Transition Metal Chemistry
https://doi.org/10.1007/s11243-020-00418-4

Palladium-catalyzed aminocarbonylation of aryl iodides with amines: efficient access to bidentate amide directing groups

Yanqing Wang[1] · Tao Wang[2] · Xiaosha Wang[2] · Lantao Liu[2,3] · Guoliang Mao[1]

Received: 5 July 2020 / Accepted: 5 August 2020

Abstract
A new route to bidentate amide directing groups has been developed via the palladium(II)-catalyzed aminocarbonylation. Under atmospheric carbon monoxide pressure, using commercially available aryl iodides and aromatic amine derivatives as substrates, the three-component reaction proceeded smoothly to give the desired products in moderate-to-excellent yields with good functional-group compatibility.

Introduction

Transition metal-catalyzed C–H bond activation and functionalization is one of the most important and frequently used methods for the formation of carbon–carbon as well as carbon–heteroatom bonds in modern organic synthetic chemistry [1–9].[1] Among these, the C–H functionalization assisted by bidentate amide directing group has attracted considerable attention because the chelation-directed strategy can provide a reliable and robust tool to enhance the efficiency and control the selectivity of C–H activation via the formation of a pincer-type metallacycle (Scheme 1) [10]. Since the pioneering work of Daugulis et al. [11], a wide variety of bidentate amide directing groups have been synthesized and applied in the C–H functionalizations such as 8-aminoquinoline [12–19], amide-oxazoline [20–27], 2-(pyridin-2-yl)isopropylamine [28–33], 2-aminopyridine 1-oxide [34–37], 2-aminophenylpyrazole [38], etc. In recent times, significant advancement has been made in the highly selective C–H activation of bidentate amides using Pd, Ni, Cu and Co as catalysts. Hence, the development of simple and efficient approaches for the synthesis of bidentate amide directing groups containing various heteroatoms is an attractive research topic. Traditionally, the synthesis of amides with such a scaffold involves the acylation of acyl chlorides with amines [27, 37]. Nevertheless, the direct aminocarbonylation of aryl halides with amines provides a more straightforward option [39–41]. The reason is that, CO is an inexpensive and readily available carbonyl source and it is also valued because of its simplicity and atom economy. Recently, we reported the synthesis of ferrocene indanone derivatives via the trinuclear *N*-heterocyclic carbene palladium(II)-catalyzed cyclocarbonylation of *o*-bromoarylferrocenes with CO as the suitable starting materials [42]. Inspired by above content, we herein planned to develop a general and efficient method for the synthesis of bidentate amide directing groups, which should be proved to be excellent substrates in C–H activation reaction (Scheme 2).

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11243-020-00418-4) contains supplementary material, which is available to authorized users.

✉ Tao Wang
wt67751726@126.com

✉ Guoliang Mao
maoguoliang@nepu.edu.cn

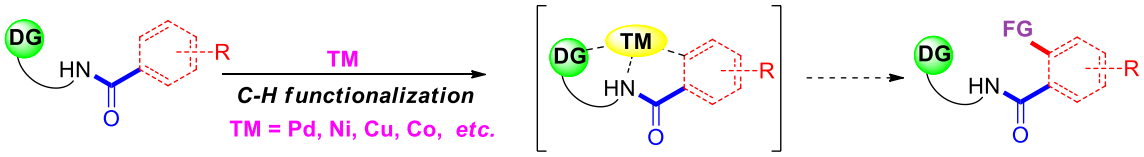
[1] College of Chemistry and Chemical Engineering, Northeast Petroleum University, Daqing 163318, People's Republic of China

[2] Henan Engineering Laboratory of Green Synthesis for Pharmaceuticals, College of Chemistry and Chemical Engineering, Shangqiu Normal University, Shangqiu 476000, People's Republic of China

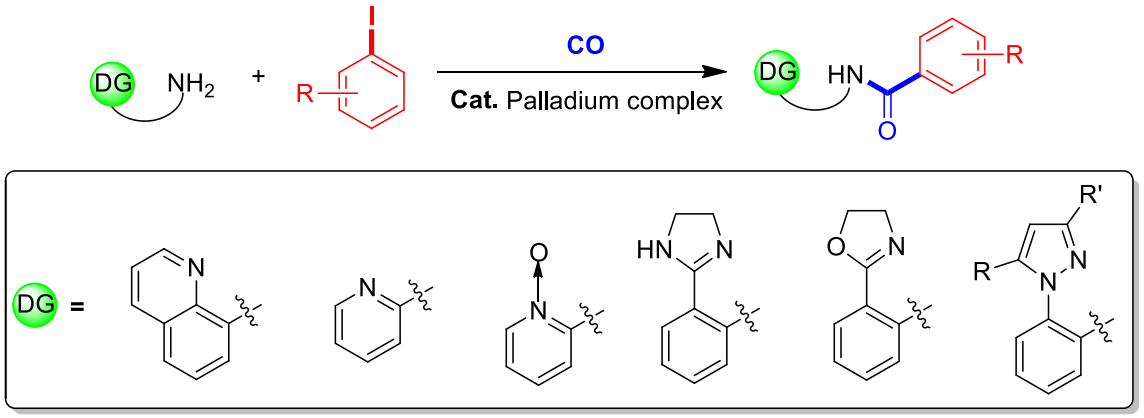
[3] College of Chemistry, Zhengzhou University, Zhengzhou 450001, People's Republic of China

[1] For selected reviews on transition metals catalyzed C–H functionalization.

Published online: 10 August 2020



Scheme 1 Transition-metal-mediated chelation-assisted C–H functionalization



Scheme 2 Synthesis of the bidentate amide directing groups

Experimental

General remarks

Solvents were dried by standard methods and freshly distilled prior to use if needed. All other chemicals were used as purchased. The aromatic amine derivatives were prepared according to the literature methods [27, 37, 43, 44]. NMR spectra were recorded on a Bruker DPX 400 instrument using TMS as an internal standard.

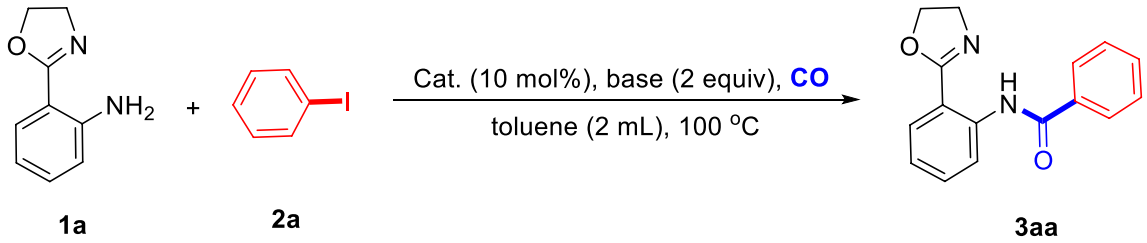
General procedure for the catalytic aminocarbonylation

Toluene (2.0 mL), K_3PO_4 (84.9 mg, 0.40 mmol), $PdCl_2(CH_3CN)_2$ (5.2 mg, 10 mol %), iodobenzene (61.2 mg, 0.30 mmol), and the 2-(4,5-dihydrooxazol-2-yl) aniline (32.4 mg, 0.20 mmol) were stirred under an Ar atmosphere at room temperature for 10 min. The mixture was flushed with CO and fitted with a CO filled balloon. The reaction mixture was heated to 100 °C with vigorous stirring for 15 h. After cooling, the mixture was evaporated and the product was isolated by preparative TLC on silica gel plates to afford the corresponding bidentate directing group complex. The purified products were identified by NMR spectra, and their analytical data are given in the Supporting Information.

Results and discussion

Our initial studies focused on developing an optimum set of reaction conditions for the carbonylative reaction. The experiments were carried out using 2-(4,5-dihydrooxazol-2-yl)aniline (0.20 mmol) and iodobenzene (0.30 mmol) as the reactants, plus $Pd(OAc)_2$ (10.0 mol%) as the catalyst, in toluene (2.0 mL) at 100 °C under a CO atmosphere, with the results shown in Table 1. The yield of *N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)benzamide (**3aa**) was strongly dependent on the choice of the base (Table 1, entries 1–13) [45]. K_3PO_4 was by far the most effective base (Table 1, entry 8). We have also explored the effect on the reaction yield of other variables, such as the palladium catalyst, the temperature, and the reaction time (Table 1, entries 14–22). The optimum reaction conditions thus far developed employ 1 atm of carbon monoxide, 1 equiv of the 2-(4,5-dihydrooxazol-2-yl)aniline (0.20 mmol), 1.5 equiv of the iodobenzene (0.30 mmol), 10 mol% of commercially available $PdCl_2(CH_3CN)_2$, and 2 equiv of anhydrous potassium phosphate in toluene (2 mL) at 100 °C for 15 h; this procedure provided a yield of 96% (Table 1, entry 15).

Table 1 Optimization of reaction conditions for the carbonylative of iodobenzene with 2-(4,5-dihydrooxazol-2-yl)aniline[a]



1a **2a** **3aa**

Entry	Cat	Base	Yield (%)[b]
1	$Pd(OAc)_2$	KO^tBu	73
2	$Pd(OAc)_2$	NaO^tBu	65
3	$Pd(OAc)_2$	Cs_2CO_3	52
4	$Pd(OAc)_2$	Na_2CO_3	72
5	$Pd(OAc)_2$	K_2CO_3	74
6	$Pd(OAc)_2$	Li_2CO_3	19
7	$Pd(OAc)_2$	$NaHCO_3$	49
8	$Pd(OAc)_2$	K_3PO_4	83
9	$Pd(OAc)_2$	$K_3PO_4{\cdot}3H_2O$	81
10	$Pd(OAc)_2$	KH_2PO_4	24
11	$Pd(OAc)_2$	NaOAc	33
12	$Pd(OAc)_2$	NaOH	5
13	$Pd(OAc)_2$	Et_3N	29
14	$Pd(PPh_3)_4$	K_3PO_4	90
15	$PdCl_2(CH_3CN)_2$	K_3PO_4	96
16	$PdCl_2(PPh_3)_2$	K_3PO_4	83
17	$PdCl_2$(dppf)	K_3PO_4	84
18	$Pd_2(dba)_3$	K_3PO_4	81
19	$PdCl_2$	K_3PO_4	66
20[c]	$PdCl_2(CH_3CN)_2$	K_3PO_4	86
21[d]	$PdCl_2(CH_3CN)_2$	K_3PO_4	80
22[e]	$PdCl_2(CH_3CN)_2$	K_3PO_4	85

[a]All reactions were carried out using 2-(4,5-dihydrooxazol-2-yl)aniline (0.20 mmol), iodobenzene (0.30 mmol), base (2.0 equiv), plus catalyst (10.0 mol%) in toluene (2.0 mL) at 100 °C for 15 h

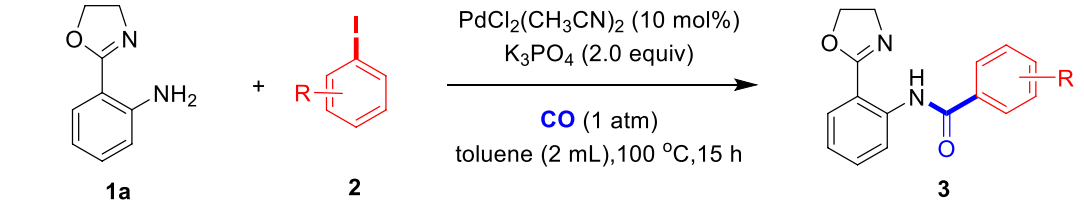
[b]Isolated yields

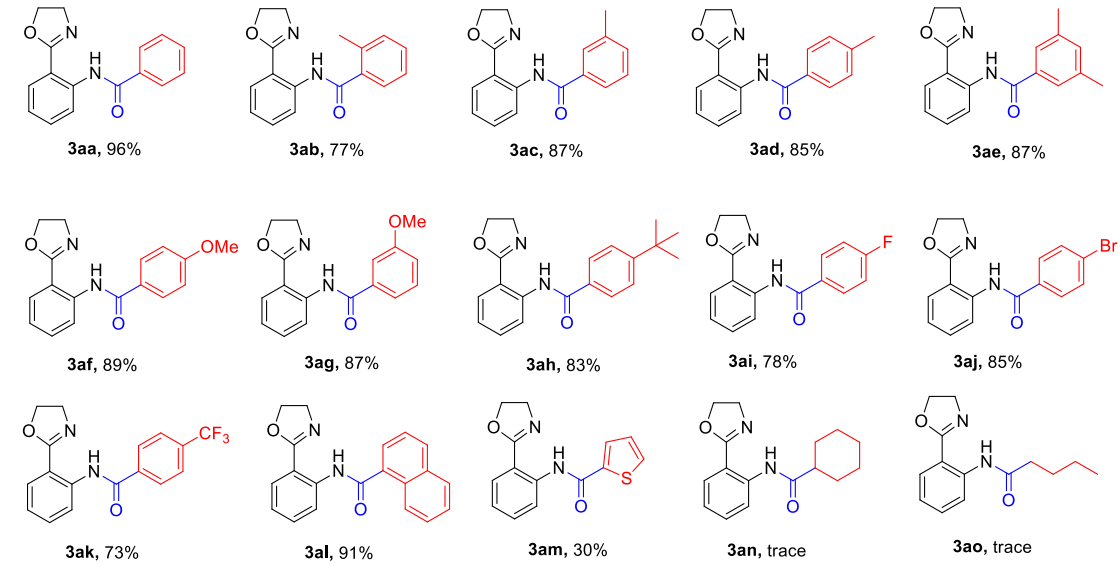
[c]Reaction temperature was 80 °C

[d]Reaction temperature was 60 °C

[e]Reaction time was 12 h

Under the optimized reaction conditions, a variety of aryl iodides were employed to further investigate the scope of the catalyst system. As demonstrated in Scheme 3, most of the carbonylations proceeded efficiently to give the corresponding bidentate directing group complexes **3aa–3al** in good to excellent yields. Both electron-donating including $–CH_3$ (**3ab–3ae**), $–OCH_3$ (**3af–3ag**), $–^tBu$ (**3ah**) and withdrawing substitutes including –F (**3ai**), –Br (**3aj**), $–CF_3$ (**3ak**) on the aryl iodides were well tolerated and gave good to excellent yields (73–89%). Meaningfully, the case of 1-iodonaphthalene also afforded the desired product in satisfactory yield under the present reaction conditions (**3al**). However, when heteroaromatic aryl iodides, such as 2-iodothiophene were used as the substrate, a relatively low yield was obtained (30% for **3am**). We have also attempted to employ iodocyclohexane and 1-iodobutane in our method. The yields of products **3an** and **3ao**





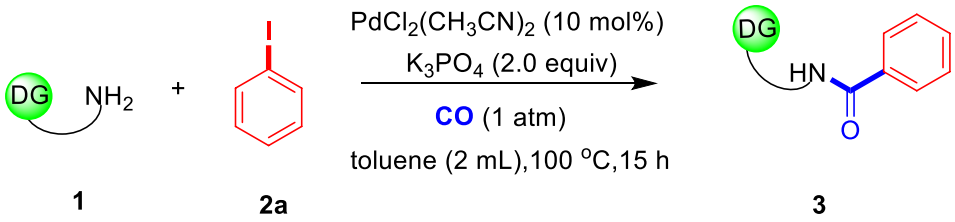
[a]All reactions were carried out using 2-(4,5-dihydrooxazol-2-yl)aniline (0.20 mmol), aryl iodides (0.30 mmol), K_3PO_4 (2.0 equiv), plus $PdCl_2(CH_3CN)_2$ (10.0 mol%) in toluene (2.0 mL) at 100 °C for 15 h.

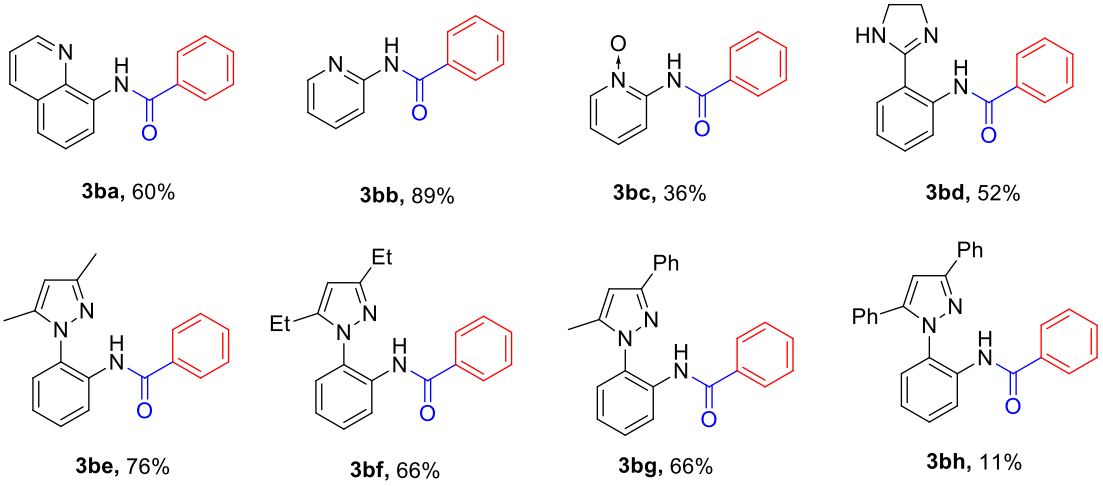
Scheme 3 Substrate scope for the carbonylative of aryl iodides with 2-(4,5-dihydrooxazol-2-yl)aniline[a]

were relatively low, but they were difficult to synthesize in present methods.

After evaluating the scope of the aryl iodide coupling partner, we tested a wide range of aromatic amine derivatives to demonstrate the generality of the protocol (Scheme 4). For example, aromatic amine derivatives including 8-aminoquinoline, 2-aminopyridine, 1-oxide 2-aminopyridine, 2-(4,5-dihydro-1*H*-imidazol-2-yl)aniline could serve as viable substrates in the reaction for the successful production of the corresponding bidentate directing group complexes (**3ba**–**3bd**). The various substituted 2-(1*H*-pyrazol-1-yl) anilines were also applicable under the current reaction conditions, affording the desired products in acceptable yields (**3be**–**3bg**, 66–76%). As for product **3bh**, the possible reason for the decrease in yield was the steric hindrance effect during the reaction. Overview, bidentate directing group building blocks were synthesized in a convenient mode with CO as the suitable starting material.

On the basis of the mechanism of previous reports [39, 40] and our results, a putative reaction mechanism was then proposed in Scheme 5. First, aryl iodides **2** are oxidatively added to the in situ formed palladium(0) complexes resulting in intermediate **I**, followed by CO insertion to





[a]All reactions were carried out using aromatic amine derivatives (0.20 mmol), iodobenzene (0.30 mmol), K_3PO_4 (2.0 equiv), plus $PdCl_2(CH_3CN)_2$ (10.0 mol%) in toluene (2.0 mL) at 100 °C for 15 h.

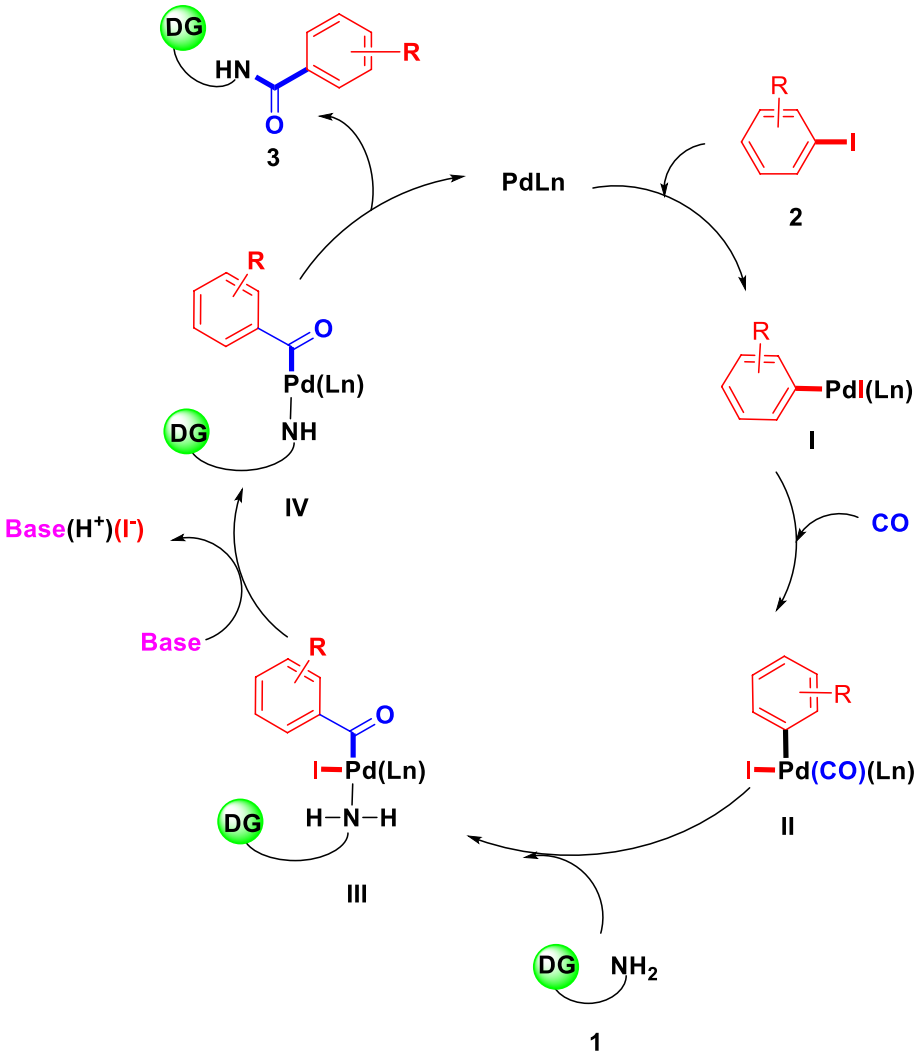
Scheme 4 Substrate scope for the carbonylative of iodobenzene with aromatic amine derivatives[a]

produce the coordination of carbon monoxide **II**, which is inserted into the Pd–C bond to give the intermediate **III**. Then the intermediate **III** is ready for the coordination of the amine nucleophile **1** and to convert to intermediate **IV** vis eliminating a molecule of HI by a base. The reductive elimination leads to the product **3** with simultaneous regeneration of the palladium(0) catalyst.

Conclusion

In summary, we have developed for the first time the palladium(II)-catalyzed carbonylation of aryl iodides and aromatic amine derivatives with CO as the suitable starting material. The transformation features high efficiency, atom economy, and broad substrate scope. The obtained bidentate amide directing groups can be applied as versatile intermediates for various useful transformations.

Scheme 5 Proposed reaction mechanism



Further studies to illuminate the reaction mechanism and extend the application of this methodology are ongoing in our laboratory.

Acknowledgements We are grateful to the Key Science Research of Education Committee in Henan Province (19A150035), the Key Scientific and Technological Project of Henan Province (192102110222), the Program for Science & Technology Innovation Talents in Universities of Henan Province (14HASTIT016) and the Program of Science and Technology Innovation Talents of Henan Province (No. 2018JQ0011).

References

1. Ma W, Kaplaneris N, Fang X, Gu L, Mei R, Ackermann L (2020) Org Chem Front 7:1022
2. Borpatra PJ, Deka B, Deb ML, Baruah PK (2019) Org Chem Front 6:3445
3. Dey A, Thrimurtulu N, Volla CMR (2019) Org Lett 21:3871
4. Rao W-H, Shi B-F (2016) Org Chem Front 3:1028
5. Chen Z, Wang B, Zhang J, Yu W, Liu Z, Zhang Y (2015) Org Chem Front 2:1107
6. Yang L, Huang H (2015) Chem Rev 115:3468
7. Gao K, Yoshikai N (2014) Acc Chem Res 47:1208
8. Wencel-Delord J, Droge T, Liu F, Glorius F (2011) Chem Soc Rev 40:4740
9. Giri R, Shi BF, Engle KM, Maugel N, Yu JQ (2009) Chem Soc Rev 38:3242
10. Guo X-K, Zhang L-B, Wei D, Niu J-L (2015) Chem Sci 6:7059
11. Zaitsev VG, Shabashov D, Daugulis O (2005) J Am Chem Soc 127:13154
12. Li Q, Huang J, Chen G, Wang S-B (2020) Org Biomol Chem 18:4802
13. Liu X, Zhang H, Yang F (2019) Bo Wang. Org Biomol Chem 17:7564
14. Ueno R, Natsui S, Chatani N (2018) Org Lett 20:1062
15. Kommagalla Y, Yamazaki K, Yamaguchi T, Chatani N (2018) Chem Commun 54:1359
16. Zhu L, Cao X, Li Y, Liu T, Wang X, Qiu R, Yin S-F (2017) Chin J Org Chem 37:1613
17. Vinayak B, NavyaSree P, Chandrasekharam M (2017) Org Biomol Chem 15:9200
18. Lin C, Chen Z, Liu Z, Zhang Y (2017) Org Lett 19:850

19. Iwasaki M, Miki N, Tsuchiya Y, Nakajima K, Nishihara Y (2017) Org Lett 19:1092
20. Sun S-Z, Shang M, Xu H, Cheng T-J, Li M-H, Dai H-X (2020) Chem Commun 56:1444
21. Hu F-P, Cui X-F, Lu G-Q, Huang G-S (2020) Org Biomol Chem 18:4376
22. Gao T-H, Wang C-M, Tang K-X, Xu Y-G, Sun L-P (2019) Eur J Org Chem 19:3005
23. Wan L, Qiao K, Yuan X, Zheng M-W, Fan B-B, Di ZC, Zhang D, Fang Z, Guo K (2017) Adv Synth Catal 359:2596
24. Liu J, Xue Z, Zeng Z, Chen Y, Chen G (2016) Adv Synth Catal 358:3694
25. Wang H-L, Shang M, Sun S-Z, Zhou Z-L, Laforteza BN, Dai H-X, Yu J-Q (2015) Org Lett 17:1228
26. Shang M, Sun S-Z, Dai H-X, Yu J-Q (2014) J Am Chem Soc 136:3354
27. Shang M, Wang H-L, Sun S-Z, Dai H-X, Yu J-Q (2014) J Am Chem Soc 136:11590
28. Ding Y, Han Y-Q, Wu L-S, Zhou T, Yao Q-J, Feng Y-L, Li Y, Kong K-X, Shi B-F (2020) Angew Chem Int Ed. https://doi.org/10.1002/anie.202004504
29. Zhou T, Jiang M-X, Yang X, Yue Q, Han Y-Q, Ding Y, Shi B-F (2020) Chin J Chem 38:242
30. Han Y-Q, Ding Y, Zhou T, Yan S-Y, Song H, Shi B-F (2019) J Am Chem Soc 141:4558
31. Yan S-Y, Han Y-Q, Yao Q-J, Nie X-L, Liu L, Shi B-F (2018) Angew Chem Int Ed 57:9093
32. Li Y, Liu Y-J, Shi B-F (2017) Adv Synth Catal 359:4117
33. Chen F-J, Zhao S, Hu F, Chen K, Zhang Q, Zhang S-Q, Shi B-F (2013) Chem Sci 4:4187
34. Fan C-L, Zhang L-B, Liu J, Hao X-Q, Niu J-L, Song M-P (2019) Org Chem Front 6:2215
35. Du C, Li P-X, Zhu X, Suo J-F, Niu J-L, Song M-P (2016) Angew Chem Int Ed 55:13571
36. Zhang L-B, Hao X-Q, Liu Z-J, Zheng X-X, Zhang S-K, Niu J-L, Song M-P (2015) Angew Chem Int Ed 54:10012
37. Hao X-Q, Chen L-J, Ren B, Li L-Y, Yang X-Y, Gong J-F, Niu J-L, Song M-P (2014) Org Lett 16:1104
38. Shen Y, Cindy Lee W-C, Gutierrez DA, Li JJ (2017) J Org Chem 82:11620
39. Mane RS, Bhanage BM (2017) Adv Synth Catal 359:2621
40. Gergely M, Boros B, Kollar L (2017) Tetrahedron 73:6736
41. Liu S, Deng Q, Fang W, Gong J-F, Song M-P, Xu M, Tu T (2014) Org Chem Front 1:1261
42. Wang T, Wang R, Wang W, Zhang A, Liu L (2018) J Organomet Chem 858:62
43. Mukherjee A, Subramanyam U, Puranik VG, Mohandas TP, Sarkar A (2005) Eur J Inorg Chem 1254
44. Korshin EE, Sabirova LA, Levin YA (2012) Synthesis 44:3512
45. Ouyang K, Xi Z (2013) Acta Chim Sin 71:13