

Cite this: *Chem. Sci.*, 2012, **3**, 2202

www.rsc.org/chemicalscience

MINIREVIEW

Catalytic intermolecular hydroacylation of C–C π -bonds in the absence of chelation assistance

Joyce C. Leung and Michael J. Krische*

Received 19th March 2012, Accepted 11th April 2012

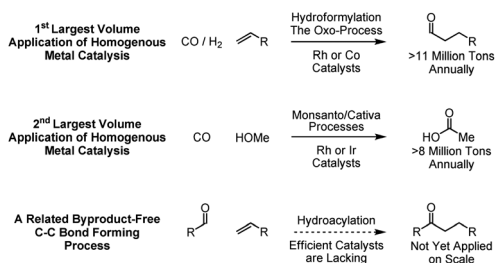
DOI: 10.1039/c2sc20350b

Intermolecular rhodium catalyzed hydroacylation in the absence of chelation assistance remains a largely unmet challenge due to competing decarbonylation of the acylrhodium intermediates to form catalytically inactive carbonyl complexes. Here, catalytic systems for intermolecular hydroacylation in the absence of chelation assistance are reviewed, with an emphasis on recently described processes that operate through mechanistic pathways beyond aldehyde C–H oxidative addition.

1. Introduction and scope of review

The two largest volume applications of homogenous metal catalysis, hydroformylation (the oxo-process)¹ and methanol carbonylation (the Monsanto/Cativa process),² are each byproduct-free C–C bond forming processes applicable to vastly abundant feedstocks. These “process-relevant” characteristics are shared by hydroacylation,³ however, implementation of hydroacylation on scale remains an unmet challenge, largely due to a mechanistic impasse associated with the use of conventional rhodium catalysts (Scheme 1).

In this account, the challenges posed by intermolecular rhodium catalyzed hydroacylation are summarized, followed by a survey of intermolecular hydroacylations employing catalysts beyond rhodium, and mechanistic pathways beyond aldehyde C–H oxidative addition. For metal catalyzed intramolecular hydroacylation and intermolecular hydroacylations that rely upon reactant-based chelation assistance, the reader is referred to the review literature.³ Radical mediated hydroacylation is not covered, but leading references are provided.⁴



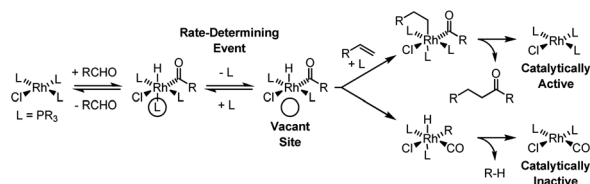
Scheme 1 Byproduct-free C–C bond forming processes applicable to abundant feedstocks: hydroformylation, methanol carbonylation and hydroacylation.

Department of Chemistry and Biochemistry, University of Texas at Austin, 1 University Station A5300, Austin, TX 78712, USA. E-mail: mkrische@mail.utexas.edu; Fax: +1 613 9418447; Tel: +1 512 2325892

2.1 Rhodium catalysts

Following the observation that Wilkinson's complex $\text{Rh}(\text{PPh}_3)_3\text{Cl}$ reacts with aldehydes stoichiometrically to provide products of decarbonylation (1968),^{5,6} the first alkene hydroacylation was reported by Sakai *et al.* in 1972.⁷ Sakai's hydroacylation, an intramolecular process or cycloisomerization,⁸ heralded a large body of work on the cyclization of olefinic aldehydes to form ketone products.³ However, attempted intermolecular rhodium catalyzed hydroacylations were found to suffer notoriously from competing decarbonylation of the acylrhodium intermediates to furnish catalytically inactive carbonyl complexes. Partitioning decarbonylation and hydroacylation pathways in reactions of simple aliphatic aldehydes and α -olefins is especially difficult as both pathways diverge from a common intermediate. As established in a stoichiometric transformation,⁹ aldehyde oxidative addition to Wilkinson's catalyst provides the *cis*-(hydrido)(acyl)rhodium complex, which is subject to rate-determining dissociation of the phosphine ligand *trans* to the hydride, due to the large hydride *trans* effect.¹⁰ The resulting coordinatively unsaturated complex is subject to either hydroacylation or decarbonylation (Scheme 2).

As first reported by Suggs (1978), decarbonylation is suppressed for β -chelating aldehydes, as formation of a strained four-membered metallacycle would result.¹¹ Subsequently, numerous examples of the intermolecular hydroacylation of various π -unsaturated reactants employing chelating aldehydes

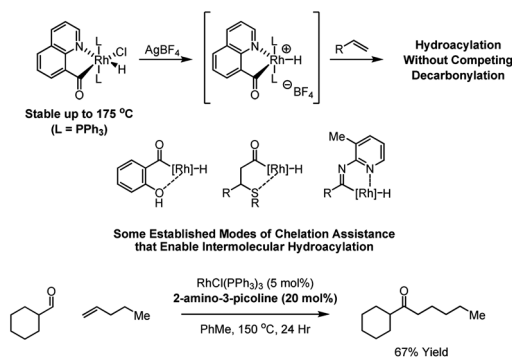


Scheme 2 Intermolecular rhodium-catalyzed hydroacylation is inefficient due to competing decarbonylation.

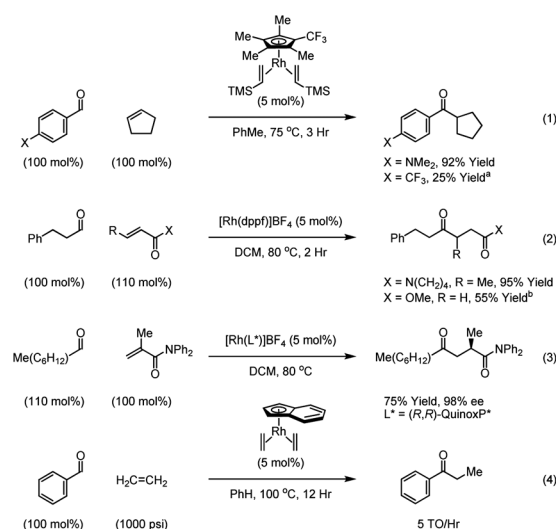
were reported, including reactions of *ortho*-(diphenylphosphino) benzaldehydes,¹² olefinic aldehydes,¹³ salicylaldehydes,¹⁴ β -sulfinyl-aldehydes¹⁵ and (*N*-2-pyridyl)aldimines.¹⁶ The requirement of aldehydes that possess chelating groups is an intrinsically limiting contrivance. However, inspired by Suggs' report, Jun *et al.* found that (*N*-2-pyridyl)aldimines can be generated *in situ* by performing the hydroacylation in the presence of 2-amino-3-picoline.¹⁶ This process is perhaps the very first example of a dynamic covalent directing group in metal catalysis (Scheme 3).¹⁷

Intermolecular rhodium catalyzed hydroacylations that operate *via* aldehyde C–H oxidative addition, and that occur in the absence of chelation assistance, are rare.¹⁸ Upon consideration of these examples, however, a combination of factors required to suppress competing decarbonylation is revealed. As described by Brookhart *et al.* (Scheme 4, eqn (1)),^{18b} using carefully tailored rhodium catalysts, aromatic aldehydes hydroacylate olefins to form aryl ketones. In these transformations, the acyl C–C bond of the aryl aldehyde is relatively strong compared to aliphatic aldehydes, which decarbonylate and isomerize under identical conditions.^{18b} Secondly, the electron deficient nature of the rhodium catalyst facilitates reductive elimination, postulated to be the turn-over limiting event in this specific system, while disfavoring introduction of a π -acidic carbonyl ligand to the high valent rhodium(III) center. As illustrated by Tanaka *et al.* in the case of acrylamides (Scheme 4, eqn (2)),^{18c} decarbonylation is also suppressed for olefin partners that more effectively compete for the vacant coordination site of the acylrhodium hydride intermediate. Indeed, less strongly coordinating acrylic esters react less efficiently. Enantioselective acrylamide hydroacylations are achieved using cationic rhodium catalysts modified by (*R,R*)-QuinoxP* (Scheme 4, eqn (3)).^{18d} The importance of strongly coordinating olefin partners is consistent with Milstein *et al.*'s earlier observation that ethylene, which binds metals more strongly than higher alkyl olefins,¹⁹ participates in efficient hydroacylation, albeit under extreme conditions (Scheme 4, eqn (4)).^{18a}

Based on a preliminary study by Miura *et al.*,^{20a} the present author developed a reductive hydroacylation of anhydrides with activated olefins employing elemental hydrogen as the terminal reductant.^{20b} To achieve high levels of branch-regioselectivity and good isolated yields, a cationic rhodium catalyst modified by



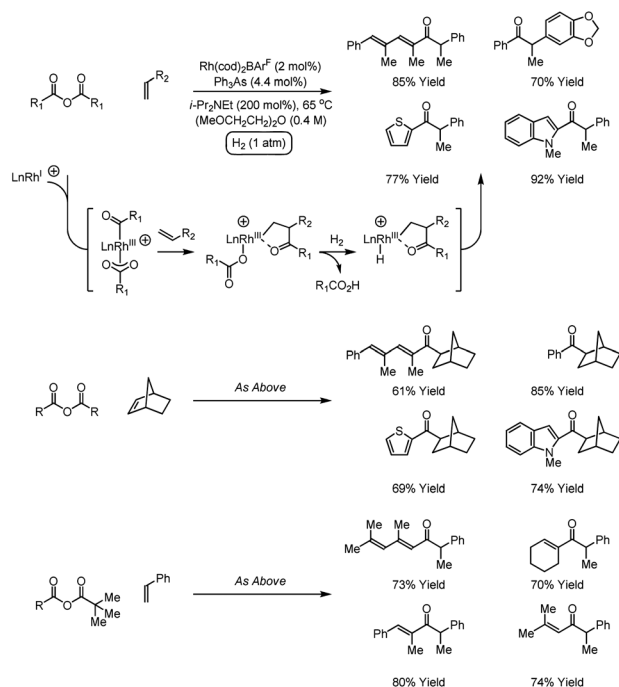
Scheme 3 Selected modes of chelation assistance that promote efficient intermolecular hydroacylation and dynamic covalent chelation assistance as described by Jun *et al.*



Scheme 4 Subtle manipulation of catalyst electronics and olefin coordinating ability enable efficient intermolecular rhodium-catalyzed hydroacylation of non-chelating aldehydes. ^a Catalyst (11 mol%), 100 °C, 48 h, GC yield. ^b Catalyst (10 mol%), 20 h, methyl acrylate as solvent.

triphenylarsine is required. The catalytic mechanism involves oxidative addition of cationic rhodium(I) to the anhydride to generate an acylrhodium(III) carboxylate.²¹ Olefin insertion followed by hydrogenolysis of the carboxylate ligand delivers an alkylrhodium hydride, which upon reductive elimination provides the product of hydroacylation as the branched regioisomer exclusively. Computational studies on related transformations suggest that hydrogenolysis of the rhodium carboxylate occurs by way of a six-centered transition for σ -bond metathesis,²² which may account for the observation that anhydrides are superior to acid chlorides and acid fluorides as acyl donors. Aromatic anhydrides or α,β -unsaturated anhydrides are required for efficient hydroacylation, again suggesting that decarbonylation is suppressed for aldehydes possessing strong sp^2 – sp^2 acyl C–C bonds. Whereas simple unactivated olefins do not engage in efficient reductive hydroacylation, good isolated yields are observed using a more strongly coordinating olefin in the form of norbornene. Finally, mixed anhydrides based on pivalic acid selectively transfer the sterically less demanding acyl moiety with exclusive branched regioselectivity (Scheme 5).

To summarize, it appears that a combination of three principal features contribute to the suppression of competing decarbonylation pathways in rhodium catalyzed hydroacylation: (1) electron deficient rhodium catalysts, typically those that are cationic, disfavor decarbonylation presumably to avoid destabilization associated with introduction of a π -acidic carbonyl ligand onto an electrophilic high valent rhodium(III) center. (2) Acyl donors with relatively strong acyl C–C bonds, such as aromatic aldehydes with electron releasing *para*-substituents, are more resistant to decarbonylation. (3) The use of strongly coordinating olefin partners is advantageous as they better compete for the vacant coordination site of the acylrhodium hydride intermediate, which would otherwise mediate decarbonylation. Notably, despite the collective mechanistic insights, efficient rhodium catalyzed



Scheme 5 Reductive intermolecular rhodium-catalyzed hydroacylation using anhydrides as non-chelating acyl donors.

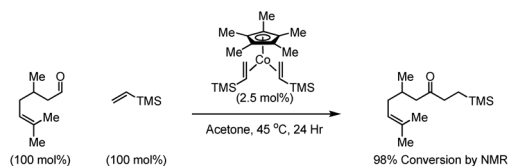
hydroacylations of simple aliphatic aldehydes and α -olefins remain elusive.

2.2 Cobalt catalysts

The challenges associated with rhodium catalyzed intermolecular hydroacylation of non-chelating acyl donors have driven investigations into the use of other metal catalysts. Cobalt, an inexpensive group 9 metal, is a logical starting point, however, like the parent rhodium based catalysts, deactivation *via* decarbonylation of acylmetal intermediates is a significant liability. To our knowledge, only a single example of cobalt catalyzed hydroacylation is reported from the laboratory of Brookhart.²³ Diverse aromatic and aliphatic aldehydes are tolerated, but the reaction is limited to the use of vinyl silanes as acyl acceptors (Scheme 6).

2.3 Ruthenium catalysts

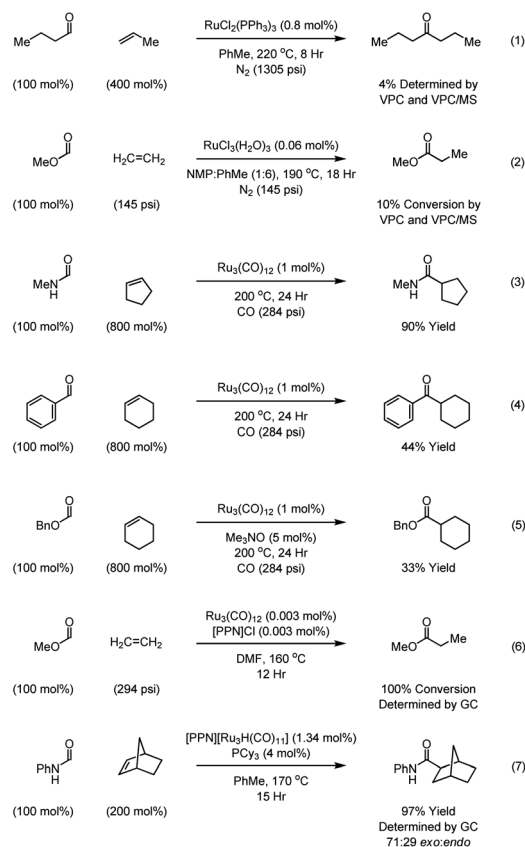
Early examples of ruthenium catalyzed hydroacylations of non-chelating aldehydes that operate *via* C–H oxidative addition are inefficient largely due to the requirement for high reaction temperatures, which contribute to competing side reactions. For example, using aliphatic aldehydes as acyl donors,^{24a} hydroacylation competes with the formation of aldol, Cannizzaro and



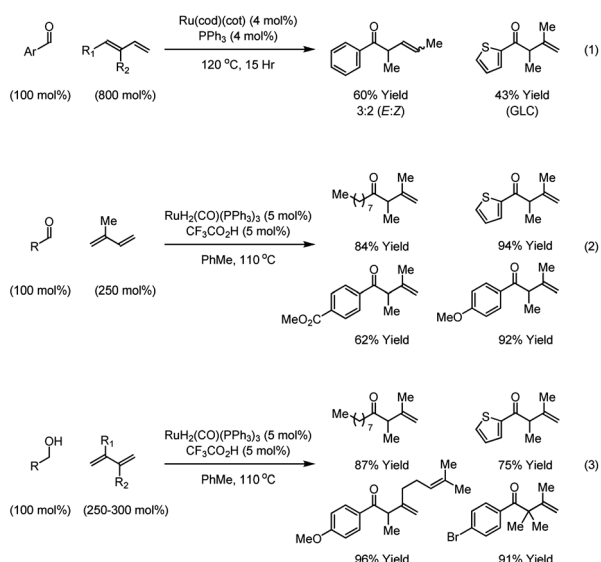
Scheme 6 Cobalt catalyzed hydroacylation of vinylsilanes.

Tischenko products (Scheme 7, eqn (1)). Whereas formate esters react inefficiently (Scheme 7, eqn (2)),^{24b} Watanabe and Kondo *et al.* report that formamides engage in efficient hydroacylation using $\text{Ru}_3(\text{CO})_{12}$ as a precatalyst under carbon monoxide pressure in the absence of solvent (Scheme 7, eqn (3)).^{24c} The $\text{Ru}_3(\text{CO})_{12}$ catalyzed hydroacylation is also applicable to aromatic aldehydes^{24d,h} and formate esters,^{24f} although modest yields are obtained (Scheme 7, eqn (4) and (5)). Attempted hydroacylation using aliphatic aldehydes under these conditions results in transhydroformylation.^{24h} Lavigne and Kalck *et al.* later found that $[\text{PPN}]\text{Cl}$, $[\text{Ph}_3\text{P}=\text{N}=\text{PPh}_3]\text{Cl}$, improves the efficiency of the $\text{Ru}_3(\text{CO})_{12}$ catalyzed hydroacylation of ethylene using methyl formate in the absence of exogenous carbon monoxide (Scheme 7, eqn (6)).^{24j} Although DMF is used as solvent, the authors apparently do not observe products of formamide-mediated hydroacylation, which is interesting as Kondo *et al.* subsequently developed the ruthenium catalyst $[\text{PPN}][\text{Ru}_3\text{H}(\text{CO})_{11}]/\text{PCy}_3$, which promotes the efficient hydroacylation of ethylene and norbornene using formamides (Scheme 7, eqn (7)).^{24k}

In 1998, Watanabe and Kondo *et al.* reported that the catalyst generated upon the combination of $\text{Ru}(\text{cod})(\text{cot})$ and PPh_3 promotes efficient hydroacylation of aromatic aldehydes with conjugated dienes to provide β,γ -enones (Scheme 8, eqn (1)).^{25a} A carbon monoxide pressure was not required. A mechanism involving aldehyde C–H oxidative addition was proposed. In 2008, following Krische *et al.*'s report of the coupling of dienes to



Scheme 7 Ruthenium catalyzed olefin hydroacylation. PPN = bis(triphenylphosphoranylidene)ammonium, $[\text{Ph}_3\text{P}=\text{N}=\text{PPh}_3]$.

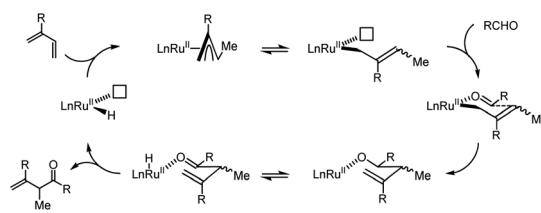


Scheme 8 Ruthenium catalyzed diene hydroacylation from the alcohol or aldehyde oxidation level.

either alcohols or aldehydes to furnish homoallylic alcohols,^{25b} Krische *et al.*^{25c} and Ryu *et al.*^{25d} independently reported that ruthenium(II) hydrides modified by phosphine ligands catalyze efficient intermolecular diene hydroacylation to form β,γ -enones using aromatic, aliphatic and α,β -unsaturated aldehydes. Furthermore, Krische demonstrated that identical hydroacylation products are generated from the alcohol or aldehyde oxidation level of the acyl donor under the same reaction conditions (Scheme 8, eqn (2) and (3)).

The mechanism of the ruthenium catalyzed diene hydroacylations described by Krische and Ryu represents a departure from conventional aldehyde C–H oxidative addition pathways. Isotopic labeling studies performed by Krische and double labeling crossover experiments performed by Ryu are consistent with the indicated catalytic mechanism, which begins with diene hydroacylation to form a π -allylruthenium species. This step in the mechanism finds precedent in the stoichiometric reaction of $\text{RuHCl}(\text{CO})(\text{PPh}_3)_3$ with 1,2- and 1,3-dienes to form π -allyl complexes that have been characterized by single crystal X-ray diffraction and NMR, respectively.²⁶ Aldehyde addition by way of a chair like transition structure is corroborated by Krische's studies, which establish that (*E*)- and (*Z*)-allylruthenium species engage in stereospecific aldehyde addition to form diastereomeric *anti*- and *syn*-homoallylic alcohols, respectively.²⁷ Dehydrogenation of the resulting homoallylic ruthenium alkoxide *via* β -hydride elimination delivers the hydroacylation product and regenerates the starting ruthenium hydride to close the catalytic cycle. The corresponding reactions of alcohols are oxidative, and likely involve initial alcohol–diene transfer hydrogenation to form the requisite aldehyde along with the mono-olefin. As ruthenium trifluoroacetate complexes are known to promote “acceptorless” alcohol dehydrogenation with evolution of elemental hydrogen,²⁸ sacrificial diene oxidant may not be required. Otherwise, a related catalytic cycle is envisioned (Scheme 9).

Using $\text{Ru}(\text{O}_2\text{CCF}_3)_2(\text{CO})(\text{PPh}_3)_2$ as a precatalyst, hydrogen is transferred from primary alcohols to 2-butyne to generate

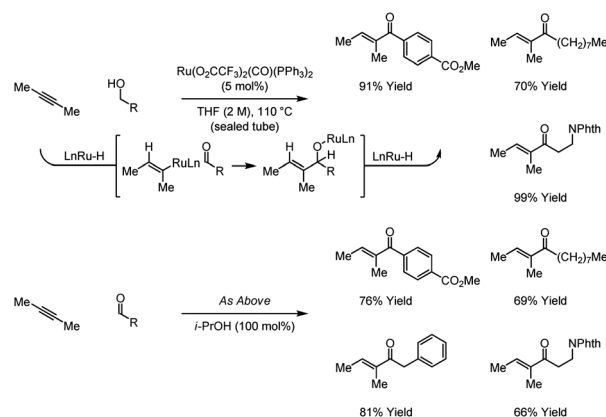


Scheme 9 A general catalytic mechanism for ruthenium catalyzed diene hydroacylation.

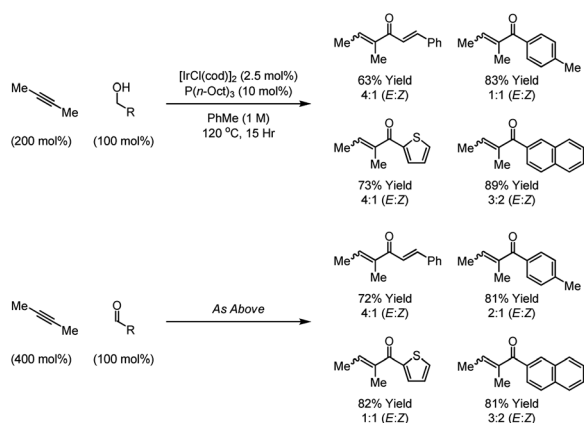
aldehyde–vinylruthenium pairs, which react to give allylic alcohols.^{29a} However, as established by Krische *et al.* in 2009, at higher reaction temperatures, higher concentrations and longer reaction times, the initially formed allylic alcohols dehydrogenate to form α,β -unsaturated ketones.^{29b} Under nearly identical conditions, 2-butyne couples to aldehydes to provide identical reaction products. Thus, intermolecular alkyne hydroacylation is achieved from the alcohol or aldehyde oxidation level (Scheme 10).

2.4 Iridium catalysts

To date, examples of iridium catalyzed hydroacylations that operate *via* aldehyde C–H oxidative addition have not been described due to the predominance of competing decarbonylation, which itself represents a preparatively useful procedure for the catalytic conversion of aldehydes to alkanes.³⁰ However, in 2010 Obora and Ishii *et al.* demonstrated that alkynes are subject to hydroacylation using alcohols or aldehydes as acyl donors through a transfer hydrogenation mechanism.^{31a} Specifically, upon exposure to an iridium catalyst generated *in situ* from $[\text{Ir}(\text{OH})(\text{cod})]_2$ and $\text{P}(n\text{-Oct})_3$, primary alcohols transfer hydrogen to 2-butyne to generate aldehyde–vinylruthenium pairs, which combine to form products of hydroacylation. As observed in the aforementioned ruthenium catalyzed process, such alkyne hydroacylations are possible from the alcohol or aldehyde oxidation level (Scheme 11). It should be noted that under closely related conditions, 1-aryl-2-methylalkynes hydro-metalate to provide vinylmetal species, which isomerize to generate allyliridium intermediates that couple to primary



Scheme 10 Ruthenium catalyzed alkyne hydroacylation from the alcohol or aldehyde oxidation level.

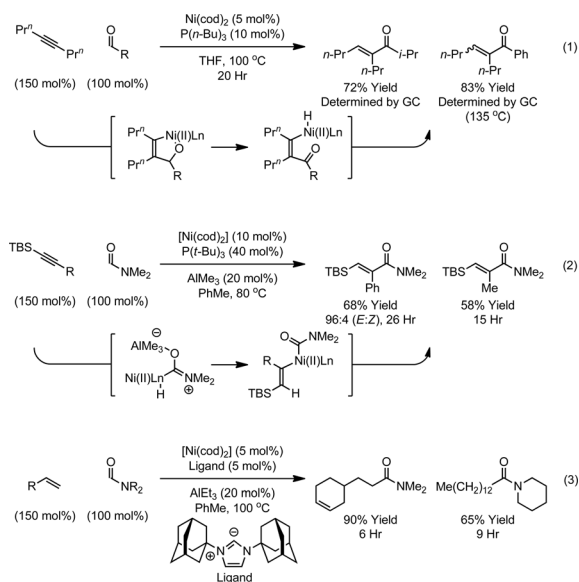


Scheme 11 Iridium catalyzed alkyne hydroacylation from the alcohol or aldehyde oxidation level.

alcohols to furnish homoallylic alcohols with complete branched regioselectivity and excellent levels of diastereoselectivity.^{31b}

2.5 Nickel catalysts

In 1990, Tsuda and Saegusa *et al.* reported the nickel catalyzed hydroacylation of alkynes employing aliphatic and aromatic aldehydes (Scheme 12, eqn (1)).^{32a} The authors proposed two possible reaction pathways: (a) a conventional hydroacylation mechanism involving aldehyde C–H oxidation, and (b) alkyne–aldehyde oxidative coupling to form an oxa-metalacyclopentene, which β -hydride eliminates to form the conjugated enone. In subsequent work by Ogoshi *et al.*, nickel(0) mediated oxidative coupling of diphenylacetylene to pivalaldehyde in the presence of PCy_3 was found to furnish an oxanickelacyclopentene, which was unambiguously characterized by single crystal X-ray diffraction analysis.³³ Additionally, work by Montgomery and Jamison reveals that under the



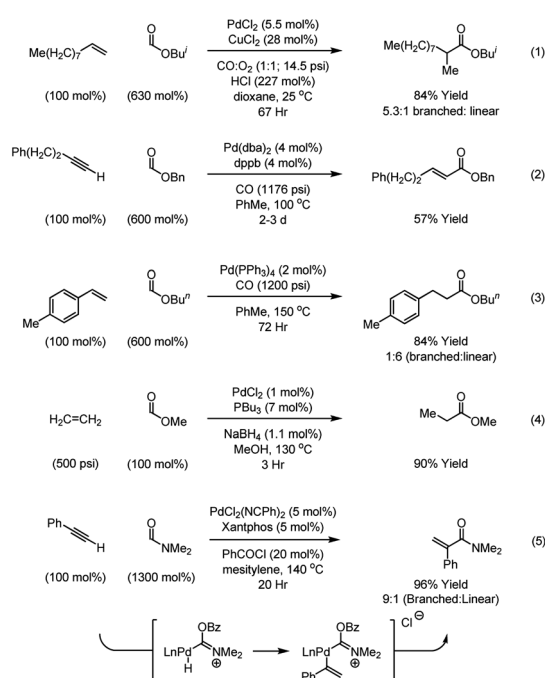
Scheme 12 Nickel catalyzed hydroacylation *via* oxidative coupling and Lewis acid assisted C–H oxidative addition.

conditions of nickel catalysis in the presence of stoichiometric reductants, the oxa-metalacyclopentene intermediates obtained upon alkyne–aldehyde oxidative coupling may be diverted to products of carbonyl vinylation, that is, allylic alcohols.³⁴ These data corroborate intervention of the oxidative coupling pathway.

Later, in 2009, Nakao and Hiyama *et al.* found that formamides engage in efficient nickel catalyzed hydroacylation of alkynes to furnish α,β -unsaturated carboxamides (Scheme 12, eqn (2)).^{32b} Rather than alkyne–aldehyde oxidative coupling, the authors propose that the Lewis acid cocatalyst accelerates C–H oxidative addition to generate an acylnickel(II)hydride, which engages in alkyne hydrometallation and C–C reductive elimination to deliver the product. In a powerful expansion of scope,^{32c} Nakao and Hiyama *et al.* later found that nickel catalysts modified by *N*-heterocyclic carbene ligands promote the hydroacylation of formamides and terminal alkenes (Scheme 12, eqn (3)).

2.6 Palladium catalysts

In 1987, Alper *et al.* reported the first palladium catalyzed hydroacylation, which employed formate esters as acyl donors and α -olefins as acceptors (Scheme 13, eqn (1)).^{35a} The branched products of hydroacylation are generated predominantly in fair to good yields. A complex catalytic system incorporating carbon monoxide, oxygen, hydrochloric acid, and copper chloride was required. Far simpler conditions later were employed in the hydroacylation of alkynes and substituted styrenes using formate esters (Scheme 13, eqn (2) and (3)).^{34b,c} In subsequent work (not shown),^{34d} a purported hydroacylation of vinylarenes employing formic acid as the acyl donor was developed. However, under pressures of ^{13}CO , incorporation of the ^{13}C label was observed, and when formic acid- ^{13}C was employed the ^{13}C label was not



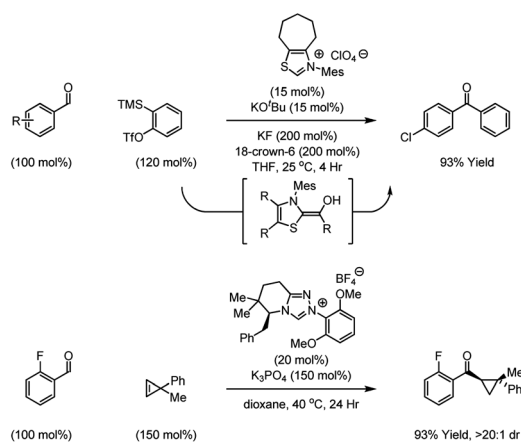
Scheme 13 Palladium catalyzed hydroacylations employing formates and formamides as acyl donors.

incorporated, suggesting C–H oxidation pathways are not operative. Here, it is possible that synthesis gas promotes hydrocarboxylation or a classical Koch-type carboxylic acid synthesis is operative.

Whereas in the preceding catalytic systems carbon monoxide is required, in 1994 Kalck *et al.* reported a carbon monoxide free catalytic system for the hydroacylation of ethylene by methyl formate (Scheme 13, eqn (4)).^{35e} Here, the complex presumed to be $\text{PdH}(\text{Cl})(\text{PBU}_3)_2$ is generated upon addition of one equivalent of NaBH_4 to $\text{PdCl}_2(\text{PBU}_3)_2$. Finally, a palladium catalyzed hydroacylation of alkynes employing formamides as acyl donors was reported by Tsuji and coworkers in 2010 (Scheme 13, eqn (5)).^{35f} Benzoyl chloride is used as a cocatalyst, and likely facilitates C–H oxidative addition through generation of a transient iminium species akin to the AlR_3 Lewis acid effect observed in the aforementioned nickel catalyzed hydroacylations of formamides.^{32b,c} The applicability of this process to terminal alkynes is notable (Scheme 13).

2.7 Organocatalytic hydroacylation

As exemplified by the Stetter reaction,³⁶ another mechanistic pathway for the hydroacylation of $\text{C}=\text{C}$ π -bonds is the conjugate addition of aldehydes to α,β -unsaturated carbonyl compounds by way of acyl anion intermediates. While the literature on conventional Stetter-type reactions is vast and beyond the scope of this review, recent studies by Glorius *et al.* reveal that the Breslow intermediate can be engaged by π -unsaturated partners that are not activated by anion stabilizing groups, thus enabling intra-³⁷ and intermolecular³⁸ hydroacylation under metal-free conditions. The first intermolecular process of this type involved the *N*-heterocyclic carbene (NHC) catalyzed hydroacylation of arynes.^{38a} In subsequent studies, Glorius *et al.* found that cyclopropenes participate in diastereoselective NHC catalyzed hydroacylation, providing access to functionalized acylcyclopropanes.^{38b} By tuning the steric and electronic features of the NHC catalyst, such transformations can be conducted with control of both relative and absolute stereochemistry.^{38c} These studies suggest the potential feasibility of intermolecular NHC catalyzed hydroacylations of aldehydes and α -olefins (Scheme 14).



Scheme 14 NHC-catalyzed intermolecular hydroacylation of arynes and cyclopropenes.

3. Future outlook

Despite decades of work on metal catalyzed hydroacylation, efficient catalytic systems for the hydroacylation of α -olefins using simple, non-chelating aliphatic aldehydes remain an unmet challenge. This difficulty is principally attributed to the focus on conventional rhodium catalyzed hydroacylations that operate *via* aldehyde C–H oxidative addition and which suffer from decarbonylation of the acylrhodium intermediates to form catalytically inactive carbonyl complexes. This issue may represent an intrinsic limitation for rhodium catalysts. As illustrated herein, the exploration of alternate mechanistic pathways for hydroacylation potentially provides an opportunity to overcome this limitation, while providing access to more cost effective catalysts. It is the authors' hope that this minireview will accelerate progress toward this goal.

Notes and references

- For selected reviews on hydroformylation, see: (a) M. Beller, B. Cornils, C. D. Frohning and C. W. Kohlpaintner, *J. Mol. Catal. A: Chem.*, 1995, **104**, 17; (b) C. D. Frohning, C. W. Kohlpaintner and H.-W. Bohnen, in *Applied Homogeneous Catalysis with Organometallic Compounds*, ed. B. Cornils and W. A. Herrmann, Wiley-VCH, Weinheim, 1996, pp. 29–104; (c) *Rhodium Catalyzed Hydroformylation*, ed. P. W. N. M. van Leeuwen and C. Claver, Kluwer Academic Publishers, Norwell, MA, 2000; (d) B. Breit and W. Seiche, *Synthesis*, 2001, 1; (e) K. Weissmehl and H.-J. Arpe, *Synthesis Involving Carbon Monoxide*, in *Industrial Organic Chemistry*, 4th edn, Wiley-VCH, Weinheim, 2003, pp. 127–144; (f) P. W. N. M. van Leeuwen, *Homogeneous Catalysis: Understanding the Art*, Kluwer Academic Publishers, Dordrecht, The Netherlands, 2004.
- For selected reviews on methanol carbonylation, see: (a) J. H. Jones, *Platinum Met. Rev.*, 2000, **44**, 94; (b) C. M. Thomas and G. Suss-Fink, *Coord. Chem. Rev.*, 2003, **243**, 125; (c) A. Haynes, *Top. Organomet. Chem.*, 2006, **18**, 179; (d) A. Haynes, *Adv. Catal.*, 2010, **53**, 1.
- For selected reviews on hydroacylation, see: (a) B. Bosnich, *Acc. Chem. Res.*, 1998, **31**, 667; (b) C.-H. Jun, J.-B. Hong and D. L. Lee, *Synlett*, 1999, 1; (c) M. Tanaka, K. Sakai and H. Suemune, *Curr. Org. Chem.*, 2003, **7**, 353; (d) C.-H. Jun; Y. J. Park. C–H Transformation at Aldehydes and Imines: Intermolecular and Intramolecular Hydroacylation, in *Handbook of C–H Transformations: Applications in Organic Synthesis*, ed. G. Dyker, Wiley-VCH, Germany, 2005, pp. 303–309; (e) G. C. Fu, in *Modern Rhodium-Catalyzed Organic Reactions*, ed. P. A. Evans, Wiley-VCH, Weinheim, 2005, pp. 79–91; (f) C.-H. Jun, E. A. Jo and J.-W. Park, *Eur. J. Org. Chem.*, 2007, 1869; (g) C. Gonzalez-Rodriguez and M. C. Willis, *Pure Appl. Chem.*, 2011, **83**, 577; (h) M. C. Willis, *Chem. Rev.*, 2010, **110**, 725.
- For selected examples of radical hydroacylation, see: (a) M. S. Kharasch, W. H. Urry and B. M. Kuderna, *J. Org. Chem.*, 1949, **14**, 248; (b) T. M. Patrick, Jr, *J. Org. Chem.*, 1952, **17**, 1009; (c) L. Friedman and H. Schechter, *Tetrahedron Lett.*, 1961, **2**, 238; (d) P. Gottschalk and D. C. Neckers, *J. Org. Chem.*, 1985, **50**, 3498; (e) H.-S. Dang and B. P. Roberts, *Chem. Commun.*, 1996, 2201; (f) H.-S. Dang and B. P. Roberts, *J. Chem. Soc., Perkin Trans. 1*, 1998, 67; (g) S. Tsujimoto, T. I. Iwahama, S. Sakaguchi and Y. Ishii, *Chem. Commun.*, 2001, 2352; (h) R. J. Fitzmaurice, J. M. Ahern and S. Caddick, *Org. Biomol. Chem.*, 2009, **7**, 235; (i) V. Chudasama, R. J. Fitzmaurice and S. Caddick, *Nat. Chem.*, 2010, **2**, 592; (j) V. Chudasama, J. M. Ahern, R. J. Fitzmaurice and S. Caddick, *Tetrahedron Lett.*, 2011, **52**, 1067; (k) L. X. Alvarez, E. V. Kudrik and A. B. Sorokin, *Chem.-Eur. J.*, 2011, **17**, 9298.
- (a) J. Tsuji and K. Ohno, *Tetrahedron Lett.*, 1965, **6**, 3969; (b) M. C. Baird, C. J. Nyman and G. Wilkinson, *J. Chem. Soc. A*, 1968, 348.
- For rhodium-catalyzed decarbonylation of aldehydes, see: (a) D. H. Dougherty and L. H. Pignolet, *J. Am. Chem. Soc.*, 1978, **100**, 7083; (b) J. M. O'Conner and J. Ma, *J. Org. Chem.*, 1992, **57**, 5075;

- (c) C. M. Beck, S. E. Rathmill, Y. J. Park, J. Chen and R. H. Crabtree, *Organometallics*, 1999, **18**, 5311.
- 7 K. Sakai, J. Ide, O. Oda and N. Nakamura, *Tetrahedron Lett.*, 1972, **13**, 1287.
- 8 B. M. Trost and M. J. Krische, *Synlett*, 1998, 1.
- 9 (a) D. Milstein, *Organometallics*, 1982, **1**, 1549; (b) D. Milstein, *J. Am. Chem. Soc.*, 1982, **104**, 5227.
- 10 P. Meakin, J. P. Jesson and C. A. Tolman, *J. Am. Chem. Soc.*, 1972, **94**, 3240.
- 11 (a) J. W. Suggs, *J. Am. Chem. Soc.*, 1978, **100**, 640; (b) J. W. Suggs, *J. Am. Chem. Soc.*, 1979, **101**, 489.
- 12 H. Lee and C.-H. Jun, *Bull. Korean Chem. Soc.*, 1995, **16**, 1.
- 13 K. P. Vora, C. F. Lochow and R. G. Miller, *J. Organomet. Chem.*, 1980, **192**, 257.
- 14 For selected examples of intermolecular rhodium catalyzed hydroacylation employing salicylaldehydes, see: (a) K. Kokubo, K. Matsumasa, M. Miura and M. Nomura, *J. Org. Chem.*, 1997, **62**, 4564; (b) K. Kokubo, K. Matsumasa, Y. Nishinaka, M. Miura and M. Nomura, *Bull. Chem. Soc. Jpn.*, 1999, **72**, 303; (c) M. Tanaka, M. Imai, Y. Yamamoto, K. Tanaka, M. Shimowatari, S. Nagumo, N. Kawahara and H. Suemune, *Org. Lett.*, 2003, **5**, 1365; (d) M. Imai, M. Tanaka, K. Tanaka, Y. Yamamoto, N. Imai-Ogata, M. Shimowatari, S. Nagumo, N. Kawahara and H. Suemune, *J. Org. Chem.*, 2004, **69**, 1144; (e) K. Tanaka, M. Tanaka and H. Suemune, *Tetrahedron Lett.*, 2005, **46**, 6053; (f) M. Imai, M. Tanaka, S. Nagumo, N. Kawahara and H. Suemune, *J. Org. Chem.*, 2007, **72**, 2543; (g) R. T. Stemmler and C. Bolm, *Adv. Synth. Catal.*, 2007, **349**, 1185; (h) Y. Inui, M. Tanaka, M. Imai, K. Tanaka and H. Suemune, *Chem. Pharm. Bull.*, 2009, **57**, 1158; (i) M. M. Coulter, K. G. M. Kou, B. Galligan and V. M. Dong, *J. Am. Chem. Soc.*, 2010, **132**, 16330; (j) D. H. T. Phan, K. G. M. Kou and V. M. Dong, *J. Am. Chem. Soc.*, 2010, **132**, 16354; (k) S. K. Murphy, D. A. Petrone, M. M. Coulter and V. M. Dong, *Org. Lett.*, 2011, **13**, 6216; (l) H.-J. Zhang and C. Bolm, *Org. Lett.*, 2011, **13**, 3900.
- 15 For selected examples of intermolecular rhodium catalyzed hydroacylation employing β -sulfinyl-aldehydes, see: (a) M. C. Willis, S. J. McNally and P. J. Beswick, *Angew. Chem., Int. Ed.*, 2004, **43**, 340; (b) M. C. Willis, H. E. Randell-Sly, R. L. Woodward and G. S. Currie, *Org. Lett.*, 2005, **7**, 2249; (c) G. L. Moxham, H. E. Randell-Sly, S. K. Brayshaw, R. L. Woodward, A. S. Weller and M. C. Willis, *Angew. Chem., Int. Ed.*, 2006, **45**, 7618; (d) M. C. Willis, H. E. Randell-Sly, R. L. Woodward, S. J. McNally and G. S. Currie, *J. Org. Chem.*, 2006, **71**, 5291; (e) G. L. Moxham, H. E. Randell-Sly, S. K. Brayshaw, A. S. Weller and M. C. Willis, *Chem.-Eur. J.*, 2008, **14**, 8383; (f) J. D. Osborne, H. E. Randell-Sly, G. S. Currie, A. R. Cowley and M. C. Willis, *J. Am. Chem. Soc.*, 2008, **130**, 17232; (g) H. E. Randell-Sly, J. D. Osborne, R. L. Woodward, G. S. Currie and M. C. Willis, *Tetrahedron*, 2009, **65**, 5110; (h) C. Gonzalez-Rodriguez, S. R. Parsons, A. L. Thompson and M. C. Willis, *Chem.-Eur. J.*, 2010, **16**, 10950; (i) C. Gonzalez-Rodriguez, R. J. Pawley, A. B. Chaplin, A. L. Thompson, A. S. Weller and M. C. Willis, *Angew. Chem., Int. Ed.*, 2011, **50**, 5134; (j) P. Lenden, D. A. Entwistle and M. C. Willis, *Angew. Chem., Int. Ed.*, 2011, **50**, 10657; (k) A. B. Chaplin, J. F. Hooper, A. S. Weller and M. C. Willis, *J. Am. Chem. Soc.*, 2012, **134**, 4885.
- 16 For selected examples of intermolecular rhodium catalyzed hydroacylation employing (N-2-pyridyl)aldimines, see: (a) C.-H. Jun, H. Lee and J.-B. Hong, *J. Org. Chem.*, 1997, **62**, 1200; (b) C.-H. Jun, C.-W. Huh and S.-J. Na, *Angew. Chem., Int. Ed.*, 1998, **37**, 145; (c) C.-H. Jun, D.-Y. Lee, H. Lee and J.-B. Hong, *Angew. Chem., Int. Ed.*, 2000, **39**, 3070; (d) C.-H. Jun, J.-W. Chung, D.-Y. Lee, A. Loupy and S. Chatti, *Tetrahedron Lett.*, 2001, **42**, 4803; (e) M. C. Willis and S. Sapmaz, *Chem. Commun.*, 2001, 2558; (f) C.-H. Jun, H. Lee, J.-B. Hong and B.-I. Kwon, *Angew. Chem., Int. Ed.*, 2002, **41**, 2146; (g) E.-A. Jo and C.-H. Jun, *Eur. J. Org. Chem.*, 2006, 2504; (h) N. R. Vautravers, D. D. Regent and B. Breit, *Chem. Commun.*, 2011, **47**, 6635.
- 17 For selected reviews on dynamic covalent chemistry in metal catalysis, see: (a) G. Rousseau and B. Breit, *Angew. Chem., Int. Ed.*, 2011, **50**, 2450; (b) K. L. Tan, X. Sun and A. D. Worth, *Synlett*, 2012, 321.
- 18 (a) T. B. Marder, D. C. Roe and D. Milstein, *Organometallics*, 1988, **7**, 1451; (b) A. H. Roy, C. P. Lenges and M. Brookhart, *J. Am. Chem. Soc.*, 2007, **129**, 2082; (c) K. Tanaka, Y. Shibata, T. Suda, Y. Hagiwara and M. Hirano, *Org. Lett.*, 2007, **9**, 1215; (d) Y. Shibata and K. Tanaka, *J. Am. Chem. Soc.*, 2009, **131**, 12552.
- 19 (a) R. Cramer, *J. Am. Chem. Soc.*, 1967, **89**, 4621; (b) A. C. Jesse, E. H. P. Cordfunke and W. Ouweltjes, *Thermochim. Acta*, 1979, **30**, 293.
- 20 (a) K. Kokubo, M. Miura and M. Nomura, *Organometallics*, 1995, **14**, 4521; (b) Y.-T. Hong, A. Barchuk and M. J. Krische, *Angew. Chem., Int. Ed.*, 2006, **45**, 6885.
- 21 J. A. Miller and J. A. Nelson, *Organometallics*, 1991, **10**, 2958, and references cited therein.
- 22 (a) Y. Musashi and S. Sakaki, *J. Am. Chem. Soc.*, 2002, **124**, 7588; (b) V. M. Williams, J.-R. Kong, B.-J. Ko, Y. Mantri, J. S. Brodbelt, M.-H. Baik and M. J. Krische, *J. Am. Chem. Soc.*, 2009, **131**, 16054; (c) P. Liu, M. J. Krische and K. N. Houk, *Chem.-Eur. J.*, 2011, **17**, 4021.
- 23 (a) C. P. Lenges and M. Brookhart, *J. Am. Chem. Soc.*, 1997, **119**, 3165; (b) C. P. Lenges, P. S. White and M. Brookhart, *J. Am. Chem. Soc.*, 1998, **120**, 6965.
- 24 (a) P. Isnard, B. Denise, R. P. A. Sneed, J. M. Cognion and P. Durual, *J. Organomet. Chem.*, 1982, **240**, 285; (b) P. Isnard, B. Denise, R. P. A. Sneed, J. M. Cognion and P. Durual, *J. Organomet. Chem.*, 1983, **256**, 135; (c) Y. Tsuji, S. Yoshii, T. Ohsumi, T. Kondo and Y. Watanabe, *J. Organomet. Chem.*, 1987, **331**, 379; (d) T. Kondo, Y. Tsuji and Y. Watanabe, *Tetrahedron Lett.*, 1987, **28**, 6229; (e) W. Ueda, T. Yokoyama, Y. Morikawa, Y. Moro-Oka and T. Ikawa, *J. Mol. Catal.*, 1988, **44**, 197; (f) T. Kondo, S. Yoshii, Y. Tsuji and Y. Watanabe, *J. Mol. Catal.*, 1989, **50**, 31; (g) E. M. Nahmed and G. Jenner, *J. Mol. Catal.*, 1990, **59**, L15; (h) T. Kondo, M. Akazome, Y. Tsuji and Y. Watanabe, *J. Org. Chem.*, 1990, **55**, 1286; (i) C. Legrand, Y. Castanet, A. Mortreux and F. Petit, *J. Chem. Soc., Chem. Commun.*, 1994, 1173; (j) N. Lugan, G. Lavigne, J. M. Soulié, S. Fabre, P. Kalck, J. Y. Saillard and J. F. Halet, *Organometallics*, 1995, **14**, 1712; (k) T. Kondo, T. Okada and T.-a. Mitsudo, *Organometallics*, 1999, **18**, 4123.
- 25 (a) T. Kondo, N. Hiraishi, Y. Morisaki, K. Wada, Y. Watanabe and T.-A. Mitsudo, *Organometallics*, 1998, **17**, 2131; (b) F. Shibahara, J. F. Bower and M. J. Krische, *J. Am. Chem. Soc.*, 2008, **130**, 6338; (c) F. Shibahara, J. F. Bower and M. J. Krische, *J. Am. Chem. Soc.*, 2008, **130**, 14120; (d) S. Omura, T. Fukuyama, J. Horiguchi, Y. Murakami and I. Ryu, *J. Am. Chem. Soc.*, 2008, **130**, 14094.
- 26 (a) K. Hiraki, N. Ochi, Y. Sasada, H. Hayashida, Y. Fuchita and S. Yamanaka, *J. Chem. Soc., Dalton Trans.*, 1985, 873; (b) P. Xue, S. Bi, H. H. Y. Sung, I. D. Williams, Z. Lin and G. Jia, *Organometallics*, 2004, **23**, 4735.
- 27 (a) E. Skucas, J. R. Zbieg and M. J. Krische, *J. Am. Chem. Soc.*, 2009, **131**, 5054; (b) J. R. Zbieg, J. Moran and M. J. Krische, *J. Am. Chem. Soc.*, 2011, **133**, 10582; (c) J. R. Zbieg, E. Yamaguchi, E. L. McInturff and M. J. Krische, *Science*, 2012, DOI: 10.1126/science.1219274.
- 28 (a) A. Dobson and S. D. Robinson, *Inorg. Chem.*, 1977, **16**, 137; (b) T. C. Johnson, D. J. Morris and M. Wills, *Chem. Soc. Rev.*, 2010, **39**, 81.
- 29 (a) R. L. Patman, M. R. Chaulagain, V. M. Williams and M. J. Krische, *J. Am. Chem. Soc.*, 2009, **131**, 2066; (b) V. M. Williams, J. C. Leung, R. L. Patman and M. J. Krische, *Tetrahedron*, 2009, **65**, 5024.
- 30 For selected examples of iridium catalyzed aldehyde decarbonylation, see: (a) T. Iwai, T. Fujihara and Y. Tsuji, *Chem. Commun.*, 2008, 6215; (b) F. M. A. Geilen, T. vom Stein, B. Engendahl, S. Winterle, M. A. Liauw, J. Klankermayer and W. Leitner, *Angew. Chem., Int. Ed.*, 2011, **50**, 6831; (c) A. E. Roa, V. Salazar, J. Lopez-Serrano, E. Onate, M. Paneque and M. L. Poveda, *Organometallics*, 2012, **31**, 716.
- 31 (a) S. Hatanaka, Y. Obora and Y. Ishii, *Chem.-Eur. J.*, 2010, **16**, 1883; (b) Y. Obora, S. Hatanaka and Y. Ishii, *Org. Lett.*, 2009, **11**, 3510.
- 32 (a) T. Tsuda, T. Kiyoi and T. Saegusa, *J. Org. Chem.*, 1990, **55**, 2554; (b) Y. Nakao, H. Idei, K. S. Kanyiva and T. Hiyama, *J. Am. Chem. Soc.*, 2009, **131**, 5070; (c) Y. Miyazaki, Y. Yamada, Y. Nakao and T. Hiyama, *Chem. Lett.*, 2012, **41**, 298.
- 33 M. Ohashi, H. Saijo, T. Arai and S. Ogoshi, *Organometallics*, 2010, **29**, 6534.
- 34 For selected reviews, see: (a) J. Montgomery, *Angew. Chem., Int. Ed.*, 2004, **43**, 3890; (b) J. Montgomery and G. J. Sormunen, *Top. Curr. Chem.*, 2007, **279**, 1; (c) R. M. Moslin, K. Miller-Moslin and T. F. Jamison, *Chem. Commun.*, 2007, 4441.

- 35 (a) M. Mlekuz, F. Joo and H. Alper, *Organometallics*, 1987, **6**, 1593; (b) H. Alper, M. Saldana-Maldonado and I. J. B. Lin, *J. Mol. Catal.*, 1988, **49**, L27; (c) I. J. B. Lin and H. Alper, *J. Chem. Soc., Chem. Commun.*, 1989, 248; (d) B. El Ali and H. Alper, *J. Mol. Catal.*, 1992, **77**, 7; (e) J. Grévin and P. Kalck, *J. Organomet. Chem.*, 1994, **476**, c23; (f) T. Fujihara, Y. Katafuchi, T. Iwai, J. Terao and Y. Tsuji, *J. Am. Chem. Soc.*, 2010, **132**, 2094.
- 36 For selected reviews of the Stetter reaction, see: (a) D. Enders, O. Niemeier and A. Henseler, *Chem. Rev.*, 2007, **107**, 5606; (b) J. Read de Alaniz and T. Rovis, *Synlett*, 2009, 1189; (c) H. U. Vora and T. Rovis, *Aldrichimica Acta*, 2011, **44**, 3; (d) P. Dominguez de Maria and S. Shanmuganathan, *Curr. Org. Chem.*, 2011, **15**, 2083; (e) A. T. Biju, N. Kuhl and F. Glorius, *Acc. Chem. Res.*, 2011, **44**, 1182; (f) D. A. DiRocco and T. Rovis, Asymmetric Benzoin and Stetter Reactions, in *Science of Synthesis, Stereoselective Synthesis*, ed. J. G. De Vries, G. A. Molander and P. A. Evans, Georg Thieme Verlag, Stuttgart, 2011, pp. 835–862.
- 37 For intramolecular transformations, see: (a) J. He, S. Tang, J. Liu, Y. Su, X. Pan and X. She, *Tetrahedron*, 2008, **64**, 8797; (b) K. Hirano, A. T. Biju, I. Piel and F. Glorius, *J. Am. Chem. Soc.*, 2009, **131**, 14190; (c) A. T. Biju, N. E. Wurz and F. Glorius, *J. Am. Chem. Soc.*, 2010, **132**, 5970; (d) I. Piel, M. Steinmetz, K. Hirano, R. Fröhlich, S. Grimme and F. Glorius, *Angew. Chem., Int. Ed.*, 2011, **50**, 4983.
- 38 For intermolecular transformations, see: (a) A. T. Biju and F. Glorius, *Angew. Chem., Int. Ed.*, 2010, **49**, 9761; (b) X. Bugaut, F. Liu and F. Glorius, *J. Am. Chem. Soc.*, 2011, **133**, 8130; (c) F. Liu, X. Bugaut, M. Scheler, R. Fröhlich and F. Glorius, *Angew. Chem., Int. Ed.*, 2011, **50**, 12626.