ChemComm
Chemical Communications

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: M. K. Bisai, S. Yadav, T. Das, K. Vanka and S. S. Sen, *Chem. Commun.*, 2019, DOI: 10.1039/C9CC05783H.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/chemcomm

View Article Online
DOI: 10.1039/C9CC05783H

ChemComm

COMMUNICATION

Lithium compounds as single site catalysts for hydroboration of alkenes and alkynes

Milan Kumar Bisai,[ab] Sandeep Yadav,[ab] Tamal Das,[bc] Kumar Vanka,[bc] and Sakya S. Sen*[ab]

Received 00th January 20xx,
Accepted 00th January 20xx

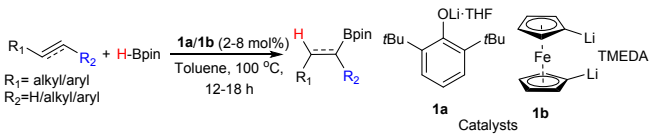
DOI: 10.1039/x0xx00000x

www.rsc.org/

The hydroboration of alkenes and alkynes using easily accessible lithium compounds [2,6-ditertbutyl phenolatelithium (1a) and 1,1' dilithioferrocene (1b)] have been achieved with good yields, high functional group tolerance and excellent chemoselectivity. Deuterium-labeling experiments confirm the *cis*-addition of pinacolborane. The methodology has been further extended to myrcene, which undergoes selective 4,3- hydroboration. DFT calculations provide insights into the mechanism.

Hydroboration of functionalized alkynes and alkenes using excess pinacolborane (HBpin) is known,[1] but their catalytic conversion usually requires a late transition metal catalyst.[2] Recently, the demand for supplanting the transition metal catalysts by more earth abundant and less toxic main group surrogates is ever increasing. Hydroboration using compounds with group 2 elements has been limited tothe catalytic reduction of unsaturated polar bonds, such as aldehydes, ketones, imines, amides, esters etc.[3-14] Although compounds with p-block elements are emerging as proficient catalysts for alkyne[15-20] and alkene[21-23] hydroboration, there are very limited reports on s-block metal catalyzed alkene or alkyne hydroboration. While Rueping and coworkers reported the first magnesium catalyzed hydroboration of terminal and internal alkynes,[24] the group of Parkin demonstrated styrene hydroboration by a terminal magnesium hydride.[25] Besides, Zhao and co-workers reported the hydroboration of carbonyl groups and styrene substrates using NaOH powder, although the scope of styrene substrates was somewhat limited.[26]

The advantages of using lithium compounds are (i) cheap, (ii) moderately abundant (65 ppm in the Earth's crust), (iii) readily accessible, and (iv) they do not involve in Schlenk equilibrium like group 2 elements. Moreover, as most of the main group catalysts are frequently prepared from the corresponding lithium reagents, taking advantage of the direct use of lithium compounds in catalysis, would obviate the need for such additional transformations. In fact, the group of Mulvey demonstrated the use of lithium aluminates as catalysts for the hydroboration of aldehydes, ketones, and imines,[27,28] and the group of Cowley and Thomas used $LiAlH_4$ for the hydroboration of alkenes,[23] but it was aluminum which is the active catalyst in both these cases and lithium only influences the reactivity. This was confirmed by using $AlEt_3$ (a surrogate of AlH_3) as a single site catalyst to accomplish the hydroboration.

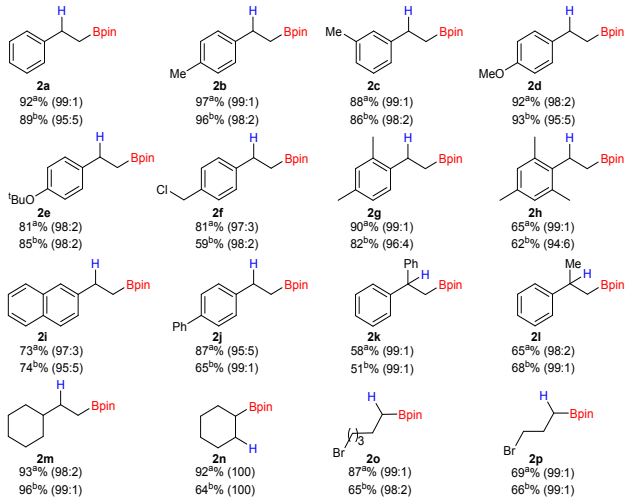


Scheme 1. Lithium compound catalyzed hydroboration of alkene and alkynes.

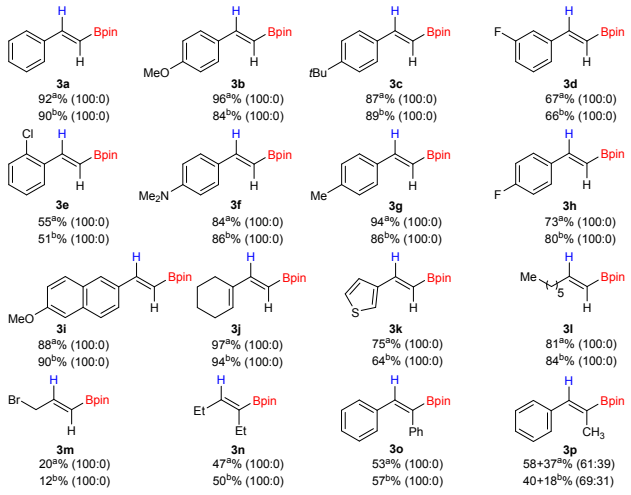
Hence, the utilization of lithium compounds as catalysts has been largely neglected. It is only recently that the groups of Okuda, Mulvey and others have started to use lithium compounds as single site catalysts for hydroboration of aldehydes and ketones.[29-33] Recently, *n*-BuLi was shown as an efficient catalyst for the hydroboration of alkynes with HBpin.[34] However, the substrate scope of the methodology was limited, and the mechanism was not elaborated. Thus, there remains a need for the development of alkene and alkyne hydroboration with lithium compounds as single site catalysts. Last year, we have reported the hydroboration and cyanosilylation of a range of aldehydes and ketones using 2,6-ditert-butyl phenolate lithium (**1a**), and 1,1'-dilithioferrocene (**1b**), and [$Dipp_2$nacnac]Li·THF (**1c**) and compared how the electronegativity of ligand associated with the Li center influences the catalytic activity.[32] The reason to select **1b** over monolithiated ferrocene can be attributed to more to sterics of the former as well as the ease of synthesis (monolithiated ferrocene preparation usually needs *t*BuLi, while **1b** can be

[a] *Inorganic Chemistry and Catalysis Division, CSIR-National Chemical Laboratory, Dr.Homi Bhabha Road, Pashan, Pune 411008, India. E-mail: ss.sen@ncl.res.in*
[b] *Academy of Scientific and Innovative Research (AcSIR), Ghaziabad-201002, India.*
[c] *Physical and Material Chemistry Division, CSIR-National Chemical Laboratory, Dr. Homi Bhabha Road, Pashan, Pune 411008, India.*
Electronic Supplementary Information (ESI) available: Experimental details, theoretical calculations, kinetic analysis and representative NMR spectra.

prepared from *n*BuLi).[35] Although these compounds are prepared from alkyllithium reagents, they are solid in nature, easy to handle, and stable under inert conditions for a long time. Herein, we report efficient hydroboration of more challenging alkenes and alkynes by **1a** and **1b** (Scheme 1). Only trace amount of conversion was observed when **1c** was used as the catalyst.



Scheme 2 Hydroboration Scope with alkene substrates. Reaction conditions: Alkene (0.50 mmol), HBpin (0.55 mmol, 1.1equiv), 4.0-8.0 mol% catalyst, 18 h reaction at 100 °C temperature in neat or in toluene. Yields were determined by the ^{1}H NMR integration relative to mesitylene. Henceforth superscripts a and b stand for the catalysts 1a and 1b respectively. Ratios in parentheses report the distribution of regioisomers (linear vs branched).

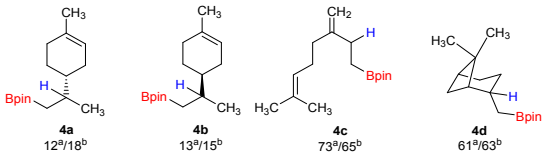


Scheme 3 Scope of hydroboration with alkyne substrates. Reaction conditions: Alkyne (0.50 mmol), HBpin (0.55 mmol, 1.1 equiv), 2.0 mol% catalyst, 12 h reaction at 100 °C in toluene. Yields were determined by the ^{1}H NMR integration relative to mesitylene.

A brief screening of catalyst loading, temperature and time has been carried out for the hydroboration of styrene or phenylacetylene with 1.1 equivalent of HBpin (See Supporting Information, Table S1 and S3) to achieve the best conversion. For hydroboration of alkynes, catalyst loadings are 2.0 mol% and the reactions were over around 12 h when heated at 100 °C. Note that, the catalyst loading is substantially lesser than *n*BuLi (10 mol%) catalyzed alkyne hydroboration.[35] For comparison purpose, cyclopentadienyllithium (CpLi) was employed as the catalyst. With 2.0 mol% catalyst loading CpLi afforded 65% yield under the same reaction condition for the hydroboration of phenylacetylene (See Supporting Information, Table S3, entry 6). Slightly higher catalyst loading (4.0 mol% for **1b** and 8.0 mol% for **1a**) and time (18 h) are required for hydroboration of alkenes. Both aliphatic and aromatic alkene/alkynes underwent hydroboration to form the corresponding alkyl or vinyl-boronates in good to excellent yields (Scheme 2 and Scheme 3), reflecting the high efficiency of the catalysts.

View Article Online DOI: 10.1039/C9CC05782J

Smooth hydroboration of different aromatic alkenes or alkynes with electron donating or withdrawing substituents at *o*/*m*/*p* position was observed. Both catalysts tolerate functional groups such as halogens (**2f**, **2o**, **2p**, **3d**, and **3h**), alkoxy (**2d**, **2e**, **3b**, and **3i**), heterocycle (**3k**), amino (**3f**) containing substrates. However, in addition to alkyne hydroboration, lithium-halide exchange was also observed for **3e** in 29% yield. The lithium halide exchange was more pronounced for **3m** as the metathesis product was obtained in more than 70% yield. Intramolecular chemoselective hydroboration of alkyne over alkene was observed for **3j**. In contrast to terminal alkynes, internal alkynes (**3n, 3o**, **and 3p**) form their corresponding boronates in moderate yields under the optimization conditions. However, similar to Rueping's magnesium catalyst, by increasing the catalyst loading (5 mol%) and reaction time (36 h), good yields are achieved for **3o** (80%). We have also tested unsymmetrical alkyne, phenylpropyne for hydroboration which afforded a mixture of α- and *β*-vinyl boranates (**3p**) in 2:3 and 3:7 ratio for **1a** and **1b**, respectively. Aliphatic alkenes (**2m-2p**) or alkynes (**3l-3n)** were effectively converted to their corresponding products. Increase of sterics has little effect on the yield as seen in the cases of hydroboration of **2h**, **2k**, **3n**, and **3o**.

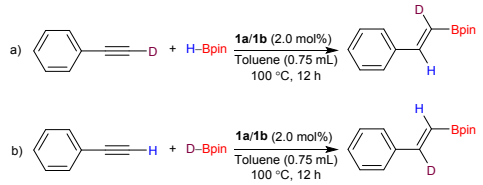


Scheme 4. Selective alkene hydroboration for terpenes.

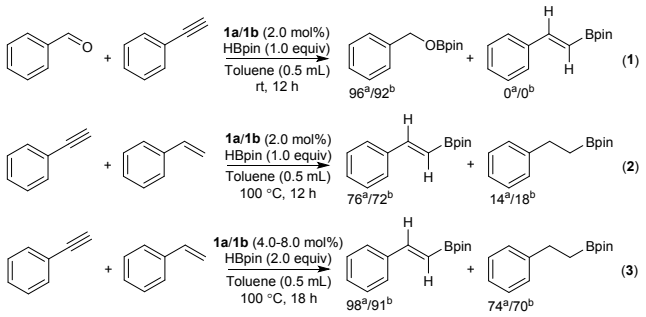
To further explore the catalytic potential of **1a** and **1b**, naturally occurring terpenes have been chosen for the selective hydroboration of the olefinic bond. Although poor yields were obtained for R- or S- limonene (**4a** and **4b**), myrcene (**4c**) and *β*-pinene (**4d**) were converted to the corresponding alkyl boronate ester in good yield with excellent selectivity. Interestingly, 4,3-selective hydroboration of 2-substituted 1,3-diene (**4c**) was observed for both the catalysts. Note that, hydroboration of dienes to access allylboranes is less-established, and only known with transition metals such as Fe,[36] Co,[37] Ni,[38] Ir,[39] etc. This is the first report of a main group element catalyzed selective hydroboration of myrcene.

Deuterium labelling experiments were carried out for the catalytic hydroboration of alkyne to understand the stereoselectivity. A sharp resonance at δ 6.18 ppm in the ^{2}H

NMR for the catalytic reduction of PhC≡CD with HBpin designates a cis configuration of the deuterium and phenyl ring [(a), Scheme 5]. Similarly, the cis arrangement of deuterium and the Bpin moiety was confirmed from the resonance at δ 7.28 ppm in the ^{2}H NMR spectrum for the catalytic reaction of PhC≡CH and DBpin [(b), Scheme 5]. This experiment attests a *cis* stereoselectivity, which is in good agreement with ScOTf mediated alkyne hydroboration, reported by Geetharani and coworkers.[40] Intermolecular chemoselective hydroboration of aldehydes, alkene and alkyne were also studied in three different sets of the reactions and the results are summarized in Scheme 6.



Scheme 5. Deuterium labelling experiment: (a) Hydroboration of phenylacetylene-D with HBpin. (b) Hydroboration of phenylacetylene with DBpin.

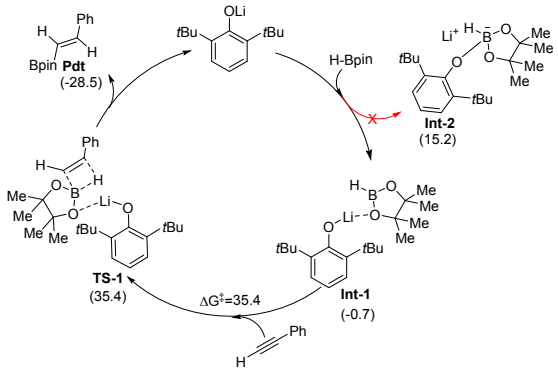


Scheme 6. Competitive experiment for chemoselective hydroboration.

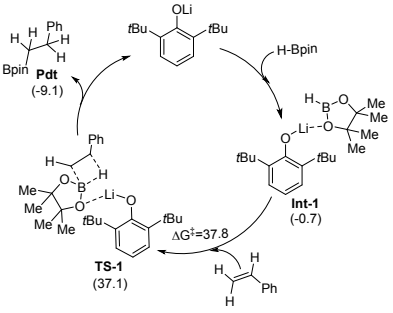
No appreciable changes in the ^{1}H NMR was observed from the stoichiometric reaction of **1a** with styrene or phenylacetylene, even after heating at 100 °C overnight. However, the reaction between **1a** and HBpin in toluene-d_8 shows a new set of resonance in the ^{11}B NMR at δ 4.7 ppm, indicating the formation of an intermediate (**Int-1**)[32,41] along with a singlet at δ 21.6 and a quintet at –39.8 ppm for the formation of a trialkoxyborane [2,6-*t*Bu$_2$-C$_6$H$_3$-OBpin] and BH_4^- anion, respectively. In addition, a singlet at δ 86.9 and a quartet at -25.4 ppm were also observed, probably due to the decomposition of HBpin and Lewis base·BH_3 adduct.[42] A white precipitate is formed in the NMR tube after 3-4 h and the filtrate part shows only three peaks at δ 4.7, 21.6 and -39.8 ppm in the ^{11}B NMR spectrum (see Supporting Information, Scheme S8). The elimination of LiH could lead to the formation of both trialkoxyborane and $LiBH_4$.[43] However, due to the very high lattice energy and poor solubility, the involvement of LiH in the catalytic activity is very unlikely, which was also noted by the groups of Mulvey,[33] Thomas, and Cowley.[23] No conclusive NMR spectra were obtained from the stoichiometric reactions between **1b** and HBpin and always peak broadening was observed.

Full quantum chemical calculations were done with density functional theory (DFT) at the dispersion and solvent corrected PBE/TZVP level of theory in order to understand the mechanism (Scheme 7 and Scheme 8) of the alkene and alkyne hydroboration reaction in the presence of **1a**. [please see the Supporting Information, Figures 81 and 82 for further details].

View Article Online DOI: 10.1039/C9CC05787H



Scheme 7. The catalytic cycle and reaction mechanism for the alkyne hydroboration by catalyst **1a**, calculated at the PBE/TZVP level of theory with DFT. The relative free energy (ΔG) for each species are shown within the parenthesis of the catalytic cycle. ΔG‡ represent the Gibbs free energy of activation respectively. All values are in kcal/mol.



Scheme 8. The catalytic cycle and reaction mechanism for the alkene hydroboration by catalyst **1a**.

In the first step of the reaction, a weakly coordinating complex (**Int-1**) is formed between catalyst **1a** and HBpin, with one of the oxygen atoms of pinacolborane approaching towards the lithium atom of **1a**. The reaction energy (ΔE) and the Gibbs free energy (ΔG) for this step are -11.5 kcal/mol and -0.7 kcal/mol respectively. Another possibility of coordinating phenolate oxygen to boron atom of pinacolborane leading to a four-coordinate boron complex (**Int-2**) was found to be thermodynamically unfavorable due to high ΔG (15.2 Kcal/mol) of the reaction. Following this, the alkene or alkyne substrate approaches towards the B-H bond of **Int-1**. This is the overture to the nucleophilic attack by the C-C double or triple bond of alkene or alkyne to the boron centre of the HBpin, with the hydride being transferred from the boron centre to the alkene or alkyne carbon centre having minimum hydrogen. This occurs through a four-membered transition state (**TS-1**)/(**TS-1'**) and leads to the hydroboration product (**Pdt-1**)/(**Pdt-1'**) along with the regeneration of the catalyst. The ΔE (-32.8 kcal/mol and -11.9 kcal/mol) and ΔG (-28.5 kcal/mol and -9.1 kcal/mol) values for these steps are highly negative and the barriers (ΔG‡s) corresponding to the transition states are moderate: 35.4

kcal/mol and 37.8 kcal/mol for the alkyne and alkene respectively. The moderate barriers explain the delicate feasibility of the reaction at 100 °C. In the transition states, there is a significant amount of B-H bond activation (1.27 Å vs 1.19 Å in the intermediate complex) occurs, which allows the hydride transfer from the boron to the alkene or alkyne carbon centre, along with the simultaneous C-C double and triple bond cleavage and B-O bond formation.

Here we are unwavering the utility of very simple, cost effective and almost non-toxic lithium compounds (**1a** and **1b**) for the catalytic hydroboration of a range of alkenes and alkynes including conjugated terpenes. Chemoselectivity as well as regioselectivity for the described catalytic process have been investigated. DFT calculations reveal that the role of the Li compounds could be interpreted as sterically demanding Lewis acids which bind to one of the Lewis basic O atoms of HBpin, and thereby setting up a platform for the HBpin to offer its B-H bond to the unsaturated alkene and alkyne.

Science and Engineering Research Board (SERB), India (CRG/2018/000287) (SSS), and (EMR/2014/000013) (KV) is acknowledged for providing financial assistance. MKB, SY, and TD thank CSIR, India for the research fellowships.

Conflicts of interest

There are no conflicts to declare.

Notes and references

1 C. E. Tucker, J. Davidson and P. Knochel, *J. Org. Chem.*, 1992, **57**, 3483–3485.

2 For reviews on transition metal catalyzed hydroboration: (a) I. Beletskaya and A. Pelter, *Tetrahedron,* 1997, **53**, 4957–5026; (b) N. Miyaura in Catalytic Heterofunctionalization (Eds: A. Togni, H. Grützmacher), Wiley-VCH, Weinhein, 2001, pp. 1–46; (c) C. M. Vogels and S. W. Westcott, *Curr. Org. Chem.,* 2005, **9**, 687–699.

3 M. Arrowsmith, T. J. Hadlington, M. S. Hill and G. Kociok-Köhn, *Chem. Commun.,* 2012, **48**, 4567–4569.

4 M. Arrowsmith, M. S. Hill and G. Kociok-Köhn, *Chem. Eur. J.,* 2013, **19**, 2776−2783.

5 C. Weetman, M. S. Hill and M. F. Mahon, *Chem. Commun.,* 2015, **51**, 14477−14480.

6 K. Manna, P. Ji, F. X. Greene and W. Lin, *J. Am. Chem. Soc.,* 2016, **138**, 7488–7491.

7 D. Mukherjee, S. Shirase, T. P. Spaniol, K. Mashima and J. Okuda, *Chem. Commun.,* 2016, **52**, 13155–13158.

8 L. Fohlmeister and A. Stasch, *Chem. Eur. J.,* 2016, **22**, 10235–10246.

9 C. Weetman, M. D. Anker, M. Arrowsmith, M. S. Hill, G. Kociok-Köhn, D. J. Liptrot and M. F. Mahon, *Chem. Sci.*, 2016, **7**, 628–641.

10 S. Yadav, S. S. Pahar and S. S. Sen, *Chem. Commun.,* 2017, **53**, 4562–4564.

11 S. Yadav, R. Dixit, M. K. Bisai, K. Vanka and S. S. Sen, *Organometallics*, 2018, **37**, 4576-4584.

12 D. Mukherjee, A. Ellern and A. D. Sadow, *Chem. Sci.,* 2014, **5**, 959–964.

13 N. L. Lampland, M. Hovey, D. Mukherjee and A. D. Sadow, *ACS Catal.,* 2015, **5**, 4219–4226.

14 For reviews on main group compound carbonyl hydroboration, see: (a) M. L. Shegavi and S. K. Bose, *Catal. Sci. Technol.*, 2019, **9**, 3307-3336; (b) C. C. Chong and R. Kinjo, *ACS Catal.,* 2015, **5**, 3238–3259.

View Article Online DOI: 10.1039/C9CC05783H

15 Z. Yang, M. Zhong, X. Ma, K. Nijesh, S. De, P. Parameswaran and H. W. Roesky, *J. Am. Chem. Soc.,* 2016, **138**, 2548–2551.

16 A. Bismuto, S. P. Thomas and M. J. Cowley, *Angew. Chem. Int. Ed.,* 2016, **55**, 15356–15359.

17 J. S. McGough, S. M. Butler, I. A. Cade and M. J. Ingleson, *Chem. Sci.,* 2016, **7**, 3384–3389.

18 M. Fleige, J. Möbus, T. v. Stein, F. Glorius and D. W. Stephan, *Chem. Commun.,*2016, **52**, 10830−10833.

19 (a) J. R. Lawson, L. C. Wilkins and R. L. Melen, *Chem. Eur. J.*, 2017, **23**, 10997−11000; (b) J. L. Carden, L. J. Gierlichs, D. F. Wass, D. L. Browne and R. L. Melen, *Chem. Commun*., 2019, **55**, 318–321.

20 D. Franz, L. Sirtl, A. Pöthig and S. Inoue, *Z. Anorg. Allg. Chem.,* 2016, **642**, 1245–1250.

21 Q. Yin, S. Kemper, H. F. T. Klare and M. Oestreich, *Chem. Eur. J.,* 2016, **22**, 13840−13844.

22 A. Prokofjevs, A. Boussonnihre, L. Li, H. Bonin, E. Lacite, D. P. Curran and E. Vedejs, *J. Am. Chem. Soc.,* 2012, **134**, 12281–12288.

23 A. Bismuto, M. J. Cowley and S. P. Thomas, *ACS Catal*., 2018, **8**, 2001–2005.

24 M. Magre, B. Maity, A. Falconnet, L. Cavallo and M. Rueping, *Angew. Chem., Int. Ed.,* 2019, **58**, 7025–7029.

25 M. Rauch, S. Ruccolo and G. Parkin, *J. Am. Chem. Soc.,* 2017**,** **139**, 13264–13267.

26 Y. Wu, C. Shan, J. Ying, J. Su, J. Zhu, L. L. Liu and Y. Zhao, *Green Chem*., 2017, **19**, 4169−4175.

27 V. A. Pollard, M. A. Fuentes, A. R. Kennedy, R. McLellan and R. E. Mulvey, *Angew. Chem., Int. Ed.,* 2018, **57**, 10651−10655.

28 L. E. Lemmerz, R. McLellan, N. R. Judge, A. R. Kennedy, S. A. Orr, M. Uzelac, E. Hevia, S. D. Robertson, J. Okuda and R. E. Mulvey, *Chem. Eur. J.*, 2018, **24**, 9940–9948.

29 D. Mukherjee, H. Osseili, T. P. Spaniol and J. Okuda, *J. Am. Chem. Soc.,* 2016, **138**, 10790–10793.

30 H. Osseili, D. Mukherjee, K. Beckerle, T. P. Spaniol and J. Okuda, *Organometallics,* 2017, **36**, 3029–3034.

31 H. Osseili, D. Mukherjee, T. P. Spaniol and J. Okuda, *Chem. Eur. J.,* 2017, **23**, 14292–14298.

32 M. K. Bisai, T. Das, K. Vanka and S. S. Sen, *Chem. Commun.,* 2018, **54**, 6843–6846.

33 R. McLellan, A. R. Kennedy, R. E. Mulvey, S. A. Orr and S. D. Robertson, *Chem. Eur. J.*, 2017, **23**, 16853–16861.

34 D. Yan, X. Wu, J. Xiao, Z. Zhu, X. Xu, X. Bao, Y. Yao, Q. Shen and M. Xue, *Org. Chem. Front.,* 2019, **6**, 648–653.

35 S. Bruña, A. Mª González-Vadillo, M. Ferrández, J. Perles, M. M. Montero-Campillo, O. Mób and I. Cuadrado, *Dalton Trans.*, 2017, **46**, 11584–11597.

36 J. Y. Yu. B. Moreau and T. Ritter, *J. Am. Chem. Soc.,* 2009**,** **131**, 12915–12917.

37 R. J. Ely and J. P. Morken, *J. Am. Chem. Soc.,* 2010, **132**, 2534−2535.

38 J. V. Obligacion and P. J. Chirik, *J. Am. Chem. Soc.,* 2013, **135**, 19107−19110.

39 D. Fiorito and C. Mazet, *ACS Catal.,* 2018, **8**, 9382−9387.

40 S. Mandal, P. K. Verma and K. Geetharani, *Chem. Commun.*, 2018, **54**, 13690-13693.

41 (*a*) A. Bonet, H. Gulyás and E. Fernández, *Angew. Chem., Int. Ed.,* 2010, **49**, 5130–5134; (*b*) R. Dasgupta, S. Das, S. Hiwase, S. Pati and S. Khan, *Organometallics,* 2019, **38**, 1429–1435.

42 K. Burgess, W. A. vander Donk, S. A. Westcott, T. B. Marder, R. T. Baker and J. C. Calabrese, *J. Am. Chem. Soc.*, 1992, **114**, 9350-9359.

43 I. P. Query, P. A. Squier, E. M. Larson, N. A. Isley and T. B. Clark, *J. Org. Chem.,* 2011, **76**, 6452–6456.

