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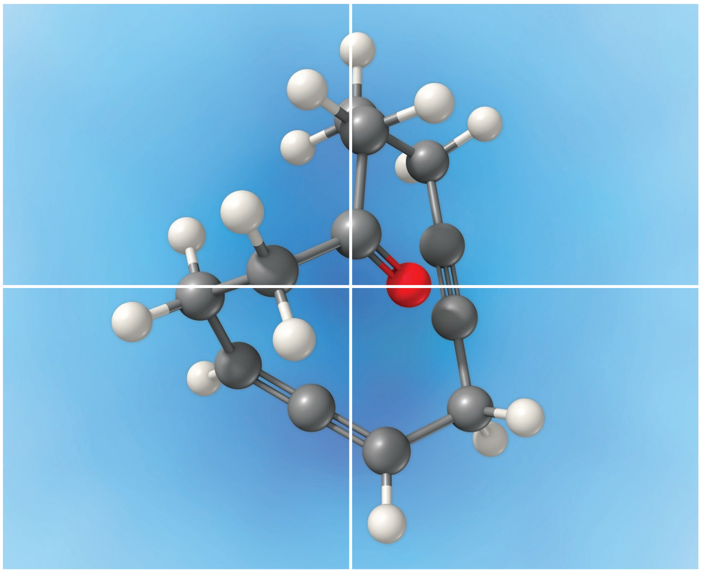

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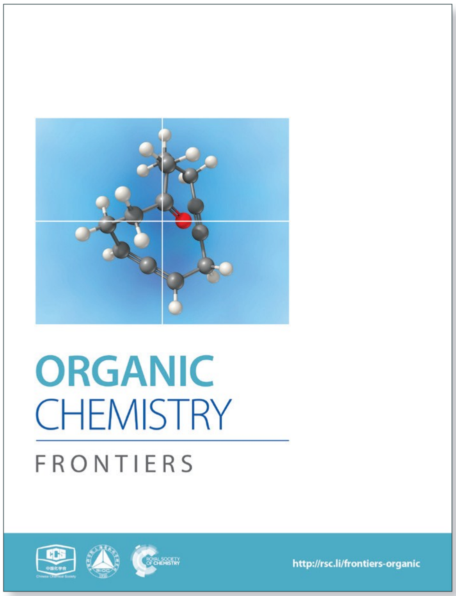

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Journal Name

Highlight

Reverse-Hydroformylation: A Missing Reaction Explored§

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Development of new and sustainable catalytic system for fundamentally important reactions is an important and an intellectually stimulating challenge. Hydroformylation, the so-called "Oxo-process" is very important and widely used reaction in the chemical industry for making value-added bulk and fine chemicals and represents one of the leading applied homogeneously catalysed reactions (Fig. 1a).[1] However, the reverse reaction, "dehydroformylation" is a thermodynamically uphill process and has been gaining much attention to chemist in recent years. It was previously observed as a side reaction in the decarbonylation and related reactions.[2b,c] Inspired by the biosynthesis of sterols *via* dehydroformylation (Fig. 1b), several transition-metal catalysed dehydroformylation of aldehydes have been attempted in the past decades.[2] However, the dehydroformylation either with the concomitant generation of synthesis gas (gaseous CO + H_2) or transfer of formyl group (-CHO) to an olefin acceptor is a missing reaction in chemical science. Thus, finding a more appropriate catalytic system for dehydroformylation reaction under mild conditions, one can efficiently utilize the renewable oxygenated biomass derivatives to value-added chemicals, such as monomers, solvents, and intermediates for bulk and fine chemicals.

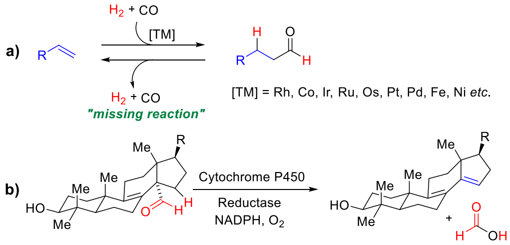

Figure 1. a) Transition-metal catalyzed hydroformylation of olefin. **b)** Dehydroformylation during biosynthesis of sterol.

In 1990, Watanabe *et al.* reported the Ru-complex catalysed intermolecular hydroacylation reaction (addition of aldehydic C-H with olefinic bond).[2a] However, the aliphatic aldehyde, n-heptanol with cyclohexene by using the same catalytic condition resulted in 29% yield of cyclohexanecarboxaldehyde along with a mixture of esters (~9%) at 200 °C. This reaction is termed as 'transfer-hydroformylation' *i.e.* transfers of CO and H_2 take place from donor aldehyde to acceptor olefin at the metal centre in the absence of synthesis gas (Fig. 2). It was observed that the aldehyde is the source of hydrogen and carbon monoxide[3] and the lower yield of formylated product clearly indicated that the transformation is kinetically controlled by CO liberation from the metal centre before the hydroformylation of acceptor olefin takes place. Notably, in the seminal work of Dong and co-workers, the kinetically as well as thermodynamically balanced 'transfer-hydroformylation' of aliphatic aldehyde to olefin has been successfully achieved by using the Rh(Xantphos) complex as a catalyst (Fig. 2). The reaction is facilitated by the introduction of strained olefin as a sacrificial carbonyl as well as hydrogen acceptor enabling the formation of thermodynamically more stable olefin from aliphatic aldehyde.[4a]

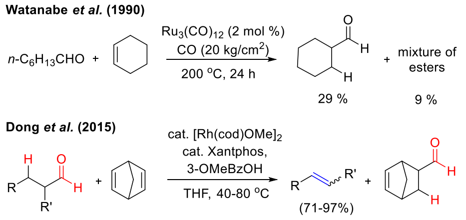

Figure 2. Transfer-hydroformylation reaction.

The mechanistic insights of transfer-hydroformylation reveals that the benzoate counter ion acts as a proton shuttle *via* reversible redox process and plays a crucial role in the conversion of aliphatic aldehyde into thermodynamically favourable olefin (Fig. 3).Initial coordination of benzoate ion triggers the oxidative addition of aldehydic C-H bond at Rh-centre. This is followed by the reductive elimination as benzoic

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acid allowing the conversion of aldehyde into olefin *via* decarbonylation and *β*-hydride elimination. The kinetically more favourable hydroformylation of strained olefin can be preceded before the liberation of gases CO and hydrogen from the metal centre. Notably, the hydroacylation of sacrificial olefin and the decarbonylation of aldehyde at Rh- metal center are equally found as critical steps in the catalytic transformation. Thus, the choice of donor aldehyde-acceptor olefin comprises the successes of transfer-hydroformylation reaction.

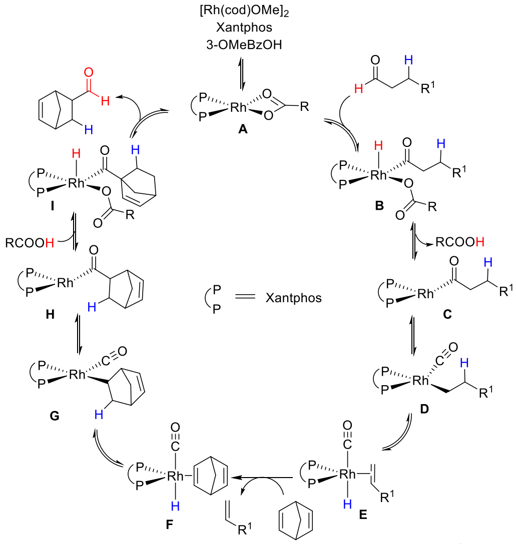

Figure 3. A proposed mechanism for the transfer-hydroformylation.[4a]

The transfer-hydroformylation has a broad substrate scope as well as functional group tolerance. Importantly, many synthetically valuable groups such as dienes, hydroxyl, amines, ethers, esters and acetals could be reserved under standard reaction condition. A noteworthy progress to convert a commercially available inexpensive (+)-yohimbine to a natural product (+)-yohimbenone with a high chemoselectivity was achieved in three step utilizing transfer-hydroformylation as one of the key steps (Fig. 4). This novel strategy might open a new avenue for the development of completely gasless (avoid syngas) hydroformylation reaction to access a complex and voluble alkenes from aldehyde feedstock by utilizing an inexpensive norbornadiene (nbd) as a sacrificial acceptor.[4]

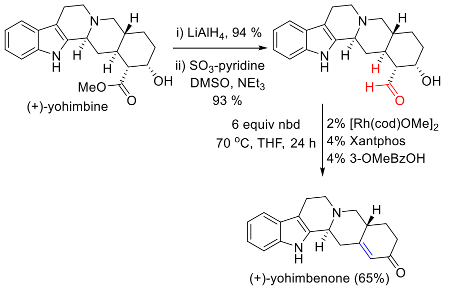

Figure 4. Synthesis of (+)-yohimbenone using the Dong's transfer-hydrogenation as one of the key steps.[4a]

In 2008, Tsuji *et al.* reported the Ir-catalyzed decarbonylation of aldehyde.[2c] The aldehydes containing *β*-hydrogen on sp^3-carbon were resulted the decarbonylation product besides a trace amount of alkenes owing to *β*-hydride elimination (Fig. 5). The formation of alkenes is due to reversible hydroformylation reaction of aldehydes. Very recently, Nozaki and co-workers have reported an unprecedented retro-hydroformylation reaction[5] catalysed by a well-defined iridium-based catalyst for the direct, selective conversion of aliphatic aldehydes into the corresponding alkenes with the concomitant generation of syngas (Fig. 5). This is the first report utilizing hydroxycyclopentadienyl iridium complex in association with *N*-heterocyclic carbene ligands, such as *N*,*N*-bis(2,6-diisopropylphenyl)imidazolylidene (IPr) as an efficient catalytic system for the acceptorless dehydroformylation reaction, though the cyclopentadienyl based metal complexes are well explored in the metal-ligand cooperation mechanism.[6] Based on mechanistic insights a possible sequential decarbonylation-dehydrogenation or dehydrogenation-decarbonylation pathway was completely ruled-out. The initial oxidative addition of aldehydic C-H bond followed by simultaneous liberation of CO and H$_2$ resulted the relatively more stable olefins.

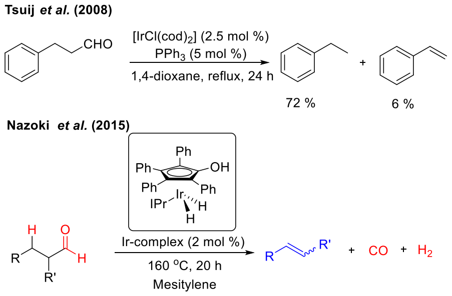

Figure 5. Retro-hydroformylation reaction

Cyclic and acyclic aliphatic aldehydes were successfully converted into corresponding olefins with concomitant elimination of syngas enabling sustainable catalytic approach to syngas production from aldehyde feedshock (Fig. 6). Cyclic aldehydes yielded the corresponding olefins along with a minor amount of reduced alcohols whereas acyclic olefins were more susceptible for hydrogenation of as-yielded olefins. In order to overcome undesired hydrogenation reaction, acyclic aldehyde transformation was carried under continuous argon bubbling. This fundamentally important reaction might provide a new strategy for the production of syngas and gasification of biomass derivatives under very mild conditions.

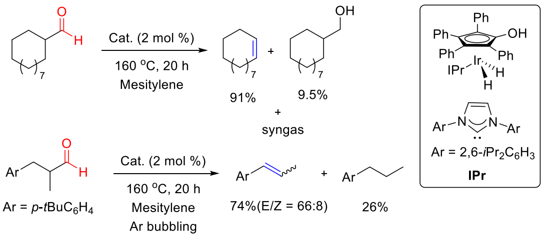

Figure 6. Retro-hydroformylation of aliphatic aldehydes.[5]

In summary, both reports reflect remarkable progress on acceptor- and acceptorless-dehydroformylation process for the conversion of large feedstock aliphatic aldehydes into more valuable olefins and marked as important milestone in the area of chemical synthesis. Future direction would be opened up for the utilization of more economical first row transition-metals for dehyroformylation process and renewable biomass derivatives as an alternative for the effective production of synthesis gas enabling sustainable approach for synthesis gas production.

Notes and references

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1 (a) J. Pospech, I. Fleischer, R. Franke, S. Buchholz and M. Beller, *Angew. Chem. Int. Ed.* 2012, **52**, 2852; (b) R. Franke, D. Selent and A. Börner, *Chem. Rev.* 2012, **112**, 5675.

2 (a) T. Kondo, M. Akazome, Y. Tsuji and Y. Watanabe, *J. Org. Chem*. 1990, 55, 1286; (b) M. Kreis, A. Palmelund, L. Bunch and R. Madsen, *Adv. Synth. Catal*. 2006, **348**, 2148; (c) T. Iwai, T. Fujihara and Y. Tsuji, *Chem. Commun*. 2008, 6215.

3 Paraformaldehyde as a C1 source for carbonylation reaction, see: (a) L. Wu, Q. Liu, R. Jackstell and M. Beller, *Angew. Chem. Int. Ed*. 2014, **53**, 6310; (b) B. Sam, B. Breit and M. J. Krische, *Angew. Chem. Int. Ed*. 2015, **54**, 3267.

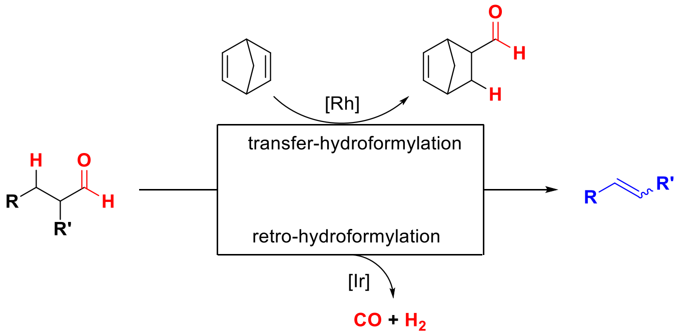
4 (a) S. K. Murphy, J. Park, F. A. Cruz andVy M. Dong, *Science*, 2015, **347**, 56; (b) C. R. Landis, *Science*, 2015, **347**, 29.

5 S. Kusumoto, T. Tatsuki and K. Nozaki, *Angew. Chem. Int. Ed.* 2015, **54**, 8458.

6 (a) S. Kusumoto, M. Akiyama and K. Nozaki, *J. Am. Chem. Soc.* 2013, **135**, 18726; (b) S. Kusumoto and K. Nozaki, *Nat. Commun.* 2015, **6**, 6296.

TOC

Transition-metal catalysed recent progress on acceptor- and acceptorless-reverse hydroformylation of aldehydes for the conversion of olefins has been discussed. The aldehyde feedstock serves as a source for syngas production and valuable alkenes.



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