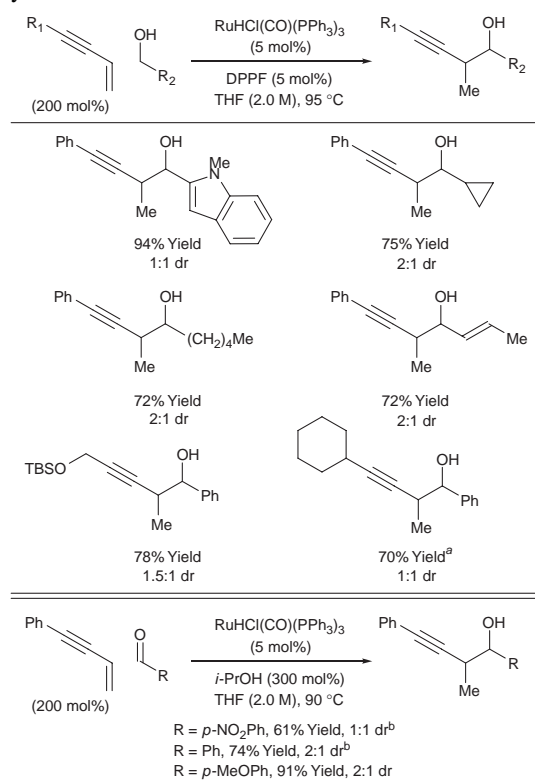
Table 4. Carbonyl propargylation via ruthenium-catalyzed transfer hydrogenative coupling of 1,3-enynes to alcohols and aldehydes

[a] m-NO$_2$BzOH (5 mol %) employed as additive. [b] Product was accompanied by ca. 10% alkyne reduction.
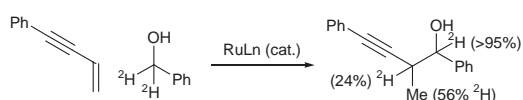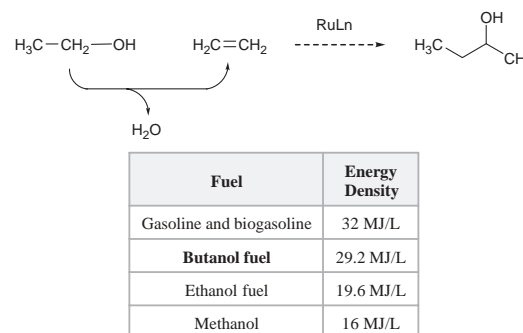

Scheme 6. Isotopic labeling experiments in ruthenium-catalyzed transfer hydrogenative couplings of 1,3-enynes.

Stereocontrolled enyne-mediated propargylation represents an important goal of ongoing research.

Enyne coupling to d_2-benzyl alcohol results in transfer of a benzylic deuteride to the allylic methyl (56% [2]H) and allylic methine (24% [2]H). Deuterium is completely retained at the benzylic methine of the coupling product (Scheme 6). These results are consistent with a catalytic cycle involving aldehyde generation via alcohol dehydrogenation followed by reversible alkene hydrometallation from the resulting ruthenium hydride to furnish an allenylmetal species. Carbonyl addition with propargylic transposition delivers the 2-propynyl alcohol.

♦ Alkyne–Carbonyl Coupling from the Alcohol Oxidation Level

Allylic alcohols are important building blocks in organic synthesis. One important strategy for their synthesis involves the catalytic asymmetric addition of vinyl–metal reagents to aldehydes.[14] More recently, direct carbonyl vinylation has
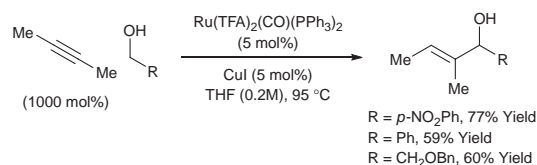
Scheme 7. Carbonyl vinylation via ruthenium-catalyzed transfer hydrogenative coupling of butyne to alcohols.

Fuel	Energy Density
Gasoline and biogasoline	32 MJ/L
Butanol fuel	29.2 MJ/L
Ethanol fuel	19.6 MJ/L
Methanol	16 MJ/L

Scheme 8. By-product-free conversion of ethanol and ethylene to sec-butanol via ruthenium-catalyzed transfer hydrogenative coupling.

been achieved via metal-catalyzed alkyne–aldehyde reductive coupling.[2b–2h,15] Transfer hydrogenative alkyne–alcohol coupling would enable direct carbonyl vinylation in the absence of any stoichiometric reductant. In a preliminary set of experiments, it was found that exposure of alcohols to butyne in the presence of Ru(TFA)(CO)(PPh$_3$)$_2$ results in formation of the desired allylic alcohols.[8e] Thus, carbonyl vinylation is achieved from the alcohol oxidation level in absence of any stoichiometrically preformed vinyl metal reagents (Scheme 7).

♦ Conclusion and Outlook

Under the conditions of ruthenium-catalyzed transfer hydrogenation, one may perform carbonyl allylation, propargylation and vinylation from the aldehyde or alcohol oxidation level. These initial findings evoke numerous possibilities for alcohol–unsaturate coupling. For example, transfer hydrogenative coupling of ethylene and alcohols would enable carbonyl ethylation from the alcohol oxidation level, eliminating the need for diethylzinc–a pyrophoric liquid. Ethylene–ethanol coupling would represent a by-product-free method for the preparation of sec-butyl alcohol, an attractive biofuel (Scheme 8).

Many challenges remain. Activation of isolated olefins in transfer hydrogenative C–C coupling is an especially important objective. Additionally, the development of stereoselective couplings and imine addition from the amine oxidation level will be required for applications in the area of fine chemical synthesis. It is the author's hope that the work described in this account will itself catalyze further progress toward these goals.

References and Notes

1 For selected reviews of hydrogenative C–C coupling, see: a) M.-Y. Ngai, J.-R. Kong, M. J. Krische, *J. Org. Chem.* **2007**, *72*, 1063. b) H. Iida, M. J. Krische, *Top. Curr. Chem.* **2007**, *279*, 77. c) E. Skucas, M.-Y. Ngai, V. Komanduri, M. J. Krische, *Acc. Chem. Res.* **2007**, *40*, 1394.

2 For hydrogenative C=X vinylation, see: a) J.-R. Kong, C.-W. Cho, M. J. Krische, *J. Am. Chem. Soc.* **2005**, *127*, 11269. b) J.-R. Kong, M.-Y. Ngai, M. J. Krische, *J. Am. Chem. Soc.* **2006**, *128*, 718. c) J. U. Rhee, M. J. Krische, *J. Am. Chem. Soc.* **2006**, *128*, 10674. d) J. R. Kong, M. J. Krische, *J. Am. Chem. Soc.* **2006**, *128*, 16040. e) V. Komanduri, M. J. Krische, *J. Am. Chem. Soc.* **2006**, *128*, 16448. f) C.-W. Cho, M. J. Krische, *Org. Lett.* **2006**, *8*, 3873. g) Y.-T. Hong, C.-W. Cho, E. Skucas, M. J. Krische, *Org. Lett.* **2007**, *9*, 3745. h) M.-Y. Ngai, A. Barchuk, M. J. Krische, *J. Am. Chem. Soc.* **2007**, *129*, 280. i) E. Skucas, J. R. Kong, M. J. Krische, *J. Am. Chem. Soc.* **2007**, *129*, 7242. j) A. Barchuk, M.-Y. Ngai, M. J. Krische, *J. Am. Chem. Soc.* **2007**, *129*, 8432. k) M.-Y. Ngai, A. Barchuk, M. J. Krische, *J. Am. Chem. Soc.* **2007**, *129*, 12644.

3 For hydrogenative aldol and Mannich addition, see: a) C.-K. Jung, S. A. Garner, M. J. Krische, *Org. Lett.* **2006**, *8*, 519. b) C.-K. Jung, M. J. Krische, *J. Am. Chem. Soc.* **2006**, *128*, 17051. c) S. A. Garner, M. J. Krische, *J. Org. Chem.* **2007**, *72*, 5843. d) C. Bee, S. B. Han, A. Hassan, H. Iida, M. J. Krische, *J. Am. Chem. Soc.* **2008**, *130*, 2746.

4 For hydrogenative acyl substitution via reductive hydroacylation, see: Y.-T. Hong, A. Barchuk, M. J. Krische, *Angew. Chem., Int. Ed.* **2006**, *45*, 6885.

5 For iridium-catalyzed hydrogenative and transfer hydrogenative carbonyl allylations employing allenes as allyl donors, see: a) E. Skucas, J. F. Bower, M. J. Krische, *J. Am. Chem. Soc.* **2007**, *129*, 12678. b) J. F. Bower, E. Skucas, R. L. Patman, M. J. Krische, *J. Am. Chem. Soc.* **2007**, *129*, 15134.

6 For rhodium- and iridium-catalyzed couplings of dienes to carbonyl compounds under hydrogenative and transfer hydrogenative conditions, respectively, see: a) H.-Y. Jang, R. R. Huddleston, M. J. Krische, *Angew. Chem., Int. Ed.* **2003**, *42*, 4074. b) J. F. Bower, R. L. Patman, M. J. Krische, *Org. Lett.* **2008**, *10*, 1033.

7 For iridium-catalyzed transfer hydrogenative carbonyl allylations employing allyl acetate as an allyl donor, see: a) I. S. Kim, M.-Y. Ngai, M. J. Krische, *J. Am. Chem. Soc.* **2008**, *130*, 6340. b) I. S. Kim, M.-Y. Ngai, M. J. Krische, **2008**, submitted for publication.

8 For ruthenium-catalyzed transfer hydrogenative coupling, see: a) F. Shibahara, J. F. Bower, M. J. Krische, *J. Am. Chem. Soc.* **2008**, *130*, 6338. b) R. L. Patman, V. M. Williams, J. F. Bower, M. J. Krische, *Angew. Chem., Int. Ed.* **2008**, *47*, 5220. c) M.-Y. Ngai, E. Skucas, M. J. Krische, *Org. Lett.* **2008**, *10*, 2705. d) F. Shibahara, J. F. Bower, M. J. Krische, **2008**, submitted for publication. e) R. L. Patman, M. Chauligain, V. M. Williams, M. J. Krische, submitted for publication.

9 Nickel catalytic intermolecular diene–aldehyde reductive coupling: a) M. Kimura, A. Ezoe, K. Shibata, Y. Tamaru, *J. Am. Chem. Soc.* **1998**, *120*, 4033. b) M. Takimoto, Y. Hiraga, Y. Sato, M. Mori, *Tetrahedron Lett.* **1998**, *39*, 4543. c) M. Kimura, H. Fujimatsu, A. Ezoe, K. Shibata, M. Shimizu, S. Matsumoto, Y. Tamaru, *Angew. Chem., Int. Ed.* **1999**, *38*, 397. d) M. Kimura, K. Shibata, Y. Koudahashi, Y. Tamaru, *Tetrahedron Lett.* **2000**, *41*, 6789. e) M. Kimura, A. Ezoe, S. Tanaka, Y. Tamaru, *Angew. Chem., Int. Ed.* **2001**, *40*, 3600. f) T.-P. Loh, H.-Y. Song, Y. Zhou, *Org. Lett.* **2002**, *4*, 2715. g) Y. Sato, R. Sawaki, N. Saito, M. Mori, *J. Org. Chem.* **2002**, *67*, 656. h) L. Bareille, P. L. Gendre, C. Moïse, *Chem. Commun.* **2005**, 775. i) M. Kimura, A. Ezoe, M. Mori, K. Iwata, Y. Tamaru, *J. Am. Chem. Soc.* **2006**, *128*, 8559. j) Y. Yang, S.-F. Zhu, H.-F. Duan, C.-Y. Zhou, L.-X. Wang, Q.-L. Zhou, *J. Am. Chem. Soc.* **2007**, *129*, 2248. k) Y. Sato, Y. Hinata, R. Seki, Y. Oonishi, N. Saito, *Org. Lett.* **2007**, *9*, 5597.

10 For reviews encompassing nickel-catalyzed diene–aldehyde reductive coupling, see: a) Y. Tamaru, *J. Organomet. Chem.* **1999**, *576*, 215. b) S. Ikeda, *Angew. Chem., Int. Ed.* **2003**, *42*, 5120. c) J. Montgomery, *Angew. Chem., Int. Ed.* **2004**, *43*, 3890. d) *Modern Organonickel Chemistry*, ed. by Y. Tamaru, Wiley-VCH, Weinheim, Germany, **2005**. e) M. Kimura, Y. Tamaru, *Top. Curr. Chem.* **2007**, *279*, 173.

11 A. Dobson, S. D. Robinson, M. F. Uttley, *J. Chem. Soc., Dalton Trans.* **1975**, 370.

12 For intermolecular hydroacylation of dienes catalyzed by ruthenium, see: T. Kondo, N. Hiraishi, Y. Morisaki, K. Wada, Y. Watanabe, T. Mitsudo, *Organometallics* **1998**, *17*, 2131.

13 For nickel-catalyzed reductive coupling of 1,3-enynes to carbonyl compounds, see: a) K. M. Miller, T. Luanphaisarnnont, C. Molinaro, T. F. Jamison, *J. Am. Chem. Soc.* **2004**, *126*, 4130. b) K. M. Miller, T. F. Jamison, *Org. Lett.* **2005**, *7*, 3077. c) K. M. Miller, E. A. Colby, K. S. Woodin, T. F. Jamison, *Adv. Synth. Catal.* **2005**, *347*, 1533.

14 For enantioselective catalytic addition of vinyl–metal reagents to aldehydes, see: a) W. Oppolzer, R. Radinov, *Helv. Chim. Acta* **1992**, *75*, 170. b) W. Oppolzer, R. Radinov, *J. Am. Chem. Soc.* **1993**, *115*, 1593. c) K. Soai, K. Takahashi, *J. Chem. Soc., Perkin Trans. 1* **1994**, 1257. d) P. Wipf, W. Xu, *Tetrahedron Lett.* **1994**, *35*, 5197. e) W. Oppolzer, R. N. Radinov, J. D. Brabander, *Tetrahedron Lett.* **1995**, *36*, 2607. f) P. Wipf, S. Ribe, *J. Org. Chem.* **1998**, *63*, 6454. g) W. Oppolzer, R. N. Radinov, E. El-Sayed, *J. Org. Chem.* **2001**, *66*, 4766. h) S. Dahmen, S. Bräse, *Org. Lett.* **2001**, *3*, 4119. i) Y. K. Chen, A. E. Lurain, P. J. Walsh, *J. Am. Chem. Soc.* **2002**, *124*, 12225. j) J.-X. Ji, L.-Q. Qiu, C. W. Yip, A. S. C. Chan, *J. Org. Chem.* **2003**, *68*, 1589. k) A. E. Lurain, P. J. Walsh, *J. Am. Chem. Soc.* **2003**, *125*, 10677. l) D.-H. Ko, S.-W. Kang, K. H. Kim, Y. Chung, D.-C. Ha, *Bull. Korean Chem. Soc.* **2004**, *25*, 35. m) C. M. Sprout, M. L. Richmond, C. T. Seto, *J. Org. Chem.* **2004**, *69*, 6666. n) S.-J. Jeon, Y. K. Chen, P. J. Walsh, *Org. Lett.* **2005**, *7*, 1729. o) F. Lauterwasser, J. Gall, S. Hoefener, S. Bräse, *Adv. Synth. Catal.* **2006**, *348*, 2068. p) S.-J. Jeon, E. L. Fisher, P. J. Carroll, P. J. Walsh, *J. Am. Chem. Soc.* **2006**, *128*, 9618. q) L. Salvi, S.-J. Jeon, E. L. Fisher, P. J. Carroll, P. J. Walsh, *J. Am. Chem. Soc.* **2007**, *129*, 16119.

15 For selected reviews encompassing intra- and intermolecular direct reductive coupling of alkynes to carbonyl partners, see: a) I. Ojima, M. Tzamarioudaki, Z. Li, R. J. Donovan,

Chem. Rev. **1996**, *96*, 635. b) J. Montgomery, *Acc. Chem. Res.* **2000**, *33*, 467. c) J. Montgomery, K. K. D. Amarashinghe, S. K. Chowdhury, E. Oblinger, J. Seo, A. V. Savchenko, *Pure Appl. Chem.* **2002**, *74*, 129. d) S.-I. Ikeda, *Angew. Chem., Int. Ed.* **2003**, *42*, 5120. e) K. M. Miller, C. Molinaro, T. F. Jamison, *Tetrahedron: Asymmetry* **2003**, *14*, 3619. f) J. Montgomery, *Angew. Chem., Int. Ed.* **2004**, *43*, 3890. g) R. M. Moslin, K. Miller-Moslin, T. F. Jamison, *Chem. Commun.* **2007**, 4441. h) J. Montgomery, G. J. Sormunen, *Top. Curr. Chem.* **2007**, *279*, 1.