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Transition Metal-Free, Iodide-Mediated Domino Carbonylation-Benzylation of Benzyl Chlorides with Arylboronic Acids under Ambient Pressure of Carbon Monoxide‡

Fengli Jin,[a]† Yanzhen Zhong,[a]† Xin Zhang ,[a] Huichun Zhang,[a] Qian Zhao[a] and Wei Han*[a]

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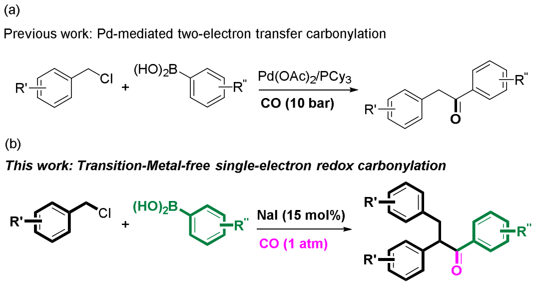
A conceptually distinct approach toward the synthesis of 1,2,3-triarylpropan-1-one by NaI-catalyzed domino carbonylation-benzylation of unactivated benzyl chlorides with arylboronic acids has been developed under ambient pressure of CO gas. The novel method represents a significant improvement over the traditional palladium-catalyzed carbonylation: the catalyst NaI is abundant, inexpensive, and bench stable, the reaction conditions are much milder, and the use of ligands and the costly need to remove metallic impurities from the end products are avoided. This apparently transition-metal-free process offers a new strategy for carbonylative cross-coupling reactions of C(sp^3) halides.

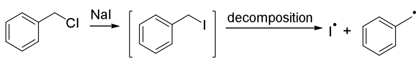
Transition-metal catalyzed reactions for selective formation of new carbon-carbon bonds have revolutionized the field of organic synthesis, enabling the facile preparation of biologically active compounds, functional organic materials, and ligands.[1] And their importance has been demonstrated by three Nobel Prizes in Chemistry in the first decade of 21st century. Among the transition-metal catalyzed strategies, palladium-catalyzed carbonylative cross-coupling reactions are attracting increasing interests owing to the direct utilization of gaseous CO, the most inexpensive and readily accessible C1-source, and introduction of synthetically versatile carbonyl groups into parent molecules.[2] In this context, the carbonylative Suzuki coupling is well known. This is attributed to a large extent to the superior properties of organoboron reagents.[3] Although this transformation has achieved a great advance, particularly in the design of transition-metal catalysts, these catalysts are mostly limited to activate aryl halides.[2] In contrast, carbonylative Suzuki couplings of alkyl or benzyl halides have been sparsely reported. This is because C(sp^3) halides are less reactive toward oxidative addition to Pd^0 than their unsaturated analogues.[4] The pioneering report was on just two examples of $PdCl_2(PPh_3)_2$-catalyzed carbonylative Suzuki coupling of benzyl bromide by Miyaura and co-workers.[5] More recently, Beller group described an efficient $Pd(OAc)_2/PCy_3$-catalyzed method for carbonylative Suzuki coupling of various challenging substrates benzyl chlorides, albeit under 10 bar of CO (Scheme 1, a).[6]



Scheme 1 Two distinct protocols for catalytic carbonylation of benzyl chlorides with arylboronic acids.

Although transition-metal catalysis has become an indispensable tool in the synthetic community, a major drawback of this strategy is associated with removing metal residue[7]: trace metals in products for human consumption are strictly regulated by stringent specifications;[8] similar concerns are also observed in the modern electronics industry, where metal residues reduce the performance of organic electronic devices.[9] Here, we report an alternative metal-free carbonylative Suzuki coupling of benzyl chlorides, which involves a hitherto unknown single-electron redox process that is driven by inorganic iodide (Scheme 1, b). This process not only addresses the issue of metal residues but also circumvents the problematic formation of alkylmetal species and the deactivation of transition-metal catalyst (CO is a strong π-acidic ligand).

Traditional free-radical carbonylation mainly relies on a xenon photolytic system or AIBN/tin hydride initiated free-radical chain reaction. And, organohalides are limited to highly reactive aliphatic iodides and high pressures of CO are required.[10] Recently, isolated examples of KO*t*Bu/1,10-phenanthroline- or visible light/an organic dye- mediated alkoxycarbonylation of activated aryl halides (mostly iodides) or diazonium salts under 50–80 atm of CO represent an important advancement in the free-radical carbonylation.[11] We herein present a novel strategy for free-radical carbonylation of unactivated benzyl chlorides via inorganic iodide mediated chain reactions.[12] This idea is based on the easy decomposition of benzyl iodide to reactive benzyl free-radical. Considering unstability and high cost of benzyl iodides, we employed halogen exchange between catalytic amount of sodium iodide and ideal substrate benzyl chloride to generate



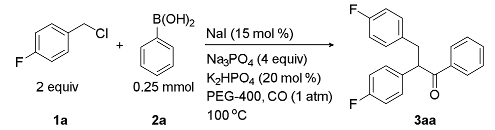
Scheme 2 Inorganic iodide mediated the formation of benzyl free-radical.

benzyl iodide *in situ* (Scheme 2).[13] A our recent work of transition-metal-free carbonylative Suzuki reactions under ambient pressure and in PEG,[14] prompted us to investigate this unprecedented iodide-mediated trimodular reactions of benzyl chlorides, arylboronic acids, and 1 atm of CO (Scheme 1, b).

Amazingly, this transformation didn't give usual product 1,2-diarylethanone,[6] but provided one-pot domino carbonylation-alkylation 1,2,3-triarylpropan-1-one (Scheme 1, b). Notably, 1,2,3-triarylpropan-1-one is a class of valuable synthetic building blocks for triarylisoxazoles, triarylpyrazoles, 2,3-diarylindenes, tri- and tetrasubstituted alkenes, and active pharmaceutical ingredients.[15]

Our investigation started with 1-(chloromethyl)-4-fluorobenzene (**1a**) and phenylboronic acid (**2a**) under 1 atm CO at 100 °C by using an inorganic iodide as catalyst in PEG-400 (Table 1) (for details see ESI, Table S1). By optimizing various reaction parameters, we found that the combination of NaI (15 mol %), and Na_3PO_4 (4 equiv)/K_2HPO_4 (20 mol%)[16] as the base in PEG-400 at 100 °C under 1 atm CO provided the best results, giving rise to 2,3-bis(4-fluorophenyl)-1-phenylpropan-1-one (**3aa**) in 91% isolated yield (entry 1). The results of control experiments in the absence of either iodide or base indicated that these species play indispensable roles in the carbonylative reaction (entries 2−5). Other iodide sources such as KI and TBAI showed less efficiency (entries 6−7). When DMF, DME, toluene, water, ethylene glycol or glycerol was in place of PEG-400, almost no desired product (**3aa**) was formed (entries 8−13).[17,18] Generally, carbonylation of C(sp^3) halides requires palladium catalyst.[4b-c] Consequently, palladium contamination of NaI or reaction system concerned us. To explore this possibility, we employed ultrapure NaI (99.999% based on trace metals) and found that a slightly better yield of **3aa** was obtained (entry 14). Meanwhile, $Pd(OAc)_2$ instead of NaI led to no conversion of **1a** (entry 15). Moreover, inductively coupled plasma atomic emission spectroscopy (**ICP–AES**) analysis of the reaction system under standard conditions confirmed that the concentrations of transition metals, such as Pd, Rh, Ru, and Ni were below the detection limit of the machine. A transition-metal scavenger QuadraPure^t TU[19] was also used to examine the normal catalytic system and didn't affect the transformation at all. These results suggest not only the critical role of the NaI in the reaction, but also that transition metals are not active catalytic species. Therefore, the possibility of transition metal-catalyzed the reaction owing to transition metal contamination can be precluded, confirming that the reaction is a true transition metal-free transformation.

Table 1 Iodide-mediated domino carbonylation-benzylation reaction of **1a** with **2a**.[a]



Entry	Variation from standard conditions	Yield **3aa** (%)
1	None	91[b]
2	Without NaI	0
3	Without Na_3PO_4	7
4	Without K_2HPO_4	80
5	Without Na_3PO_4 and K_2HPO_4	0
6	KI instead of NaI	86
7	TBAI[c] instead of NaI	64
8	DMF[d] instead of PEG-400	<5
9	DME[e] instead of PEG-400	0
10	Toluene instead of PEG-400	0
11	H_2O instead of PEG-400	0
12	Ethylene glycol instead of PEG-400	0
13	Glycerol instead of PEG-400	0
14	Ultrapure NaI[f] instead of NaI	92
15	$Pd(OAc)_2$[g] instead of NaI	0

[a] *Standard conditions*: **1a** (0.5 mmol), **2a** (0.25 mmol), CO (1 atm), Na_3PO_4 (1.0 mmol), K_2HPO_4 (0.05 mmol), PEG-400 (2.0 mL), and 6 h at 100 °C. [b] When the reaction was carried out under dark, the yield was not affected at all. [c] TBAI = tetrabutylammonium iodide. [d] DMF = *N,N'*-_ dimethylformamide. [e] DME = 1,2-dimethoxyethane. [f] Ultrapure NaI (99.999% based on trace metals, Across). [g] $Pd(OAc)_2$ (1 mol%).

Under the standard conditions, we find that about 10−20% of 2-(4-fluorophenyl)-1-phenylethan-1-one (**2a'**) (according to GC-MS analysis) is present throughout the reaction, the concentration of 2-(4-fluorophenyl)-1-phenylethan-1-one decreasing only toward the end of the carbonylation reaction (Figure 1). This result can be rationalized by a domino reaction sequence of *in situ* NaI-catalyzed conversion of **1a** into the 2-(4-fluorophenyl)-1-phenylethan-1-one **2a'** followed by the benzylation of the resulting ketone and also indicates that the rate of carbonylation step is comparable to or exceeds the rate of the benzylation of the resulting ketone intermediate.

With the newly developed protocol of domino carbonylation-benzylation, an array of benzyl chlorides were next subjected to the standard conditions (Table 2). Inductive electron-deprived fluoro, chloro, and trifluoromethyl groups were compatible well and the desired products were produced in excellent yields (**3aa**-**3ia**). More specifically, the position of the fluoro or trifluoromethyl substituent at the phenyl ring seems to have a negligible impact on the product yield. It should also be noted that dichloro-substituted substrates were successfully transformed into the desired ketones (**3da** and **3ea**), versatile intermediates for further synthetic manipulations. Furthermore, substrates with electron-donating

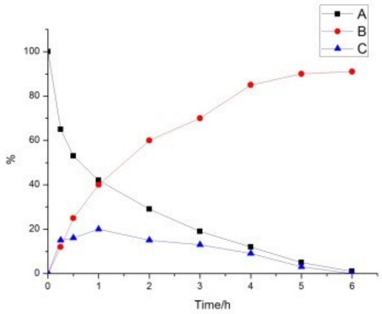
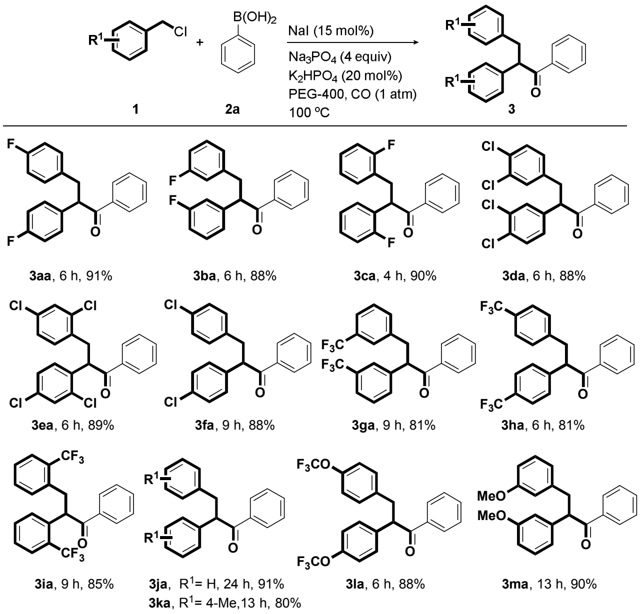


Figure 1 NaI-mediated carbonylation-benzylation of **1a** with **2a** under the standard conditions (A: chloride **1a**, B: product **3aa**, C: **2a'**).

Table 2 NaI- mediated domino carbonylation-benzylation reactions of **1** with **2a**.[a]



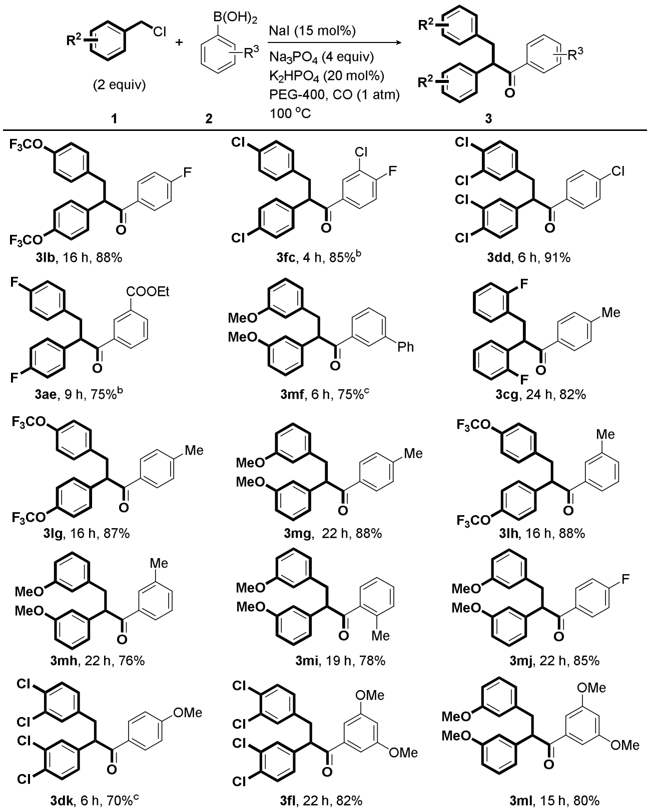
3aa, 6 h, 91% **3ba**, 6 h, 88% **3ca**, 4 h, 90% **3da**, 6 h, 88%

3ea, 6 h, 89% **3fa**, 9 h, 88% **3ga**, 9 h, 81% **3ha**, 6 h, 81%

3ia, 9 h, 85% **3ja**, R^1= H, 24 h, 91% **3ka**, R^1= 4-Me,13 h, 80% **3la**, 6 h, 88% **3ma**, 13 h, 90%

[a] Reaction conditions: **1** (0.5 mmol), **2a** (0.25 mmol), NaI (15 mol %), Na_3PO_4 (1.0 mmol), K_2HPO_4 (0.05 mmol), PEG-400 (2.0 mL), CO (1 atm), and 6 h at 100 °C.

Table 3 NaI- mediated domino carbonylation-benzylation reactions of **1** with **2**.[a]



3lb, 16 h, 88% **3fc**, 4 h, 85%[b] **3dd**, 6 h, 91%

3ae, 9 h, 75%[b] **3mf**, 6 h, 75%[c] **3cg**, 24 h, 82%

3lg, 16 h, 87% **3mg**, 22 h, 88% **3lh**, 16 h, 88%

3mh, 22 h, 76% **3mi**, 19 h, 78% **3mj**, 22 h, 85%

3dk, 6 h, 70%[c] **3fl**, 22 h, 82% **3ml**, 15 h, 80%

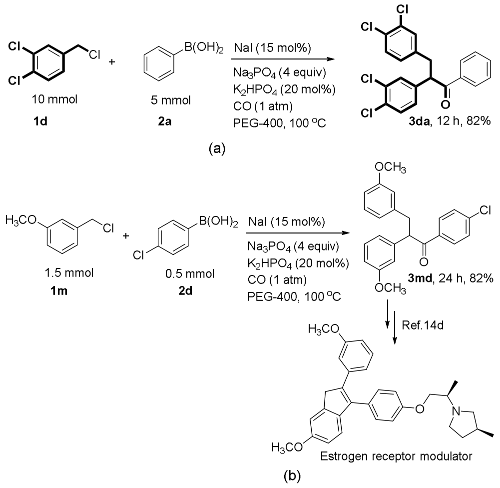
[a] Reaction conditions: **1** (0.5 mmol), **2** (0.25 mmol), NaI (15 mol %), Na_3PO_4 (1.0 mmol), K_2HPO_4 (0.05 mmol), PEG-400 (2.0 mL), CO (1 atm), and 6 h at 100 °C. [b] $NaHCO_3$ (0.5 mmol) instead of Na_3PO_4 (1.0 mmol) and K_2HPO_4 (0.05 mmol). [c] TBAI (15 mol %) instead of NaI (15 mol %).

groups such as methyl, trifluoromethoxy, and methoxy were effective under the standard conditions, affording the desired products in 80-90% yields (**3ka**-**3ma**). However, 1-(chloromethyl)naphthalene as a benzyl chloride resulted in a complex mixture and (1-chloroethyl)benzene when tested failed to give desired product. Cinnamyl chloride and *tert*-butyl chloride were also totally ineffective chloride substrates.

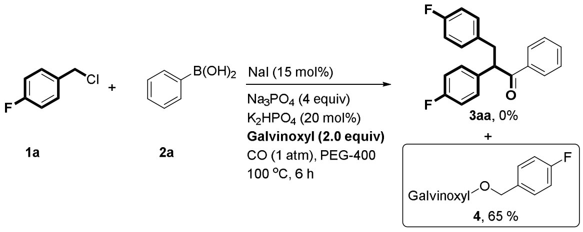
To further extend the scope of the method, variation of arylboronic acids was investigated. As displayed in Table 3, arylboronic acids bearing both electron-poor and electron-rich moieties worked well with various benzyl chlorides in our catalytic system. To our delight, reactive fluoride (**3lb**, **3fc**, and **3lj**), chloride (**3fc** and **3dd**), and ester (**3ae**) functionalities remained intact albeit a weaker base $NaHCO_3$ was better for the formation of **3fc** and **3ae**. A biphenylboronic acid gave the corresponding ketone **3mf** in 75% yield when TBAI was in the place of NaI. Additionally, the tansformation was not hampered by *ortho* substitution (**3mi**). Methoxy and dimethoxy substituted boronic acids could be also utilized as well, affording **3dk**, **3fl**, and **3ml** in good to excellent yields.

Notably, the reaction can be effectively scaled up with the comparable efficiency. For instance, the reaction of 1,2-dichloro-4-(chloromethyl)benzene (**1d**, 10 mmol) with phenylboronic acid (**2a**, 5 mmol) furnished the domino carbonylation-benzylation ketone **3da**, a versatile synthetic building block, in 82% yield (1.73 g) (Scheme 3, a). Significantly, a key intermediate **3md** for the construction of an important estrogen receptor modulator that is implicated in numerous cancer diseases, such as lung cancer, colon cancer, breast cancer, ovarian cancer, uterrine cancer, endometrial cancer, and prostate cancer, is readily accessable in a single step (Scheme 3, b), avoiding traditional multistep procedures.[15d]

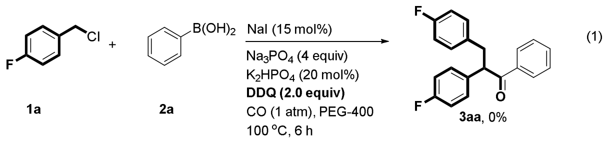
Ryu et al. proposed a free-radical mechanism for Pd/light induced carbonylative reactions of alkyl iodides and arylboronic acids.[13b] To gain further insight into our novel NaI-catalyzed carbonylation of benzyl chlorides with arylboronic acids, a free-

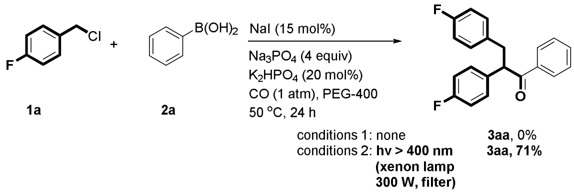


Scheme 3 (a) Gram-scale synthesis; (b) A synthetic application.

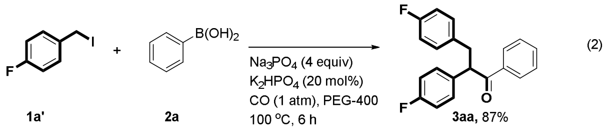


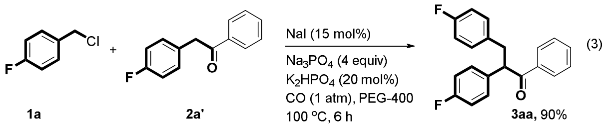
Scheme 4 Effect of a free-radical scavenger.

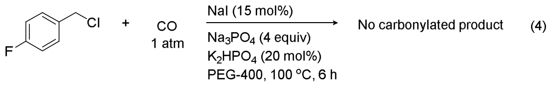


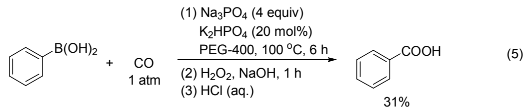


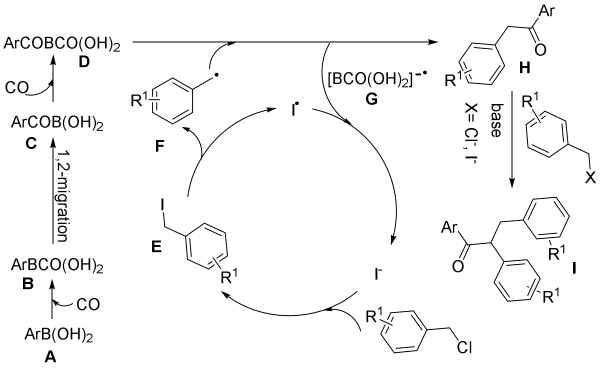
Scheme 5 Effect of visible light.











Scheme 6 Proposed reaction mechanism for the iodide-mediated domino carbonylation-benzylation process.

radical scavenger Galvinoxyl was utilized in the model reaction (Scheme 4). Consequently, the desired product can not be accessed, implicating that the catalytic cycle was completely inhibited. Moreover, the product from the interception of benzyl radical by the radical scavenger galvinoxyl was detected by HRMS (See the ESI). A single-electron-acceptor DDQ was employed and also resulted in total inhibition of the model reaction [Eqn (1)]. Furthermore, visible-light (*hv* > 400 nm, xenon lamp 300 W, filter) (See the ESI) mediated the model reaction under normal conditions at 50 ^oC still provided the desired product in 71% yield, while at 50 ^oC in the absence of the light the same reaction can not proceed at all (Scheme 5). These results indicated that the present transformation involved free-radical intermediates. To further clarify the iodide-mediated free-radical transformation, control experiments were carried out: a benzyl iodide **1a'**, a potential intermediate, was pre-prepared and reacted with **2a** under standard conditions except the absence of NaI to give a comparable result (**3aa** in 87% yield) [Eqn (2)] with the model reaction; the potential intermediate **2a'** was also directly used as a starting material, giving **3aa** in 90% yield under normal conditions [Eqn (3)]. These findings suggested that a benzyl iodide and a 1,2-diarylethanone formed as intermediates during a reaction. Additionally, in the absence of **2a** any carbonylated product was not observed under normal conditions [eqn (4)]. However, **2a** gave a carbonylated product benzoic acid in 31% yield in the absence of **1a** [eqn (5)], consistent with previous report.[20] These results indicate that the carbonylation process starting from arylboronic acid is reasonable.

Based on these observations and previous studies,[11, 13, 20, 21] a free radical mechanism for the domino carbonylation-benzylation of benzyl chloride is proposed (Scheme 5). Initially, arylboronic acid is to react with carbon monoxide to form carbonylated intermediate **A**, which further gives key intermediate **C** by carbonyl 1,2-migration insertion.[20] The organoborane intermediate **C** is also carbonylated in the presence of carbon monoxide to give intermediate **D**.[20] A benzyl iodide **E** generates through halogen exchange between a benzyl chloride and NaI and subsequently decomposes into a benzyl free radical **F** and an iodine free radical. Then, the active benzyl free radical **F** is intercepted by the intermediate **D** to generate 1,2-diarylethanone intermediate **H** with accompanying liberation of $[BCO(OH)_2]$ radical anion **G**. Finally, the intermediate **H** undergoes benzylation with the assistance of a base to give desired product **I** and the $[BCO(OH)_2]$ radical anion **G** reacts with iodine free radical through single electron transfer to give iodide ion, thus completing a radical chain.

In summary, we have developed a conceptually distinct and highly efficient intermolecular domino carbonylation-benzylation reactions catalyzed by NaI, which is abundant, inexpensive, readily available and bench stable. This protocol has been applied to an array of unactivated and inexpensive benzyl chlorides and to a number of arylboronic acids under mild conditions. Experiments indicated that radical intermediates were involved in this transformation. Although detailed mechanistic descriptions are still desired, it is believed that this finding represents a conceptual breakthrough in carbonylative cross-coupling, particularly in carbonylation of challenging aliphatic halides by using a non-transition-metal catalyst.

Notes and references

[a] *Jiangsu Collaborative Innovation Center of Biomedical Functional Materials, Jiangsu Key Laboratory of Biofunctional Materials, Key Laboratory of Applied Photochemistry, School of Chemistry and Materials Science, Nanjing Normal University, Wenyuan Road NO.1, 210023 Nanjing (China). Fax: (+) 86-(0)25-8589-1455*
E-mail:whhanwei@gmail.com
† The authors contributed equally.

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1. (a) A. de Meijere and F. Diederich, *Metal-Catalyzed Cross-Coupling Reactions*, Wiley-VCH: Weinheim, 2004; (b) A. Roglans, A. Pla-Quintana and M. Moreno-Manas, *Chem. Rev.*, 2006, **106**, 4622; (c) J. Magano and J. R. Dunetz, *Chem. Rev.*, 2011, **111**, 2177; (d) C. A. Busacca, D. R. Fandrick, J. J. Song and C. H. Senanayake, *Adv. Synth. Catal.*, 2011, **353**, 1825.
2. For some selective reviews on Pd-catalyzed carbonylations of aryl halides or aryl pseudohalides with CO, see: (a) X.-F. Wu and M. Beller, *Transition Metal Catalyzed Carbonylation Reactions-Carbonylative Activation of C–X Bonds*, Springer-Verlag Berlin, Heidelberg, 2013; (b) L. Kollár, *Modern carbonylation methods*, Wiley-VCH, Verlag GmbH & Co. KgaA, Weinheim, 2008; (c) X.-F. Wu, H. Neumann and M. Beller, *Chem. Rev.*, 2013, **113**, 1; (d) X.-F. Wu, H. Neumann and M. Beller, *Chem. Soc. Rev.*, 2011, **40**, 4986; (e) J. Magano and J. R. Dunetz, *Chem. Rev.*, 2011, **111**, 2177; (f) R. Grigg and S. P. Mutton, *Tetrahedron*, 2010, **66**, 5515; (g) A. Brennfuhrer, H. Neumann and M. Beller, *Angew. Chem., Int. Ed.*, 2009, **48**, 4114; (h) W. W. Fang, H. B. Zhu, Q. Y. Deng, S. L. Liu, X. Yu. Liu, Y. J. Shen and T. Tu, *Synthesis*, 2014, **46**, 1689; (i) S. T. Gadge and B. M. Bhanage, *RSC Adv.*, 2014, **4**, 10367.
3. D. G. Hall, *Boronic Acids-Preparation and Applications in Organic Synthesis, Medicine and Materials*, Wiley-VCH, Weinheim, 2011.
4. (a) D. J. Cardenas, *Angew. Chem., Int. Ed.*, 2003, **42**, 384; For recent reviews on carbonylation of C(sp^3) halides, see: (b) B. Liégault, J.-L. Renaud and C. Bruneau, *Chem. Soc. Rev.*, 2008, **37**, 290; (c) L. P. Wu, X. J. Fang, Q. Liu, R. Jackstell, M. Beller and X.-F. Wu, *ACS Catal.*, 2014, **4**, 2977.
5. T. Ishiyama, H. Kizaki, T. Hayashi, A. Suzuki and N. Miyaura, *J. Org. Chem.*, 1998, **63**, 4726.
6. (a) X.-F. Wu, H. Neumann and M. Beller, *Adv. Synth. Catal.*, 2011, **353**, 788; (b) X.-F. Wu, H. Neumann and M. Beller, *Tetrahedron Lett.*, 2010, **51**, 6146.
7. For reviews on transition-metal-free catalysis, see: (a) C. -L. Sun and Z.-J. Shi, *Chem. Rev.*, 2014, **114**, 9219; (b) V. P. Mehta and B. Punji, *RSC Advances*, 2013, **3**, 11957; (c) S. Yanagisawa and K. Itami, *ChemCatChem* 2011, **3**, 827; (d) E. Shirakawa and T. Hayashi, *Chem. Lett.*, 2012, **41**, 130.
8. (a) C. E. Garrett and K. Prasad, *Adv. Synth. Catal.*, 2004, **346**, 889; (b) C. J. Welch, J. Albaneze-Walker, W. R. Leonard, M. Biba, J. DaSilva, D. Henderson, B. Laing, D. J. Mathre, S. Spencer, X. Bu and T. Wang, *Org. Process Res. Dev.*, 2005, **9**, 198.
9. ö. Usluer, M. Abbas, G. Wantz, L. Vignau, L. Hirsch, E. Grana, C. Brochon, E. Cloutet and G. Hadziioannou, *ACS Macro Lett.*, 2014, **3**, 1134.
10. (a) I. Ryu, *Chem. Soc. Rev.*, 2001, **30**, 16; (b) S. Sumino, A. Fusano, T. Fukuyama and I. Ryu, *Acc. Chem. Res.*, 2014, **47**, 1563; (c) I. Ryu and N. Sonoda, *Angew. Chem., Int. Ed.*, 1996, **35**, 1050; recent important examples of radical carbonylations, see: (d) P. Xie, Y. J. Xie, B. Qian, H. Zhou, C. G. Xia and H. M. Huang, *J. Am. Chem. Soc.*, 2012,**134**, 9902; (e) P. Xie, C. G. Xia and H. M. Huang, *Org. Lett.*, 2013, **15**, 3370; (f) S. Kobayashi, T. Kawamoto, S. Uehara, T. Fukuyama and I. Ryu, *Org. Lett.*, 2010, **12**, 1548; (g) T. Kawamoto, T. Okada, D. P. Curran, and I. Ryu, *Org. Lett.*, 2013, **15**, 2144; (h) T. Kawamoto, H. Matsubara, I. Ryu, *Chem. Lett.*, 2014, **43**, 1140; (i) T. Kawamoto, A. Sato and I. Ryu, *Chem. Eur. J.*, 2015, **21**, 14764; (j) L. J. Gu, C. Jin and J. Y. Liu, *Green Chem.*, 2015, **17**, 3733; (k) S. Sumino, T. Ui and I. Ryu, *Org. Chem. Front.*, 2015, **2**, 1085.
11. (a) H. Zhang, R. Shi, A. Ding, L. Lu, B. Chen and A. Lei, *Angew. Chem., Int. Ed.*, 2012, **51**, 12542; (b) M. Majek and A. Jacobi von Wangelin, *Angew. Chem., Int. Ed.*, 2015, **54**, 2270; (c) W. Guo, L.-Q. Lu, Y. Wang, Y.-N. Wang, J.-R. Chen and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2015, **54**, 2265.
12. For selective reviews on iodide catalysis, see: (a) M. Uyanik and K. Ishihara, *ChemCatChem* 2012, **4**, 177; (b) R. Samanta, K. Matcha and A. P. Antonchick, *Eur. J. Org. Chem.*, 2013, 5769; (c) M. S. Yusubov and V. V. Zhdankin, *Resource-Efficient Technologies*, 2015, **1**, 49.
13. (a) W. Müller-Markgraf and J. Troe, *J. Phys. Chem.*, 1988, **92**, 4905; (b) S. Sumino, T. Ui and I. Ryu, *Org. Lett.*, 2013, **15**, 3142.
14. F. L. Jin and W. Han, *Chem. Commun.*, 2015, **51**, 9133.
15. (a) X. Zhu, Y.-F. Wang, W. Ren, F.-L. Zhang and S. Chiba, *Org. Lett.*, 2013, **15**, 3214; (b) G. M. Anstead, R. J. Altenbach, S. R. Wilson and J. A. Katzenellenbogen, *J. Med. Chem.*, 1988, **31**, 1316; (c) Z. Y. Wang, C. Dufresne, Y. Leblanc, C. S. Li, J. Y. Gauthier, C. K. Lau, M. Therien and P. Roy, *US 6174874*, 2001; (d) S. P. Govek and N. D. Smith, *WO 159769*, 2011.
16. During optimization of various bases, we found out that a byproduct 1,2-diarylethanone was formed in less than 10% yield. When K$_2$HPO$_4$ was used as a base, 1,2-diarylethanone was not observed. Although Na$_3$PO$_4$ as a base gave an excellent yield of desired product, 1,2-diarylethanone byproduct also formed in 6% yield. In order to achieve a higher selectivity, the combination of Na$_3$PO$_4$/K$_2$HPO$_4$ was chosen and indeed the byproduct 1,2-diarylethanone was completely suppressed.
17. Replacing PEG 400 with other PEGs, such as PEG-200 or PEG-600 resulted in lower yields (41% and 76%, respectively).
18. Polyethylene glycol (PEG) is often used as a good phase transfer agent. This property favors gas-liquid-solid multiphase catalytic reaction. Additionally, PEG is a highly polar solvent and thus can cause strong solvation effects on polar molecule carbon monoxide to reduce mass transfer resistance. The dual positive properties probably enable PEG to show excellent performance in the transformation.
19. (a) M. T. Ankner, P.-O. Norrby, O. Wiest and P. Helquist, *J. Am. Chem. Soc.*, 2015, **137**, 7019; (b) A. Hinchcliffe, C. Hughes, D. A. Pears and M. R. Pitts, *Org. Process Res. Dev.*, 2007, **11**, 477.
20. For a review on carbonylation of organoboranes, see: H. C. Brown, *Acc. Chem. Res.*, 1969, **2**, 65
21. Z. W. Chen, H. F. Jiang, A. Z. Wang and S. R. Yang, *J. Org. Chem.*, 2010, **75**, 6700.

Transition Metal-Free, Iodide-Mediated Domino Carbonylation-Benzylation of Benzyl Chlorides with Arylboronic Acids under Ambient Pressure of Carbon Monoxide

Fengli Jin, Yanzhen Zhong, Xin Zhang, Huichun Zhang, Qian Zhao and Wei Han*

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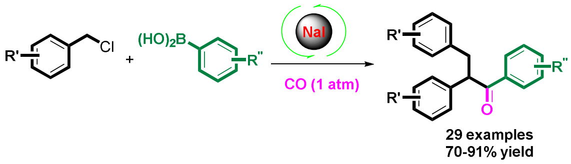

Transition metal-free, ambient-pressure domino carbonylation-benzylation reactions by iodide catalysis has been developed.