Chinese Chemical Letters 32 (2021) 1717–1720

Contents lists available at ScienceDirect

Chinese Chemical Letters

journal homepage: www.elsevier.com/locate/cclet

Communication

Selective annulation of benzamides with internal alkynes catalyzed by an electron-deficient rhodium catalyst

Ping Zhang[a], Wenju Chang[b], Hongyun Jiao[b], Yanshang Kang[a], Wenxuan Zhao[b], Peipei Cui[a], Yong Liang[b], Wei-Yin Sun[a], Yi Lu[a,*]

[a] Coordination Chemistry Institute, State Key Laboratory of Coordination Chemistry, School of Chemistry and Chemical Engineering, Nanjing National Laboratory of Microstructures, Collaborative Innovation Center of Advanced Microstructures, Nanjing University, Nanjing 210023, China
[b] State Key Laboratory of Coordination Chemistry, Jiangsu Key Laboratory of Advanced Organic Materials, School of Chemistry and Chemical Engineering, Nanjing University, Nanjing 210023, China

ARTICLE INFO

Article history:
Received 27 October 2020
Received in revised form 10 January 2021
Accepted 13 January 2021
Available online 20 January 2021

Keywords:
Electron-deficient rhodium
C—H activation
Annulation
Benzamide
Alkyne

ABSTRACT

An electron-deficient $[Cp^ERhCl_2]_2$ catalyzed annulation of *N*-pentafluorophenylbenzamides with internal alkynes was successfully established under mild reaction conditions, with the assistance of Lewis acid silver salt. Particularly, electron-deficient benzamide substrates were smoothly transformed into the desired products in this catalytic system. The catalytic system showed a broad tolerance for different substituents on the aromatic rings or aryl, alkyl-substituted alkynes.

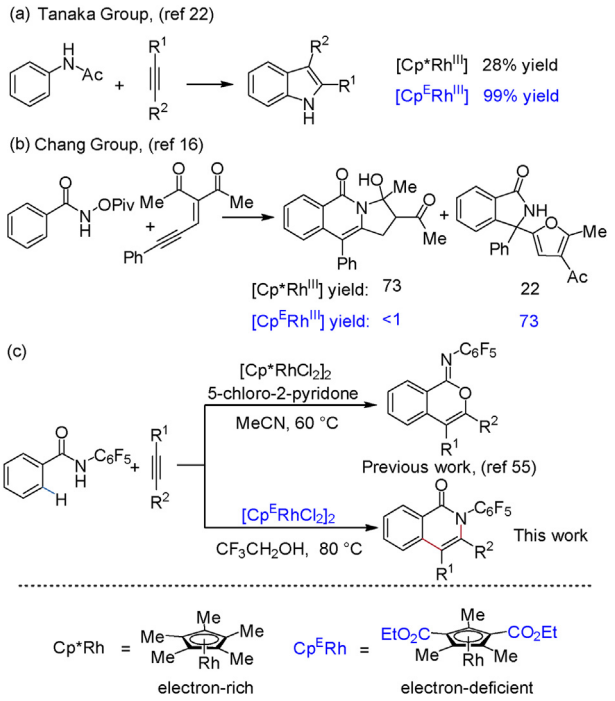
The synthesis of small molecules through rhodium-catalyzed C—H activation has been greatly developed in the past few years [1–4]. Generally, a commercially available $[Cp^*RhCl_2]_2$ (Cp^* = pentamethylcyclopentadienyl) and its cationic complex are nearly universally considered to be privileged catalysts for these transformations [5–15]. It attributes the success to the strong π-electron donating ability of the Cp^* ligand to obtain labile intermediates such as cationic or high-valent metal species [16,17]. Recent studies have showed that some sterically or electronically tuned Cp ligands can dramatically induce significant changes in reactivity, as well as chemo-, regio- and diastereo-selectivity for different reactions. Satoh and Miura groups reported that the addition of phenyl-substituted Cp used as ligands improved the reactivity and changed the chemo-selectivity in rhodium-catalyzed C—H bond activation [18–20]. With the development of the steric and electronic manipulation of Cp ligands, $[Cp^XRh]$ catalysts have been used in rhodium-catalyzed C—H bond functionalization [21–24]. Tanaka group demonstrated that electron-deficient Cp^E ligand could improve reaction reactivity in rhodium catalytic system (Scheme 1a) [22]. Chang [16] and co-workers reported that tuning the electronic property of Cp ligand could also change the chemo-selectivity (Scheme 1b). At the same time, enantioselective Rh-catalyzed C—H functionalization reactions promoted by the introduction of chiral Cp ligands were disclosed by Cramer [25–30], Li [31–34], You [35,36] and others [37–40].

The nitrogen-containing heterocycles in biologically active molecules have attracted much attention for their synthesis and functionalization in rhodium catalytic systems [6–11,41–46]. Recently, the development in Rh chemistry has demonstrated that Cp^ERh^{III}complex bearing two ester groups could successfully realize the construction of heterocycles through C—H activation [16,22–24,47–50]. Based on these progresses and our previous work [51–55], we developed an oxidative selective annulation of benzamides with alkynes catalyzed by the electron-deficient rhodium complex Cp^ERh^{III} in the air under mild conditions, with the assistance of Lewis acid silver salt.

On the basis of our work [55], we tried to employ an electron-deficient $[Cp^ERhCl_2]_2$ as a catalyst in place of $[Cp^*RhCl_2]_2$ in CH_3CN solvent at 100 °C (Table 1, entry 2). To our delight, it afforded a single isomer **3aa** in 28% yield. Subsequently, we were pleased to find that the yield was improved dramatically when CF_3CH_2OH was applied as solvent (entry 7). Investigation of oxidants proved that Ag_2CO_3 was most effective (entries 8–11). Generally speaking, $[Cp^ERhCl_2]_2$ was not suitable for the C—H bond functionalization of electron-deficient substrates according to the literature [23]. However, in this work, electron-deficient benzamides were

* Corresponding author.
E-mail address: luyi@nju.edu.cn (Y. Lu).

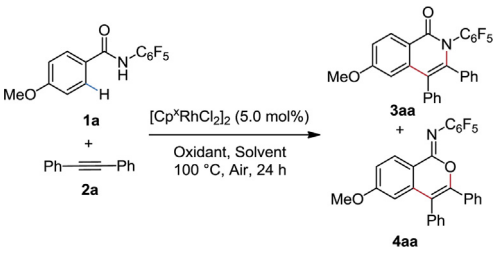
https://doi.org/10.1016/j.cclet.2021.01.024



Scheme 1. Cyclopentadienyl ligands in Rh(III)-catalyzed C—H activation reactions.

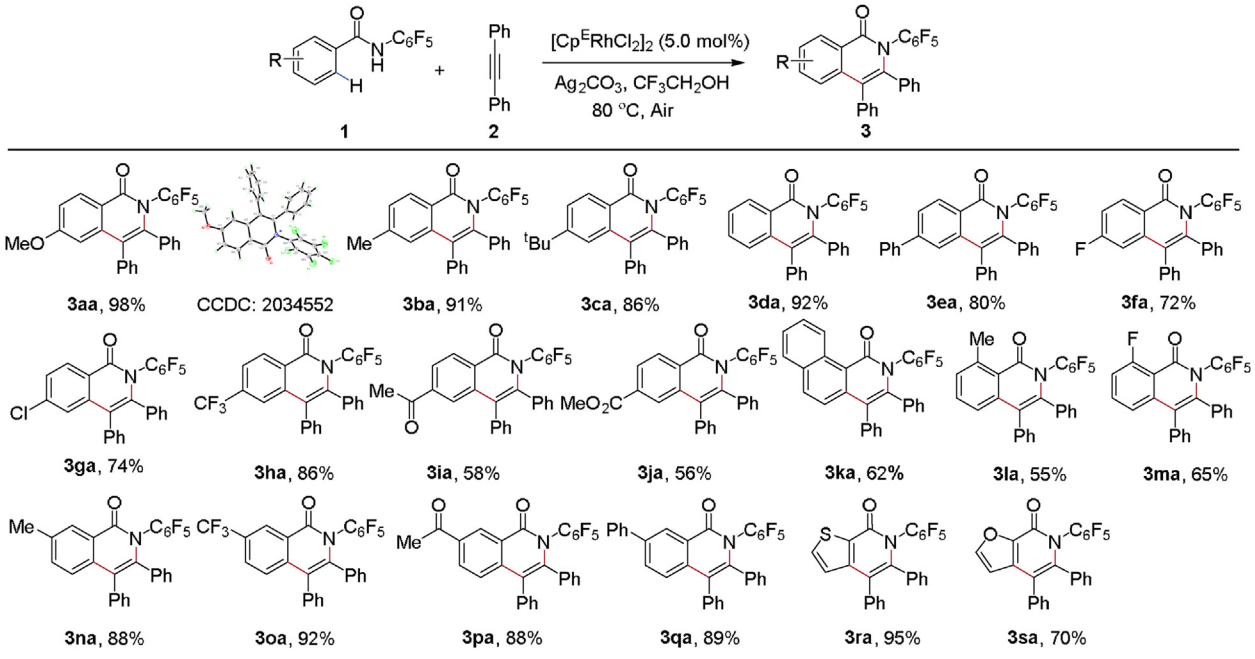
smoothly transformed into the desired products with the catalyst $[Cp^ERhCl_2]_2$, while catalysts with Cp* and Cp^{*Cy} decreased the chemo-selectivity (entries 14 and 15). It is probably because of the electronic effect of *N*-pentafluorophenyl, which enhances the acidity of the hydrogen atom on the N—H bond. With the assistance of carbonate anion from Ag_2CO_3, the nitrogen anion is more readily coordinated to the electron-deficient rhodium(III) complex. Moreover, tests of several substrates with different directing groups proves the importance of electronic effects as well (Table S5 in Supporting information). Compared to the substrates with electron-donating *N*-methyl and -benzyl groups, the substrate with *N*-methoxy group is relatively easier to be deprotonated by carbonate ion in this catalytic system. The steric and electronic properties of substrates with *N*-phenyl group are similar to the one with *N*-methoxy group. In the presence of

Table 1
Screening of reaction conditions for **3aa**.[a]

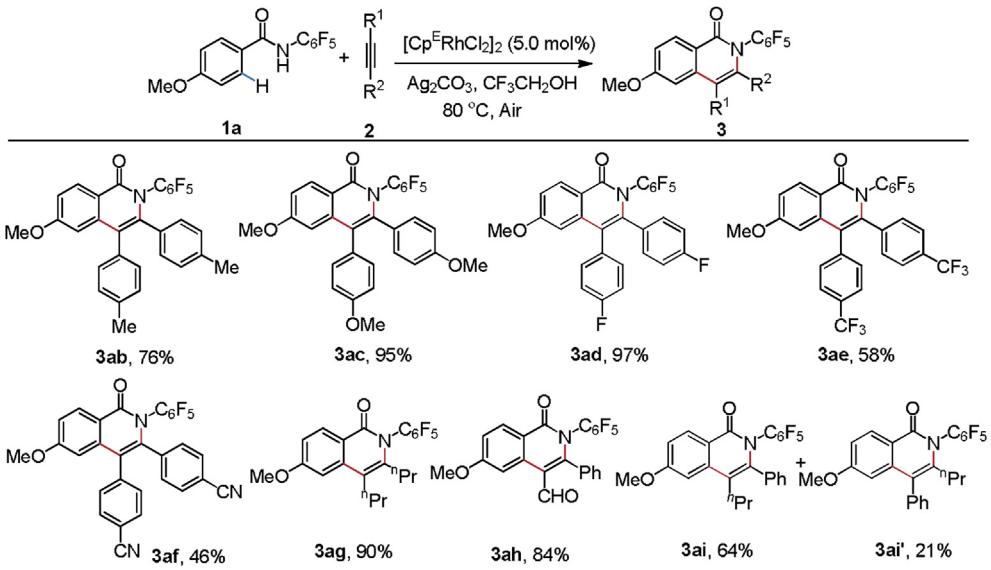


Entry	Catalyst	Oxidant	Solvent	Yield (%)[b]	
				3aa	**4aa**
1[c]	$[Cp^*RhCl_2]_2$	Ag_2CO_3	CH_3CN	11	84
2	$[Cp^ERhCl_2]_2$	Ag_2CO_3	CH_3CN	28	0
3	$[Cp^ERhCl_2]_2$	Ag_2CO_3	DCE	15	2
4	$[Cp^ERhCl_2]_2$	Ag_2CO_3	MeOH	16	0
5	$[Cp^ERhCl_2]_2$	Ag_2CO_3	EtOH	6	0
6	$[Cp^ERhCl_2]_2$	Ag_2CO_3	HFIP	16	0
7	$[Cp^ERhCl_2]_2$	Ag_2CO_3	CF_3CH_2OH	96	0
8	$[Cp^ERhCl_2]_2$	AgOAc	CF_3CH_2OH	57	0
9	$[Cp^ERhCl_2]_2$	Ag_2O	CF_3CH_2OH	64	0
10	$[Cp^ERhCl_2]_2$	AgOPiv	CF_3CH_2OH	52	0
11	$[Cp^ERhCl_2]_2$	$Cu(OAc)_2$	CF_3CH_2OH	52	0
12[d]	$[Cp^ERhCl_2]_2$	Ag_2CO_3	CF_3CH_2OH	87	0
13[e]	$[Cp^ERhCl_2]_2$	Ag_2CO_3	CF_3CH_2OH	95	0
14[e]	$[Cp^*RhCl_2]_2$	Ag_2CO_3	CF_3CH_2OH	42	54
15[e]	$[Cp^{*Cy}RhCl_2]_2$	Ag_2CO_3	CF_3CH_2OH	52	46

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), $[Cp^XRhCl_2]_2$ (5.0 mol%), and Ag_2CO_3 (1.0 equiv.) in CF_3CH_2OH (1.0 mL) at 100 °C in oil bath for 24 h under air.
[b] The yield was determined by ^1H NMR analysis of crude product using 1,3,5-trimethoxybenzene as an internal standard.
[c] 60 °C in oil bath for 24 h.
[d] 80 °C in oil bath for 24 h.
[e] 80 °C in oil bath for 36 h.



Scheme 2. Scope of benzamides.

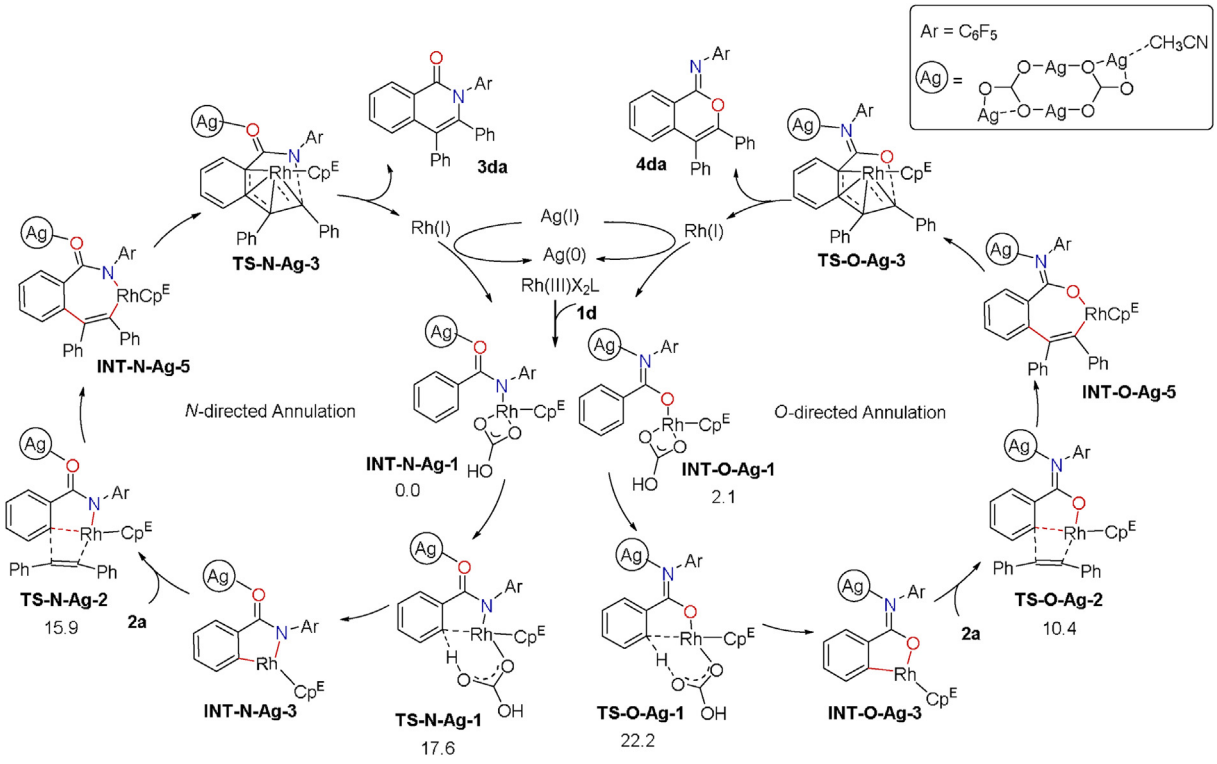


Scheme 3. Scope of alkynes. For compound **3ah**, 1-phenyl-3,3-diethoxy-1-propyne was used.

strongly electron deficient *N*-pentafluorophenyl group, hydrogen proton is more easily removed with the assistance of carbonate ion, providing the best result for this transformation.

With the optimized reaction conditions in hand, we explored the scope of this approach for products **3** by employing different substituted benzamides under the optimal reaction conditions (Scheme 2). Various substituted benzamides **1** were treated with **2a** to give the isoquinolone derivatives in moderate to excellent yields. Both electron-donating (**3aa**–**3ea**) and electron- withdrawing (**3fa**–**3ka**) groups at the *para* position on the substrates were well tolerated. Substrate **1** with methoxy-group at the *para* position showed the highest reactivity. The structure of **3aa** was confirmed by single-crystal X-ray analysis (Section 2.5 in Supporting information). 2-Fluorobenzamide afforded **3ma** in moderate yield (65%), whereas 2-methylbenzamide showed a slightly decreased efficiency (**3la**). It is noteworthy that benzamides possessing different substituents, such as methyl, trifluoromethyl, acetyl, methoxycarbonyl, and phenyl groups at the *meta*-position could lead to the formation of a single regioisomer (**3na**-**3qa**), attributing to the steric effects [56]. Furthermore, heteroaromatic benzamides also turned out to be compatible (**3ra**, **3sa**).

As shown in Scheme 3, the catalytic system was not only available to diphenylacetylene (**2a**) but also suitable for aryl- or alkyl-substituted alkynes. Symmetrical diaryl or dialkyl alkynes



Scheme 4. Proposed mechanism. Numbers associated with molecules are DFT-computed relative Gibbs free energy (kcal/mol) in CH_3CN.

led to the products in moderate to good yields (**3ab**-**3ag**). Intriguingly, unsymmetric 1-phenyl-3,3-diethoxy-1-propyne was applied as a coupling partner, and it proceeded smoothly to afford **3ah** (CCDC: 2050115) in 84% yield with high regioselectivity (Section 2.5 in Supporting information). However, when 1-phenyl-1-pentyne was applied, a mixture of regioisomers **3ai** and **3ai'** was produced.

To understand the chemo-selectivity of this reaction, we performed a series of density functional theory (DFT) calculations using 1,2-diphenylacetylene (**2a**) and amide **1d** as the substrates [57–61]. The calculations demonstrated that the reaction proceeded through a C–H activation, alkyne insertion, and metallallylcarbenoid annulation (Scheme 4, for computational details, see Section 2.6.2 in Supporting information) [62]. The chemo-selectivity was determined in the C—H activation step *via* transition states **TS-N-Ag-1** (17.6 kcal/mol) and **TS-O-Ag-1** (22.2 kcal/mol). Therefore, the *N*-directed pathway was favored over *O*-directed pathway by 4.6 kcal/mol, in agreement with that only *N*-cyclization product **3da** is observed in the presence of Cp^ERh catalyst. In the *N*-directed pathway, the C—H activation step (*via* **TS-N-Ag-1**) is 1.7 kcal/mol higher than the alkyne insertion (*via* **TS-N-Ag-2**) indicating an ambiguous kinetic isotope effect. The kinetic isotope experiments were conducted with **1d** and **1d**-d_5 under standard reaction conditions (parallel experiment: $k_H/k_D = 1.50$ and intermolecular: $k_H/k_D = 1.55$), which were consistent with DFT calculations.

In summary, we have successfully developed a selective *N*-annulation of benzamides with internal alkynes under mild reaction conditions with an electron-deficient catalyst $[Cp^ERhCl_2]_2$. The electronic effect of ligand played a vital role in controlling the chemo-selectivity of this transformation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We gratefully acknowledge the National Natural Science Foundation of China (Nos. 21671097 and 21573106) and the Fundamental Research Funds for the Central Universities for financial support.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.cclet.2021.01.024.

References

[1] J. Wencel-Delord, T. Droge, F. Liu, F. Glorius, Chem. Soc. Rev. 40 (2011) 4740–4761.
[2] K. Shin, H. Kim, S. Chang, Acc. Chem. Res. 48 (2015) 1040–1052.
[3] Z. Chen, B. Wang, J. Zhang, et al., Org. Chem. Front. 2 (2015) 1107–1295.
[4] G. Song, X. Wei, Acc. Chem. Res. 48 (2015) 1007–1020.
[5] N. Umeda, H. Tsurugi, T. Satoh, M. Miura, Angew. Chem. Int. Ed. 47 (2008) 4019–4022.
[6] S. Mochida, N. Umeda, K. Hirano, T. Satoh, M. Miura, Chem. Lett. 39 (2010) 744–746.
[7] N. Guimond, C. Gouliaras, K. Fagnou, J. Am. Chem. Soc. 132 (2010) 6908–6909.
[8] T.K. Hyster, T. Rovis, J. Am. Chem. Soc. 132 (2010) 10565–10569.
[9] G. Song, D. Chen, C.L. Pan, R.H. Crabtree, X.W. Li, J. Org. Chem. 75 (2010) 7487–7490.
[10] H. Wang, C. Grohmann, C. Nimphius, F. Glorius, J. Am. Chem. Soc. 134 (2012) 19592–19595.
[11] Y. Fukui, P. Liu, Q. Liu, et al., J. Am. Chem. Soc. 136 (2014) 15607–15614.
[12] Y. Liu, Y. Yang, Y. Shi, et al., Organometallics 35 (2016) 1350–1353.
[13] J. Mo, L. Wang, X. Cui, Org. Lett. 17 (2015) 4960–4963.
[14] Y. Zhao, S. Li, X. Zheng, et al., Angew. Chem. Int. Ed. 56 (2017) 4286–4289.
[15] G. Zheng, X. Duan, L. Chen, et al., J. Org. Chem. 85 (2020) 4543–4552.
[16] S.Y. Hong, J. Jeong, S. Chang, Angew. Chem. Int. Ed. 56 (2017) 2408–2412.
[17] T. Piou, F. Romanov-Michailidis, M. Romanova-Michaelides, et al., J. Am. Chem. Soc. 139 (2017) 1296–1310.
[18] T. Uto, M. Shimizu, K. Ueura, et al., J. Org. Chem. 73 (2008) 298–300.
[19] N. Umeda, H. Tsurugi, T. Satoh, M. Miura, Angew. Chem. Int. Ed. 47 (2008) 4019–4022.
[20] M. Shimizu, K. Hirano, T. Satoh, M. Miura, J. Org. Chem. 74 (2009) 3478–3483.
[21] F. Romanov-Michailidis, K.F. Sedillo, J.M. Neely, T. Rovis, J. Am. Chem. Soc. 136 (2015) 8892–8895.
[22] Y. Hoshino, Y. Shibata, K. Tanaka, Adv. Synth. Catal. 356 (2014) 1577–1585.
[23] M. Fukui, Y. Hoshino, T. Satoh, M. Miura, K. Tanaka, Adv. Synth. Catal. 356 (2014) 1638–1644.
[24] M. Font, B. Cendón, A. Seoane, J.L. MascareÇas, M. Gulías, Angew. Chem. Int. Ed. 57 (2018) 8255–8259.
[25] B. Ye, N. Cramer, Science 338 (2012) 504–506.
[26] S.G. Wang, N. Cramer, Angew. Chem. Int. Ed. 58 (2019) 2514–2518.
[27] S.G. Wang, Y. Liu, N. Cramer, Angew. Chem. Int. Ed. 58 (2019) 18136–18140.
[28] S.G. Wang, N. Cramer, ACS Catal. 10 (2020) 8231–8236.
[29] C. Duchemin, N. Cramer, Angew. Chem. Int. Ed. 59 (2020) 14129–14133.
[30] Y. Sun, N. Cramer, Angew. Chem. Int. Ed. 57 (2018) 15539–15543.
[31] B. Shen, B. Wan, X. Li, Angew. Chem. Int. Ed. 57 (2018) 15534–15538.
[32] M. Tian, D. Bai, G. Zheng, J. Chang, X. Li, J. Am. Chem. Soc. 141 (2019) 9527–9532.
[33] X. Yang, G. Zheng, X. Li, Angew. Chem. Int. Ed. 58 (2019) 322–326.
[34] F. Wang, Z. Qi, Y. Zhao, et al., Angew. Chem. Int. Ed. 59 (2020) 13288–13294.
[35] J. Zheng, W.J. Cui, C. Zheng, S.L. You, J. Am. Chem. Soc. 138 (2016) 5242–5245.
[36] W.J. Cui, Z.J. Wu, Q. Gu, S.L. You, J. Am. Chem. Soc. 142 (2020) 7379–7385.
[37] Z.J. Jia, C. Merten, R. Gontla, et al., Angew. Chem. Int. Ed. 56 (2017) 2429–2434.
[38] E.A. Trifonova, N.M. Ankudinov, A.A. Mikhaylov, et al., Angew. Chem. Int. Ed. 57 (2018) 7714–7718.
[39] T. Li, C. Zhou, X. Yan, J. Wang, Angew. Chem. Int. Ed. 57 (2018) 4048–4052.
[40] H. Li, X. Yan, J. Zhang, et al., Angew. Chem. Int. Ed. 58 (2019) 6732–6736.
[41] N. Guimond, S.I. Gorelsky, K. Fagnou, J. Am. Chem. Soc. 133 (2011) 6449–6457.
[42] G. Song, X. Gong, X. Li, J. Org. Chem. 76 (2011) 7583–7589.
[43] Z. Shi, C. Tang, N. Jiao, Adv. Synth. Catal. 354 (2012) 2695–2700.
[44] X. Xu, Y. Liu, C.M. Park, Angew. Chem. Int. Ed. 51 (2012) 9372–9376.
[45] D.G. Yu, F. de Azambuja, T. Gensch, C.G. Daniliuc, F. Glorius, Angew. Chem. Int. Ed. 53 (2014) 9650–9654.
[46] N.S. Upadhyay, V.H. Thorat, R. Sato, et al., Green Chem. 19 (2017) 3219–3224.
[47] M. Fukui, Y. Shibata, Y. Hoshino, et al., Chem. Asian J. 11 (2016) 2260–2264.
[48] E. Kudo, Y. Shibata, M. Yamazaki, et al., Chem. Eur. J. 22 (2016) 14190–14194.
[49] J. Terasawa, Y. Shibata, M. Fukui, K. Tanaka, Molecules 23 (2018) 3325–3337.
[50] G. Mihara, K. Ghosh, Y. Nishii, M. Miura, Org. Lett. 22 (2020) 5706–5711.
[51] Y. Lu, H.W. Wang, J.E. Spangler, et al., Chem. Sci. 6 (2015) 1923–1927.
[52] H.W. Wang, P.P. Cui, Y. Lu, W.Y. Sun, J.Q. Yu, J. Org. Chem. 81 (2016) 3416–3422.
[53] H.W. Wang, Y. Lu, B. Zhang, et al., Angew. Chem. Int. Ed. 56 (2017) 7449–7453.
[54] Y.S. Kang, P. Zhang, M.Y. Li, et al., Angew. Chem. Int. Ed. 58 (2019) 9099–9103.
[55] P. Zhang, W. Chang, Y.S. Kang, et al., Org. Lett. 22 (2020) 9462–9467.
[56] L. Li, W.W. Brennessel, W.D. Jones, Organometallics 28 (2009) 3492–3500.
[57] M.D. Lotz, N.M. Camasso, A.J. Canty, M.S. Sanford, Organometallics 36 (2017) 165–171.
[58] J.Q. Wu, S.S. Zhang, H. Gao, et al., J. Am. Chem. Soc. 139 (2017) 3537–3545.
[59] X.G. Liu, H. Gao, S.S. Zhang, Q. Li, H. Wang, ACS Catal. 7 (2017) 5078–5086.
[60] K.L. Bay, Y.F. Yang, K.N. Houk, J. Organomet. Chem. 864 (2018) 19–25.
[61] I. Funes-Ardoiz, F. Maseras, Angew. Chem. Int. Ed. 55 (2016) 2764–2767.
[62] J. Jiang, H. Liu, L. Cao, et al., ACS Catal. 9 (2019) 9387–9392.