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Aerobic Copper-Catalyzed Salicylaldehydic C_{formyl}–H Arylations with Arylboronic Acids

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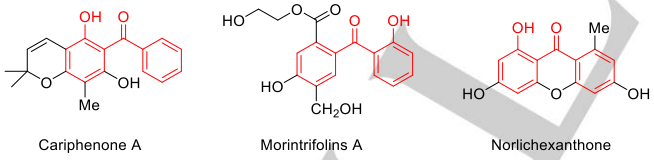
Abstract: We report a challenging copper-catalyzed C_{formyl}–H arylation of salicylaldehydes with arylboronic acids, which involves unique salicylaldehydic copper-species differing from reported salicylaldehydic rhodacycle and palladacycle. Also, this protocol has high chemoselectivity for the C_{formyl}–H bond compared to the phenolic O–H bond involving copper catalysis under high reaction temperature. This approach is compatible with a wide range of salicylaldehyde and arylboronic acid substrates, including estrone and carbazole derivatives, which leads to corresponding arylation products. Mechanistic studies show that 2-hydroxy group of salicylaldehyde substrate triggers the formation of salicylaldehydic copper complexes *via* Cu(I)/Cu(II)/Cu(III) catalytic cycle.

2-Hydroxybenzophenone scaffolds, serving as ubiquitous and valuable organic structural units, are widely present in functional materials, biologically active molecules and natural products such as Cariphenone A, Morintrifolins A and Norlichexanthone (Figure 1).[1] Therefore, the past several decades have witnessed an increasing interest in the methods for its synthesis. The classical methods such as the Friedel-Crafts acylation[2] of phenols and Fries rearrangement[3] of aryl benzoates can construct the 2-hydroxybenzophenone moiety in the absence of site-selectivity.



Cariphenone A Morintrifolins A Norlichexanthone

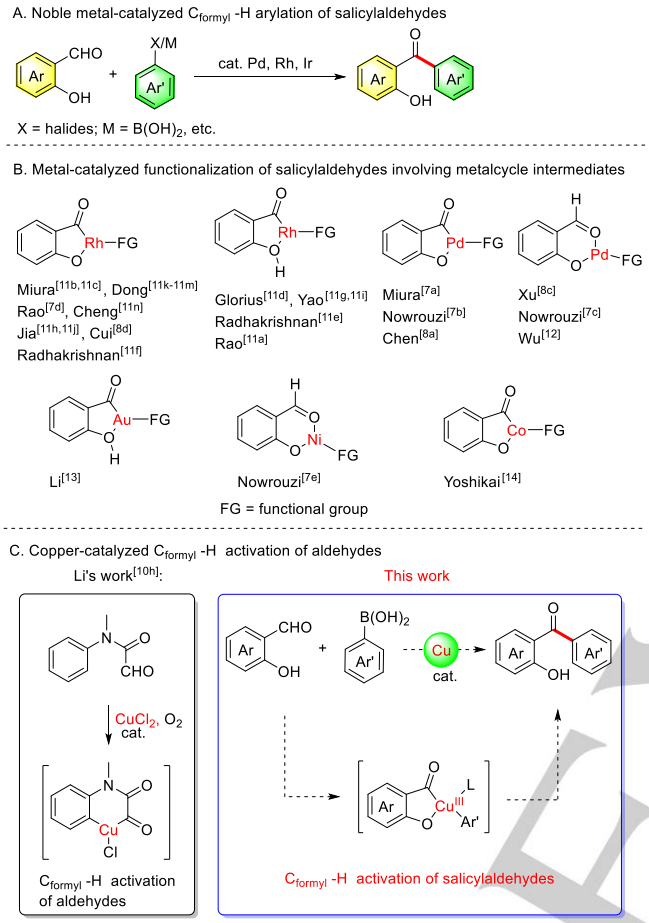
Figure 1. 2-Hydroxybenzophenone structure contained in many natural products.

Designing highly positional selectivity approaches for 2-hydroxybenzophenone is an interesting challenge in organic synthesis. A number of alternative synthetic strategies[4-8] have been successfully employed, among which C–H activation[5] is a highly efficient and atom-economical strategy, mainly including arene C_{sp2}–H hydroxylation of benzophenone[6] and C_{formyl}–H arylation of salicylaldehyde[7,8]. Because salicylaldehydes are versatile and available building blocks in organic synthesis[9], many endeavors have been devoted to functionalizing the kind of aldehydes with various coupling partners *via* a direct C(sp^2)–H activation of aldehydes[10]. To date two main pathways have been applied to constructing the structure of 2-hydroxybenzophenone *via* salicylaldehydic C_{formyl}–H activation catalyzed by precious metal catalysts: 1) the arylation of *o*-hydroxybenzaldehydes with electrophiles (aryl halides) generally involving oxidative addition of aryl halides to metal species, followed by intramolecular C–H activation of the formyl group and reductive elimination to deliver the products[7a-7e]; 2) the cross-coupling between *o*-hydroxybenzaldehydes and nucleophiles (arylboronic acids or hypervalent iodines)[8] through direct C–H activation and transmetalation[8a,8d,8e] or nucleophilic addition and oxidation[8c] (Scheme 1A).

The achievements of transition-metal-catalyzed functionalization of salicylaldehydes mainly benefit from the formation of noble metalcycle intermediates (for example, rhodacycle and palladacycle) *via* coordination of the 2-hydroxy group of salicylaldehydes to an active metal species (Scheme 1B). The C_{formyl}–H arylation[7d,8d,11a], olefination[11b-11j] and alkylation[11f,11k-11n] of salicylaldehydes catalyzed by rhodium involving rhodacycle intermediates as the key step were documented. With regard to palladium catalysis, five-membered[7a,7b,8a] and six-membered[7c,8c,12] palladacycles have been reported, in which the former experiences the cleavage of aldehyde C–H bond and the latter does not. Li[13] has also disclosed gold(I)-catalyzed C_{formyl}–H alkylation of salicylaldehyde *via* oxidative addition to afford cyclic acyl gold(III) complexes. Besides above noble metal catalysts, cheap and economical metal catalysts such as nickel[7e] and cobalt[14] are more charming. For instance, cobalt(I)-diphosphine catalysts have been used to activate salicylaldehydic C_{formyl}–H bond involving a cyclic acyl-(hydrido)cobalt(III) species[14]. Regretfully, highly economical and environmentally benign copper salts generally serve as stoichiometric oxidants in transition-metal-catalyzed aldehyde C–H activation reactions[8d,11], although some reports on Cu-catalyzed or -mediated coupling of aromatic C–H bonds with arylboron reagents have gained considerable interest[15]. One example using copper catalyst to realize the intramolecular C–H arylation of aldehyde based on a six-membered coppercycle intermediate was reported[10h]. However, C_{formyl}–H arylation of salicylaldehyde with arylboronic acid *via* five-membered coppercycle species is unknown (Scheme 1C).

We imagined alternative and more economical synthesis of 2-hydroxybenzophenones through the copper-catalyzed C_{formyl}–H arylation of salicylaldehydes with commercial arylboronic acids. However, there is a fundamental problem that needs to be solved. Evans demonstrated the copper-promoted arylation of phenols with arylboronic acids which is famous Chan-Evans-Lam reaction[16]. How to tune the C_{formyl}–H arylation and Chan-

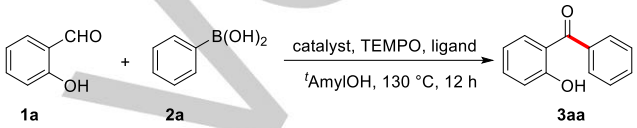
Evans-Lam reaction of salicylaldehydes with arylboronic acids in the presence of copper catalyst is an exciting challenge and has to be faced. Inspired by above studies[8,10h,16] and our previous work[17], we herein present this successful cross-coupling reaction with high chemoselectivity.



Scheme 1. Transition-metal-catalyzed functionalization of aldehydes.

According to this proposal, we selected salicylaldehyde (SA) (**1a**) and phenylboronic acid (**2a**) as representative substrates to explore the optimal conditions (Table 1). In our initial study, desired product **3aa** was obtained in 18% yield accompanied with the Chan-Evans-Lam product **4** (2-phenoxybenzaldehyde) in 14% yield in the presence of catalytic amount of CuBr at 80 °C (Table 1, entry 1). Gratifyingly, although **3aa** was accompanied by the trace amount of the product **4**, it was produced in 93% yield by HPLC (High Performance Liquid Chromatography) analysis and 90% isolated yield respectively when the reaction temperature was increased to 130 °C (Table 1, entry 2). In light of this reaction conditions, we further evaluated other factors that could affect this transformation. The reaction became sluggish in *p*-xylene or higher boiling point polar solvents such as DMF and DMSO (Table 1, entries 3-5). We proceeded to explore other commercial Cu(I) and Cu(II) salts as the catalyst and the results showed that they all led to lower or moderate yields (Table 1, entries 6-11). In the absence of copper catalyst, the performance was poor, which illustrated that CuBr as the optimal catalyst played an essential role in this reaction (Table 1, entry 12). According to previous work[8c], palladium could catalyze C–H arylation of SA and phenylboronic acid, but $PdBr_2$ instead of CuBr inhibited this transformation in our reaction system (Table 1, entry 13). It was worth note that the reaction highly depended on the ligand. Thus, the yield of **3aa** dropped significantly using other typical nitrogen-containing ligands or without the ligand (Table 1, entries 14-19). In addition, the omission of TEMPO (2,2,6,6-tetramethylpiperidine-*N*-oxyl) and the change of TEMPO equivalent resulted in lower yields of **3aa** (Table 1, entries 20-23). The product yield was increased to 97% in the oxygen atmosphere, while the yield of **3aa** was slightly reduced in the nitrogen atmosphere (Table 1, entries 24-25). Shortening the reaction time also decreased the yield of the target product to an extent (Table 1, entry 26).

Table 1. Optimization of reaction conditions.[a]



1a 2a 3aa

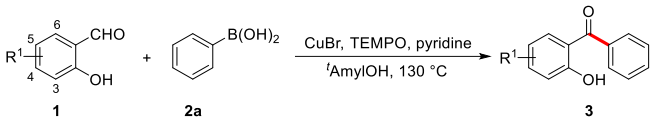
Entry	Catalyst	Ligand	Yield (%)[b]
1[c]	CuBr	pyridine	18[d]
2	CuBr	pyridine	93 (90)[e]
3[f]	CuBr	pyridine	17
4[g]	CuBr	pyridine	36
5[h]	CuBr	pyridine	34
6	CuI	pyridine	36
7	CuCl	pyridine	84
8	Cu_2O	pyridine	36
9	CuOAc	pyridine	31
10	$Cu(OAc)_2$	pyridine	21
11	$CuBr_2$	pyridine	50
12	—	pyridine	<5
13	$PdBr_2$	pyridine	0
14	CuBr	Et_3N	<5
15	CuBr	2,2'-bipyridine	<5
16	CuBr	2,2':6',2"-terpyridine	<5
17	CuBr	urea	0
18	CuBr	1,10-phenanthroline hydrate	0
19	CuBr	—	15
20[i]	CuBr	pyridine	25
21[j]	CuBr	pyridine	90
22[k]	CuBr	pyridine	78
23[l]	CuBr	pyridine	80
24[m]	CuBr	pyridine	97
25[n]	CuBr	pyridine	81
26[o]	CuBr	pyridine	80

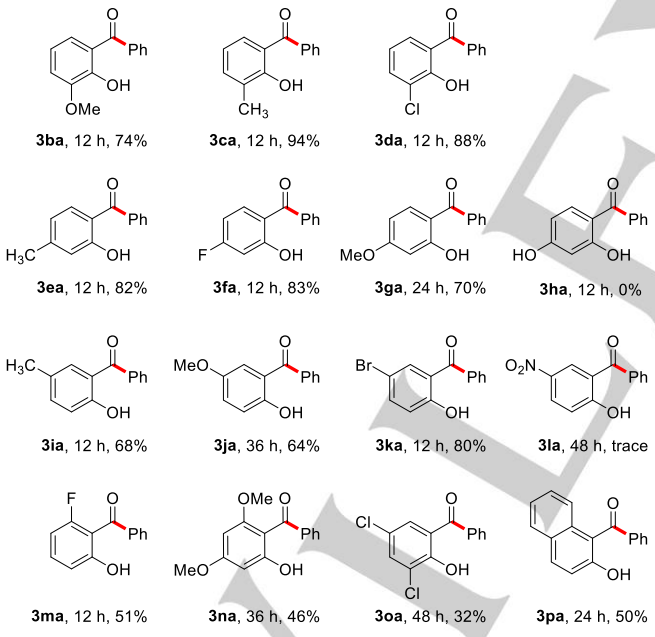
[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.5 mmol), catalyst (0.04 mmol), TEMPO (0.04 mmol), ligand (2 equiv.), ^{t}AmylOH (1 mL) in a sealed tube under air at 130 °C for 12 h. TEMPO = 2,2,6,6-tetramethylpiperidine-*N*-oxyl. ^{t}AmylOH = 2-methyl-2-butanol. [b] Yield was determined by HPLC using pure **3aa** as an external standard. [c] 80 °C. [d] The yield was accompanied by the product **4** of Chan-Evans-Lam reaction in 14% yield which was determined by HPLC using pure 2-phenoxybenzaldehyde as an external standard. [e] Isolated yield. [f] *p*-xylene instead of ^{t}AmylOH. [g] DMF instead of ^{t}AmylOH. [h] DMSO instead of ^{t}AmylOH. [i] Without TEMPO. [j] 10 mol% TEMPO. [k] 0.5 equiv. TEMPO. [l] 1 equiv. TEMPO. [m] Using an O_2 balloon. [n] Using a N_2 balloon. [o] 6 h.

The scope of salicylaldehyde derivatives **1** is shown in Table 2. Substitution of electron-donating (−Me and –OMe) or electron-withdrawing (−Cl) groups at the 3-position of SA led to a slight decrease in the reaction outcome (**3ba**-**3da**). The lower yield of **3ba** might come from the competitive coordination of methoxyl group to copper that is unfavourable to the formation of salicylaldehydic cyclocopper species. The presence of a methyl

or fluorine substituent at 4-position of SA gave good yields (**3ea**-**3fa**), while significant side effect of substituents (−OMe, −OH) at the same position of SA was observed (**3ga**-**3ha**). These results further showed that the competitive coordination of methoxyl or hydroxyl group to copper catalyst was harmful to the formation of the reactive intermediate, especially the hydroxyl substituent. 5-Methylsalicylaldehyde furnished product **3ia** in moderate yield, while 5-methoxysalicylaldehyde required longer reaction time to offer **3ja** in the comparable yield. Gratifyingly, bromine substituent at the C5 position was tolerated and the corresponding product **3ka** was obtained in 80% yield, which facilitated the further functionalization. Nitro group at the 5-position in SA reacted ineffectively and the trace amount of product **3la** was discovered. In addition, fluorine group at the C6 position offered **3ma** in 51% yield. As expected, the substrates with multiple substituents on SA could also be converted into corresponding products **3na**-**3oa** *via* prolonging the reaction time. 2-Hydroxy-1-naphthaldehyde was examined, which afforded the arylation product **3pa** in the moderate yield.

Table 2. Scope of arylation of salicylaldehyde derivatives **1**.[a]

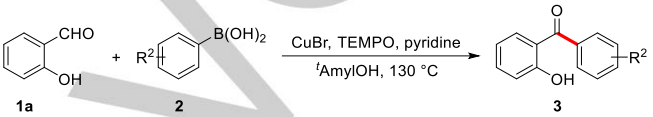


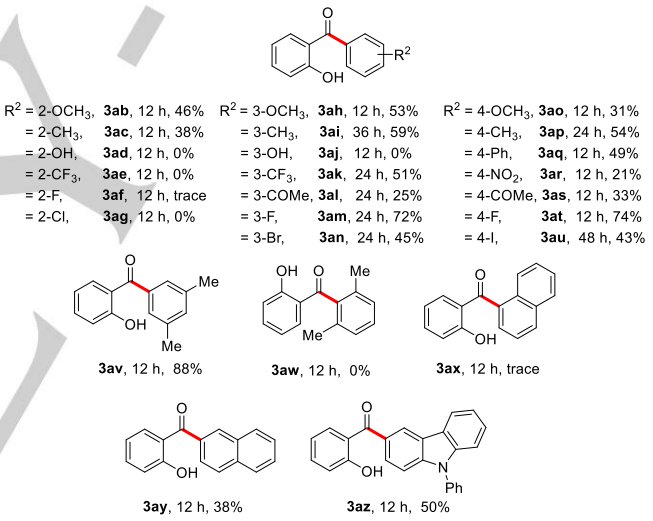


[a] Reaction conditions: **1** (0.2 mmol), **2a** (0.5 mmol), CuBr (0.04 mmol), TEMPO (0.04 mmol), pyridine (2 equiv.), ^{t}AmylOH (1 mL) in a sealed tube under air at 130 °C with isolated yields.

Next, we investigated a wide range of substituted phenylboronic acids (Table 3). In the case of *o*-substituted phenylboronic acids, these transformations were relatively poor due to the steric hindrance (**3ab**-**3ag**) and the results also showed that the performance of electron-rich phenylboronic acids was superior to that of electron-deficient phenylboronic acids. Various electron-rich or electron-poor substituents at the *meta* or *para* position of phenylboronic acid were tolerated, except for the hydroxyl group, thus providing the corresponding products (**3ah**-**3au**). (3,5-Dimethylphenyl) boronic acid gave the desired product **3av** in 88% yield, whereas (2,6-dimethylphenyl)-boronic acid cannot be converted into the corresponding product **3aw**, indicating again that this reaction is extremely sensitive to the steric hindrance. Meanwhile, the standard conditions were suitable for the coupling of naphthalene boronic acids with SA, and naphthalen-2-ylboronic acid performed better than naphthalen-1-ylboronic acid (**3ay** and **3ax**, respectively). Interestingly, (9-phenyl-9*H*-carbazol-3-yl)boronic acid serving as an intermediate of OLED materials[18], could be used to generate the desired product **3az** in moderate yield.

Table 3. Scope of phenylboronic acids **2**.[a]

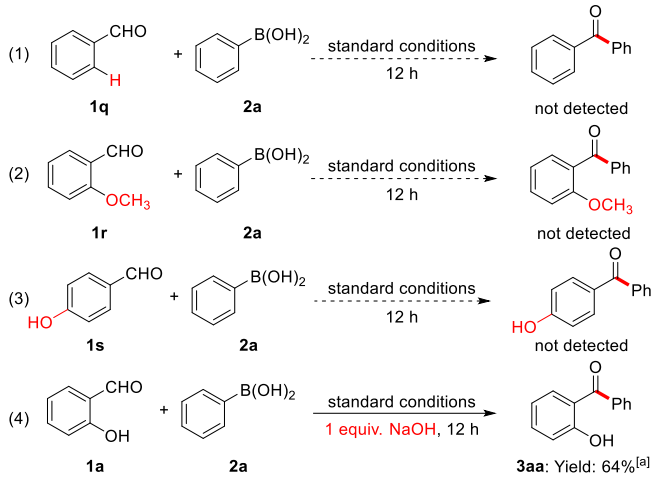




[a] Reaction conditions: **1a** (0.2 mmol), **2** (0.5 mmol), CuBr (0.04 mmol), TEMPO (0.04 mmol), pyridine (2 equiv.), ^{t}AmylOH (1 mL) in a sealed tube under air at 130 °C with isolated yields.

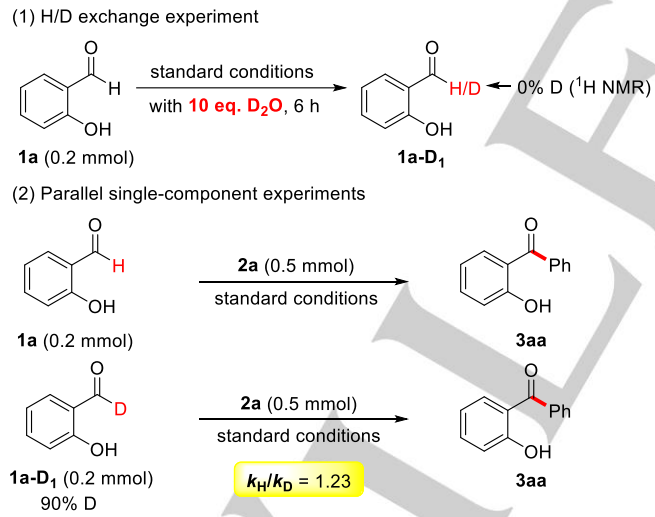
To gain insight into the mechanism, we performed a series of control experiments (Schemes 2-3). When we subjected benzaldehyde (**1q**), 2-methoxybenzaldehyde (**1r**) and 4-hydroxybenzaldehyde (**1s**) respectively to the standard conditions, the corresponding products were not observed (Scheme 2, Eq 1-3); thus 2-hydroxy group in the substrate was vital in triggering the formation of salicylaldehydic organocopper species followed by the arylation reaction. In addition, when strong base NaOH was added into the reaction system, medium reactivity was observed (Scheme 2, Eq 4). These results showed that salicylaldehydic organocopper species might involve phenoxy anionic coordination. Furthermore, kinetic isotope effect (KIE) experiments were conducted (Scheme 3). **1a** was treated with D_2O, but no deuterium incorporation was

detected (Scheme 3, Eq 1), which suggested that the C−H activation step was irreversible. Moreover, **1a** and deuterium-labelled aldehyde **1a-D₁** were subjected to the standard reaction conditions, respectively (Scheme 3, Eq 2). The KIE (k_H/k_D = 1.23) was measured in parallel single-component experiments,[19] which indicated that aldehyde C−H bond cleavage step might not be the turnover-limiting step in the copper-catalyzed cycle.



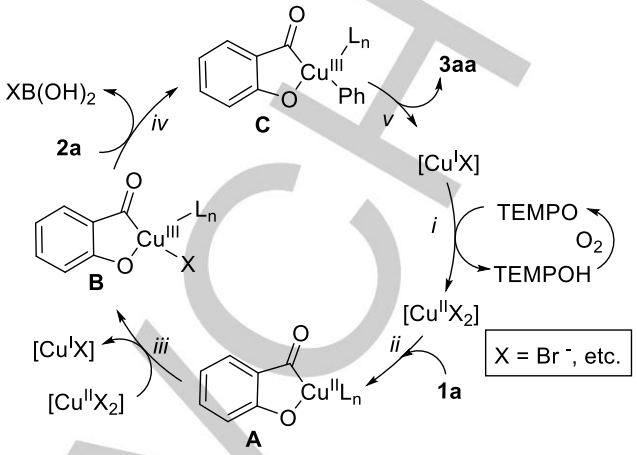
[a] Yield was determined by HPLC using pure **3aa** as an external standard.

Scheme 2. Role of 2-hydroxy group in the substrate.



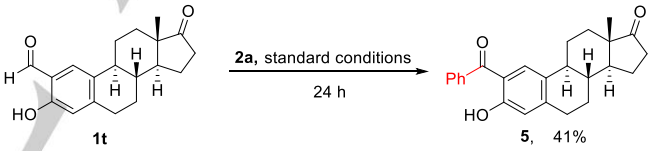
Scheme 3. Kinetic isotope effect studies.

Plausible mechanism for this copper-catalyzed C−H arylation is proposed in Scheme 4. This reaction is initiated by a one-electron oxidation of [Cu(I)X] by TEMPO to form the active Cu(II)-species (step *i*)[20], which then reacts with **1a** to afford a five-membered coppercycle **A** involving C_{formyl}–H bond activation assisted by phenoxy anionic group (step *ii*). Subsequently, the resulting intermediate **A** is oxidized by [Cu(II)] species to yield a Cu(III) intermediate **B** (step *iii*) followed by transmetalation with **2a** to generate an intermediate **C** (step *iv*). Finally, reductive elimination from the intermediate **C** gives **3aa** and regenerates [Cu(I)X] species to complete the catalytic cycle (step *v*)[16d, 21].



Scheme 4. Proposed reaction mechanism.

We further explored synthetic application of our approach (Scheme 5). Natural estrone derivative **1t** was subjected to the standard conditions extending reaction time to 24 h to afford the desired product **5** in 41% isolated yield.



Scheme 5. Synthetic application of our approach.

In conclusion, we have developed a copper-catalyzed direct C_{formyl}–H arylation of salicylaldehydes with arylboronic acids. This approach has excellent chemoselectivity for the C_{formyl}–H activation of salicylaldehydes compared to the classic Chan-Evans-Lam reaction. Furthermore, in contrast to precious metal catalysts such as palladium and rhodium, economical and environmentally benign copper catalyst performs comparative miracles.

Acknowledgements

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Keywords: copper catalysis • salicylaldehydes • C–H activation • C–C coupling • chemoselectivity

[1] a) Y. Dobashi, J.-I. Kondou, Y. Ohkatsu, *Polym. Degrad. Stab.* **2005**, *89*, 140-144; b) Z. Klimová, J. Hojerová, M. Beránková, *Food Chem. Toxicol.* **2015**, *83*, 237-250; c) J. M. Grandner, R. A. Cacho, Y. Tang, K. N. Houk, *ACS Catal.* **2016**, *6*, 4506-4511; d) A. P. M. Bernardi, A. B. F. Ferraz, D. V. Albring, S. A. L. Bordignon, J. Schripsema, R. Bridi, C. S. Dutra-Filho, A. T. Henriques, G. L. von Poser, *J. Nat. Prod.* **2005**, *68*, 784-786; e) Y. Deng, Y.-W. Chin, H. Chai, W. J. Keller, A. D. Kinghorn, *J. Nat. Prod.* **2007**, *70*, 2049-2052; f) T. Ali, M. Inagaki, H.-B. Chai, T. Wieboldt, C. Rapplye, L. H. Rakotondraibe, *J. Nat. Prod.* **2017**, *80*, 1397-1403.

[2] P. H. Gore, *Chem. Rev.* **1955**, *55*, 229-281.

[3] J. A. Miller, *J. Org. Chem.* **1987**, *52*, 322-323.

[4] a) C. Zhou, R. C. Larock, *J. Org. Chem.* **2006**, *71*, 3551-3558; b) M. L. Deb, C. D. Pegu, P. J. Borpatra, P. K. Baruah, *RSC Adv.* **2016**, *6*, 40552-40559; c) Y. Xie, *Chem. Commun.* **2016**, *52*, 12372-12375; d) S. Bera, K. Chandrasekhar, S. Chatterjee, S. K. Killi, D. Sarkar, B. Banerji, *Eur. J. Org. Chem.* **2019**, *2019*, 3877-3881; e) H. Rao, C.-J. Li, *Angew. Chem. Int. Ed.* **2011**, *50*, 8936-8939; f) J. Li, Z. Liu, S. Wu, Y. Chen, *Org. Lett.* **2019**, *21*, 2077-2080; g) R. Ruzi, J. Ma, X.-A. Yuan, W. Wang, S. Wang, M. Zhang, J. Dai, J. Xie, C. Zhu, *Chem. – Eur. J.* **2019**, *25*, 12724-12729; h) H. Cai, L. Xia, Y. R. Lee, *Chem. Commun.* **2016**, *52*, 7661-7664; i) X. Shi, Y. He, X. Zhang, X. Fan, *Org. Chem. Front.* **2017**, *4*, 1967-1971; j) K.-Q. Chen, Z. Luo, Z.-H. Gao, S. Ye, *Chem. – Eur. J.* **2019**, *25*, 3253-3256; k) X. Zhang, G. Wu, W. Gao, J. Ding, X. Huang, M. Liu, H. Wu, *Org. Lett.* **2018**, *20*, 708-711; l) Y.-M. Cai, Y.-T. Xu, X. Zhang, W.-X. Gao, X.-B. Huang, Y.-B. Zhou, M.-C. Liu, H.-Y. Wu, *Org. Lett.* **2019**, *21*, 8479-8484; m) J. Buchspies, M. Szostak, *Catalysts* **2019**, *9*, 53-75; n) C. Liu, R. Lalancette, R. Szostak, M. Szostak, *Org. Lett.* **2019**, *21*, 7976-7981.

[5] a) K. Godula, D. Sames, *Science* **2006**, *312*, 67-72; b) R. G. Bergman, *Nature* **2007**, *446*, 391-393; c) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147-1169; d) L. McMurray, F. O'Hara, M. J. Gaunt, *Chem. Soc. Rev.* **2011**, *40*, 1885-1898; e) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068-5083; f) C.-L. Sun, Z.-J. Shi, *Chem. Rev.* **2014**, *114*, 9219-9280; g) C. Liu, J. Yuan, M. Gao, S. Tang, W. Li, R. Shi, A. Lei, *Chem. Rev.* **2015**, *115*, 12138-12204; h) Z. Dong, Z. Ren, S. J. Thompson, Y. Xu, G. Dong, *Chem. Rev.* **2017**, *117*, 9333-9403; i) P. Gandeepan, T. Müller, D. Zell, G. Cera, S. Warratz, L. Ackermann, *Chem. Rev.* **2019**, *119*, 2192-2452; j) C. Shan, R. Bai, Y. Lan, *Acta Phys. -Chim. Sin.* **2019**, *35*, 940-953; k) Y. Liu, T. You, H.-X. Wang, Z. Tang, C.-Y. Zhou, C.-M. Che, *Chem. Soc. Rev.* **2020**, *49*, 5310-5358.

[6] a) G. Shan, X. Yang, L. Ma, Y. Rao, *Angew. Chem.* **2012**, *124*, 13247-13251; *Angew. Chem. Int. Ed.* **2012**, *51*, 13070-13074; b) G. Shan, X. Han, Y. Lin, S. Yu, Y. Rao, *Org. Biomol. Chem.* **2013**, *11*, 2318-2322; c) F. Mo, L. J. Trzepkowski, G. Dong, *Angew. Chem.* **2012**, *124*, 13252-13256; *Angew. Chem. Int. Ed.* **2012**, *51*, 13075-13079; d) P. Y. Choy, F. Y. Kwong, *Org. Lett.* **2013**, *15*, 270-273; e) Y.-W. Zheng, B. Chen, P. Ye, K. Feng, W. Wang, Q.-Y. Meng, L.-Z. Wu, C.-H. Tung, *J. Am. Chem. Soc.* **2016**, *138*, 10080-10083; f) L. Massignan, X. Tan, T. H. Meyer, R. Kuniyil, A. M. Messinis, L. Ackermann, *Angew. Chem.* **2020**, *132*, 3210-3215; *Angew. Chem. Int. Ed.* **2020**, *59*, 3184-3189.

[7] a) T. Satoh, T. Itaya, M. Miura, M. Nomura, *Chem. Lett.* **1996**, *25*, 823-824; b) N. Nowrouzi, S. Motevalli, D. Tarokh, *J. Mol. Catal. A* **2015**, *396*, 224-230; c) N. Nowrouzi, D. Tarokh, *J. Iran. Chem. Soc.* **2016**, *13*, 1493-1497; d) M. L. N. Rao, B. S. Ramakrishna, *Eur. J. Org. Chem.* **2017**, *2017*, 5080-5093; e) N. Nowrouzi, M. Zarei, F. Roozbin, *RSC Adv.* **2015**, *5*, 102448-102453.

[8] a) M. Xia, Z. Chen, *Synth. Commun.* **2000**, *30*, 531-536; b) D.-J. Chen, Z.-C. Chen, *Synlett* **2000**, 1175-1177; c) F. Weng, C. Wang, B. Xu, *Tetrahedron Lett.* **2010**, *51*, 2593-2596; d) D. Wang, S. Cui, *Tetrahedron* **2015**, *71*, 8511-8516; e) X. Yang, H. Wang, X. Zhou, X. Li, *Org. Biomol. Chem.* **2016**, *14*, 5233-5237.

[9] a) X. Chen, H. Wang, K. Doitomi, C. Y. Ooi, P. Zheng, W. Liu, H. Guo, S. Yang, B.-A. Song, H. Hirao, Y. R. Chi, *Nat. Commun.* **2017**, *8*, 15598; b) Y. Xie, B. List, *Angew. Chem.* **2017**, *129*, 5018-5022; *Angew. Chem. Int. Ed.* **2017**, *56*, 4936-4940; c) L. Liu, M.-C. Tang, Y. Tang, *J. Am. Chem. Soc.* **2019**, *141*, 19538-19541; d) H. Xu, X. Chen, J. Gao, J. Lin, M. Addicoat, S. Irle, D. Jiang, *Chem. Commun.* **2014**, *50*, 1292-1294; e) H.-S. Xu, S.-Y. Ding, W.-K. An, H. Wu, W. Wang, *J. Am. Chem. Soc.* **2016**, *138*, 11489-11492.

[10] For recent representative reviews and examples, see: a) Y. J. Park, J.-W. Park, C.-H. Jun, *Acc. Chem. Res.* **2008**, *41*, 222-234; b) M. A. Garralda, *Dalton Trans.* **2009**, 3635-3645; c) M. C. Willis, *Chem. Rev.* **2010**, *110*, 725-748; d) C. Pan, X. Jia, J. Cheng, *Synthesis* **2012**, *44*, 677-685; e) J. C. Leung, M. J. Krische, *Chem. Sci.* **2012**, *3*, 2202-2209; f) L. Yang, H. Huang, *Chem. Rev.* **2015**, *115*, 3468-3517; g) Z. Nairoukh, M. Cormier, I. Marek, *Nat. Rev. Chem.* **2017**, *1*, 0035; h) B.-X. Tang, R.-J. Song, C.-Y. Wu, Y. Liu, M.-B. Zhou, W.-T. Wei, G.-B. Deng, D.-L. Yin, J.-H. Li, *J. Am. Chem. Soc.* **2010**, *132*, 8900-8902; i) R. Singha, S. Dhara, M. Ghosh, J. K. Ray, *RSC Adv.* **2015**, *5*, 8801-8805; j) C. Che, Q. Huang, H. Zheng, G. Zhu, *Chem. Sci.* **2016**, *7*, 4134-4139; k) Q. Zhang, W. Wang, C. Gao, R.-R. Cai, R.-S. Xu, *RSC Adv.* **2017**, *7*, 20123-20127; l) D. H. T. Phan, K. G. M. Kou, V. M. Dong, *J. Am. Chem. Soc.* **2010**, *132*, 16354-16355; m) L.-J. Xiao, X.-N. Fu, M.-J. Zhou, J.-H. Xie, L.-X. Wang, X.-F. Xu, Q.-L. Zhou, *J. Am. Chem. Soc.* **2016**, *138*, 2957-2960; n) H. Zheng, J. Ding, J. Chen, M. Liu, W. Gao, H. Wu, *Synlett* **2011**, 1626-1630.

[11] a) M. L. N. Rao, B. S. Ramakrishna, *RSC Adv.* **2016**, *6*, 75505-75511; b) K. Kokubo, K. Matsumasa, Y. Nishinaka, M. Miura, M. Nomura, *Bull. Chem. Soc. Jpn.* **1999**, *72*, 303-311; c) M. Shimizu, H. Tsurugi, T. Satoh, M. Miura, *Chem. – Asian J.* **2008**, *3*, 881-886; d) Z. Shi, N. Schröder, F. Glorius, *Angew. Chem. Int. Ed.* **2012**, *51*, 8092-8096; e) E. Jijy, P. Prakash, M. Shimi, P. M. Pihko, N. Joseph, K. V. Radhakrishnan, *Chem. Commun.* **2013**, *49*, 7349-7351; f) A. Vijayan, T. V. Baiju, E. Jijy, P. Prakash, M. Shimi, N. Joseph, P. M. Pihko, S. Varughese, K. V. Radhakrishnan, *Tetrahedron* **2016**, *72*, 4007-4015; g) P. Sun, S. Gao, C. Yang, S. Guo, A. Lin, H. Yao, *Org. Lett.* **2016**, *18*, 6464-6467; h) H. Jia, Y. Tang, Y. Shi, L. Ma, Z. He, W. Lai, Y. Yang, Y. Wang, Y. Zang, S. Xu, *Chem. Pap.* **2017**, *71*, 1791-1795; i) L. Cai, X. Zhu, J. Chen, A. Lin, H. Yao, *Org. Chem. Front.* **2019**, *6*, 3688-3692; j) X. Zhao, H. Jia, Q. Wang, H. Song, Y. Tang, L. Ma, Y. Shi, G. Yang, Y. Wang, Y. Zang, S. Xu, *Heterocycl. Commun.* **2020**, *26*, 20-25; k) M. M. Coulter, K. G. M. Kou, B. Galligan, V. M. Dong, *J. Am. Chem. Soc.* **2010**, *132*, 16330-16333; l) M. von Delius, C. M. Le, V. M. Dong, *J. Am. Chem. Soc.* **2012**, *134*, 15022-15032; m) S. K. Murphy, M. M. Coulter, V. M. Dong, *Chem. Sci.* **2012**, *3*, 355-358; n) R. Kuppusamy, P. Gandeepan, C.-H. Cheng, *Org. Lett.* **2015**, *17*, 3846-3849.

[12] C. Shen, X.-F. Wu, *Synlett* **2016**, *27*, 1269-1273.

[13] R. Skouta, C.-J. Li, *Angew. Chem.* **2007**, *119*, 1135-1137; *Angew. Chem. Int. Ed.* **2007**, *46*, 1117-1119.

[14] J. Yang, N. Yoshikai, *Angew. Chem.* **2016**, *128*, 2920-2924; *Angew. Chem. Int. Ed.* **2016**, *55*, 2870-2874.

[15] a) I. Ban, T. Sudo, T. Taniguchi, K. Itami, *Org. Lett.* **2008**, *10*, 3607-3609; b) F. Yang, Z. Xu, Z. Wang, Z. Yu, R. Wang, *Chem. – Eur. J.* **2011**, *17*, 6321-6325; c) M. Shang, S.-Z. Sun, H.-X. Dai, J.-Q. Yu, *Org. Lett.* **2014**, *16*, 5666-5669; d) Y. Shen, J. Chen, M. Liu, J. Ding, W. Gao, X. Huang, H. Wu, *Chem. Commun.* **2014**, *50*, 4292-4295; e) W.-Y. Hu, P.-P. Wang, S.-L. Zhang, *Synthesis* **2015**, *47*, 42-48; f) Y. Liu, C. Long, L. Zhao, M.-X. Wang, *Org. Lett.* **2016**, *18*, 5078-5081; g) Q. Gui, X. Chen, L. Hu, D. Wang, J. Liu, Z. Tan, *Adv. Synth. Catal.* **2016**, *358*, 509-514; h) Q. Zhang, Y. Liu, T. Wang, X. Zhang, C. Long, Y.-D. Wu, M.-X. Wang, *J. Am. Chem. Soc.* **2018**, *140*, 5579-5587; i) L. Liu, Z. Xi, *Chin. J. Chem.* **2018**, *36*, 1213-1221.

[16] a) D. M. T. Chan, K. L. Monaco, R.-P. Wang, M. P. Winters, *Tetrahedron Lett.* **1998**, *39*, 2933-2936; b) D. A. Evans, J. L. Katz, T. R. West, *Tetrahedron Lett.* **1998**, *39*, 2937-2940; c) P. Y. S. Lam, C. G. Clark, S. Saubern, J. Adams, M. P. Winters, D. M. T. Chan, A. Combs, *Tetrahedron Lett.* **1998**, *39*, 2941-2944; d) A. E. King, T. C. Brunold, S. S. Stahl, *J. Am. Chem. Soc.* **2009**, *131*, 5044-5045; e) J. C. Vantourout, H. N. Miras, A. Isidro-Llobet, S. Sproules, A. J. B. Watson, *J. Am. Chem. Soc.* **2017**, *139*, 4769-4779; f) J. C. Vantourout, L. Li, E. Bendito-Moll, S. Chabbra, K. Arrington, B. E. Bode, A. Isidro-Llobet, J. A. Kowalski, M. G. Nilson, K. M. P. Wheelhouse, J. L. Woodard, S. Xie, D. C. Leitch, A. J. B. Watson, *ACS Catal.* **2018**, *8*, 9560-9566; g) M. J. West, J. W. B. Fyfe, J. C. Vantourout, A. J. B. Watson, *Chem. Rev.* **2019**, *119*, 12491-12523; h) X. Ma, F. Liu, D. Mo, *Chin. J. Org. Chem.* **2017**, *37*, 1069-1087; i) A. C. Brewer, P. C. Hoffman, J. R. Martinelli, M. E. Kobierski, N. Mullane, D. Robbins, *Org. Process Res. Dev.* **2019**, *23*, 1484-1498.

[17] a) T.-T. Lai, D. Xie, C.-H. Zhou, G.-X. Cai, *J. Org. Chem.* **2016**, *81*, 8806-8815; b) D. Xie, T.-T. Lai, Y.-B. Wu, C.-H. Zhou, G.-X. Cai, *Sci. Sin. Chim.* **2017**, *47*, 1198-1207; c) Y.-B. Wu, L. Xiao, C.-L. Mao, Z.-L. Zang, C.-H. Zhou, G.-X. Cai, *Adv. Synth. Catal.* **2019**, *361*, 4461-4467.

[18] J. Ji, P. Li, Q. Tian, W. Feng, C. Wu, *Dyes Pigments* **2019**, *171*, 107670-107675.

[19] Q.-L. Yang, Y.-Q. Li, C. Ma, P. Fang, X.-J. Zhang, T.-S. Mei, *J. Am. Chem. Soc.* **2017**, *139*, 3293-3298.

[20] a) Z. Ma, K. T. Mahmudov, V. A. Aliyeva, A. V. Gurbanov, A. J. L. Pombeiro, *Coordin. Chem. Rev.* **2020**, *423*, 213482-213505; b) A. E. Wendlandt, A. M. Suess, S. S. Stahl, *Angew. Chem.* **2011**, *123*, 11256-11283; *Angew. Chem. Int. Ed.* **2011**, *50*, 11062-11087; c) A. Dijksman, I. W. C. E. Arends, R. A. Sheldon, *Org. Biomol. Chem.* **2003**, *1*, 3232-3237.

[21] a) A. E. King, B. L. Ryland, T. C. Brunold, S. S. Stahl, *Organometallics* **2012**, *31*, 7948-7957; b) A. Vasilopoulos, S. L. Zultanski, S. S. Stahl, *J. Am. Chem. Soc.* **2017**, *139*, 7705-7708; c) S. Bhunia, G. G. Pawar, S. V. Kumar, Y. Jiang, D. Ma, *Angew. Chem.* **2017**, *129*, 16352-16397; *Angew. Chem. Int. Ed.* **2017**, *56*, 16136-16179.

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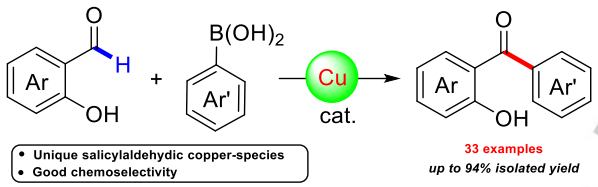

A challenging copper-catalyzed C_{formyl}−H arylation of salicylaldehydes with arylboronic acids is developed, which involves unique salicylaldehydic copper-species differing from reported salicylaldehydic rhodacycle and palladacycle, as well as high chemoselectivity for the C_{formyl}−H bond compared to the phenolic O−H bond based on copper catalysis.