Check for updates

View Article Online
View Journal

ChemComm
Chemical Communications

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: Y. Wang, X. Jiang and B. Wang, *Chem. Commun.*, 2020, DOI: 10.1039/D0CC06451C.

Volume 54
Number 1
4 January 2018
Pages 1-112

ChemComm
Chemical Communications
rsc.li/chemcomm

ISSN 1359-7345

ROYAL SOCIETY OF CHEMISTRY

COMMUNICATION
S. J. Connon, M. O. Senge *et al.*
Conformational control of nonplanar free base porphyrins: towards bifunctional catalysts of tunable basicity

This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/chemcomm

DOI: 10.1039/D0CC06451C

Journal Name

COMMUNICATION

Cobalt-Catalyzed Carboxylation of Aryl and Vinyl Chlorides with CO_2

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

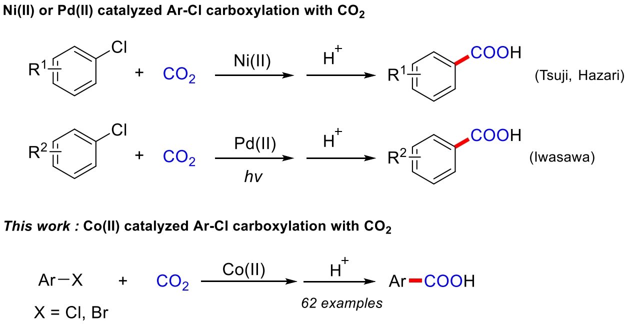
DOI: 10.1039/x0xx00000x

www.rsc.org/

Yanwei Wang[a], Xiaomei Jiang[a] and Baiquan Wang[a,b,*]

The transition-metal-catalyzed carboxylation of aryl and vinyl chlorides with CO_2 is rarely studied, and has been achieved only with Ni catalyst or combination of palladium and photoredox. In this work, the cobalt-catalyzed carboxylation of aryl and vinyl chlorides and bromides with CO_2 has been developed. These transformations proceed under mild conditions and exhibit a broad substrate scope, affording the corresponding carboxylic acids in good to high yields.

In recent years, carbon dioxide has gained increasing concentration as a C1 synthon in organic synthetic realm,[1a-m] especially for the construction of carboxylic acids, which are building blocks in many pharmaceuticals.[1] CO_2, despite its significant kinetic inertness and thermodynamic stability, could behave as weak electrophile in the transition-metal catalyzed cross-electrophile coupling reactions. In this regime, transition-metals (Ni,[2] Pd,[3] Co,[4] Cu[5]) catalyzed cross-electrophile coupling reactions of aryl halides and CO_2 exhibited enormous potential in the synthetic applications, which offering more straightforward strategies to construct aryl carboxylic acids. Among these, most works focused on the more active aryl bromides or iodides. There are only a few examples on the carboxylation of the most abundant and versatile aryl chlorides. In 2012, Tsuji and co-workers dis closed the Ni-catalyzed carboxylation of aryl and vinyl chlorides with CO_2 using manganese powder as a reductant.[2a] Then, Hazari revealed that using the homogeneous organic reductant could enable the Ni-catalyzed carboxylation of aryl chlorides with lower catalyst loading and broader substrate scope.[2e] Recently, Iwasawa and Martin employed palladium/photoredox as the catalytic system to promote the carboxylation of aryl chlorides with CO_2.[3b] Given the versatile performances of cobalt catalysts in the electrophile coupling reactions of organic (pseudo)halides,[4,6] we assume the cobalt catalyst could promote the carboxylation procedure of less reactive aryl chlorides with CO_2 under mild conditions.



Scheme 1 Transition-Metal-Catalyzed Carboxylation of Aryl Chlorides with CO_2.

We commenced the investigations by evaluating the reaction of 1-chloro-4-methoxybenzene with CO_2 at atmospheric pressure. After a series trails of the reaction parameters, the carboxylation procedure was carried out using a mixture of $CoBr_2$ (5 mol%), 2,9-dibutyl-4,7-dimethyl-1,10-phenanthroline (**L6**, 10 mol %) as ligand , Mn powder (1.5 equiv) as reductant, LiOAc (2.0 equiv) and Et_4NI (2.0 equiv) as additives, in DMA (1 mL) at 100 °C under 1 atm CO_2 for 12 h (Table1, entry 1). Control experiments showed that LiOAc played an important role in this transformation (entry 2). Changing LiOAc into NaOAc, KOAc, or Li_2CO_3 resulted in lower conversion (entries 3–5), and the reaction was totally inactive when LiCl was added as an additive (entry 6). Further investigation experiments showed that LiOAc played a double role in the reaction, offering a lithium salt and serving as a base (for details, see Table S3 in the ESI). It is known that lithium salts could work as Lewis acids to promote the insertion reactions of CO_2 into transition-metal-carbon bonds.[2e,7] Notably, the addition of Et_4NI was essential for this transformation, which afforded higher yields than other quaternary ammonium salts such as Bu_4NI or Et_4NBr, whereas no desired product detected when Et_4NCl was employed (Table S2). The reaction efficiency was also sensitive to the reaction temperatures. Only trace amount of desired product was detected at 60 °C, and the reaction was inactive when performed at room temperature (Table S2, entries 3 and 4). The effect of solvents was investigated as well, and DMA gave the best result (Table S2, entries 5–7). As

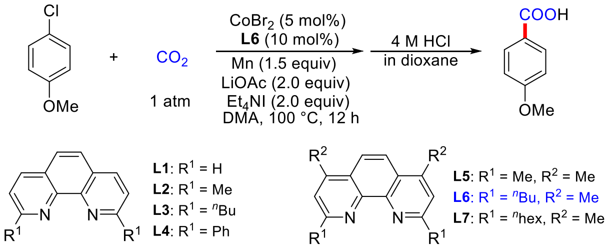
---

[a] State Key Laboratory of Elemento-Organic Chemistry, College of Chemistry, Nankai University, Tianjin 300071, P. R. China. E-mail: bqwang@nankai.edu.cn; Fax: +86 (22) 23504781; Tel: +86 (22) 23504781
[b] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P. R. China

† Electronic supplementary information (ESI) available: Full experimental details, characterization and NMR spectra of the target products. See DOI: 10.1039/x0xx00000x

View Article Online
DOI: 10.1039/D0CC06451C

Table 1 Optimization of reaction conditions[a]

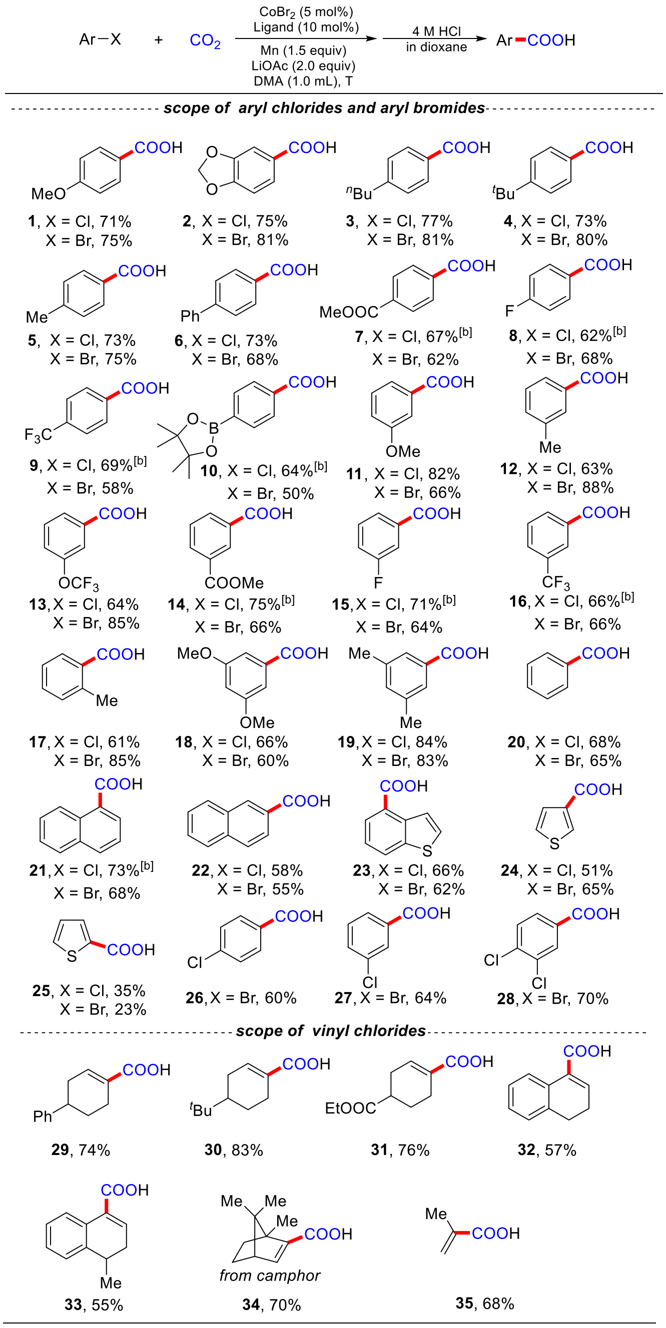


entry	alteration	yield (%)[b]
1	none	71
2	no LiOAc	0
3	NaOAc instead of LiOAc	19
4	KOAc instead of LiOAc	34
5	Li_2CO_3 instead of LiOAc	59
6	LiCl instead of LiOAc	0
7	Et_4NBr instead of Et_4NI	65
8	Et_4NCl instead of Et_4NI	0
9	**L1** instead of **L6**	trace
10	**L2** instead of **L6**	18
11	**L3** instead of **L6**	59
12	**L4** instead of **L6**	0
13	**L5** instead of **L6**	64
14	**L7** instead of **L6**	60
15	Zn instead of Mn	trace
16[c]	$Co(PPh_3)_3Cl$ instead of $CoBr_2$	12
17[d]	$Co(PPh_3)_3Cl$ instead of $CoBr_2$	0
18	without $CoBr_2$	0

[a] Reaction conditions: 1-Chloro-4-methoxybenzene (0.5 mmol, 1.0 equiv), CO_2 1 atm, $CoBr_2$ (5 mol%), ligand (10 mol%), Mn powder (1.5 equiv), LiOAc (2.0 equiv), Et_4NI (2.0 equiv), DMA (1.0 mL), 100 °C for 12 h. [b] Isolated yield. [c] $Co(PPh_3)_3Cl$ (5 mol%). [d] $Co(PPh_3)_3Cl$ (5 mol%), without **L6**.

showed in Table 1, subtle differences in the ligand backbone exhibited a profound influence on the reaction outcome (entries 9–14). An increase in the steric bulk around the nitrogen-donor ligand could minimize the homo-coupling reaction, and introduction of a butyl group at 2,9-positions gave the optimal result (entry 11). The electronic effect of methyl groups at 4,7-position of the 1,10-phenanthroline backbone may further improve the efficiency (entries 1, 13-14). Other ligands, such as terpyridine, PPh_3, or Xantphos could not promote this conversion (Table S1). When Zn powder was employed as the reductant, trace product or no product was obtained (entry 15). The different performance of Zn and Mn may be attributed to their reduction potentials (Zn^{2+}/Zn^0, -1.02 V *vs* Mn^{2+}/Mn^0, -1.44 V).[8,9] Notably, $Co(PPh_3)_3Cl$ combined with **L6** could promote this reaction as well, giving the carboxylation product in 12% yield (entries 16–17). No desired product was obtained without $CoBr_2$ (entry 18). To our delight, this catalytic system also worked well with aryl bromides under mild conditions (Table S4). Very recently, Xi group reported cobalt-catalyzed carboxylation of aryl bromides with the isolated yield up to 72%.[4a] Our procedure could work smoothly with lower catalyst loading at room temperature with higher yields (up to 88%, Table 2).

Table 2 Substrate scope[a]



1, X = Cl, 71%
X = Br, 75%

2, X = Cl, 75%
X = Br, 81%

3, X = Cl, 77%
X = Br, 81%

4, X = Cl, 73%
X = Br, 80%

5, X = Cl, 73%
X = Br, 75%

6, X = Cl, 73%
X = Br, 68%

7, X = Cl, 67%[b]
X = Br, 62%

8, X = Cl, 62%[b]
X = Br, 68%

9, X = Cl, 69%[b]
X = Br, 58%

10, X = Cl, 64%[b]
X = Br, 50%

11, X = Cl, 82%
X = Br, 66%

12, X = Cl, 63%
X = Br, 88%

13, X = Cl, 64%
X = Br, 85%

14, X = Cl, 75%[b]
X = Br, 66%

15, X = Cl, 71%[b]
X = Br, 64%

16, X = Cl, 66%[b]
X = Br, 66%

17, X = Cl, 61%
X = Br, 85%

18, X = Cl, 66%
X = Br, 60%

19, X = Cl, 84%
X = Br, 83%

20, X = Cl, 68%
X = Br, 65%

21, X = Cl, 73%[b]
X = Br, 68%

22, X = Cl, 58%
X = Br, 55%

23, X = Cl, 66%
X = Br, 62%

24, X = Cl, 51%
X = Br, 65%

25, X = Cl, 35%
X = Br, 23%

26, X = Br, 60%

27, X = Br, 64%

28, X = Br, 70%

29, 74%

30, 83%

31, 76%

32, 57%

33, 55%

from camphor
34, 70%

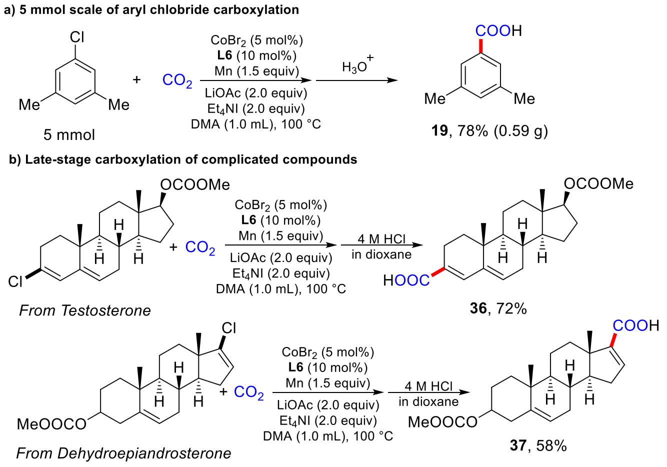
35, 68%

[a] Reaction conditions: ArX (0.5 mmol), CO_2 1 atm, $CoBr_2$ (5 mol%), ligand (10 mol%), Mn powder (1.5 equiv), LiOAc (2.0 equiv), DMA (1.0 mL), 12 h. X= Cl, with **L6**, Et_4NI (2.0 equiv), at 100 °C; X = Br, with **L2**, at room temperature. [b] With **L2**.

With the optimal reaction conditions in hand, we explored the scope of aryl chlorides and aryl bromides, as shown in Table 2. To our delight, most substrates worked smoothly to afford corresponding carboxylation products in moderate to good yields. When 4-substituted aryl chlorides and aryl bromides treated with CO_2 under the catalytic systems, higher yields were obtained for the electron-donating groups (**1**–**5**) than those for the electron-withdrawing

View Article Online
DOI: 10.1039/D0CC06451C

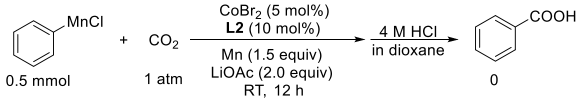
groups (**7**–**10**). Notably, the boronic acid ester (**10**) remained intact under the reaction conditions, which is beneficial for further derivatization. Next, aryl chlorides and bromides bearing different substituents at *meta*-position were tested, giving the corresponding products in 63–88% yields (**11**–**16**). Moreover, more sterically hindered 2-chlorotoluene and 2-bromotoluene proceeded smoothly in the catalytic system, providing the *o*-toluic acid (**17**) in 61% and 85% yields respectively, while only trace amount of the corresponding carboxylic acids were obtained with 1-chloro-/1-bromo-2-methoxybenzene. This is probably due to the coordination of the adjacent oxygen atom of o-anisolyl halides to the cobalt atom forming a cyclic cobalt intermediate, which hindered the insertion of CO_2 into the C–Co bond. 3,5-Disubstituted substrates were also investigated, as exemplified by **18** (ArCl 66%, ArBr 60%) and **19** (ArCl 84%, ArBr 83%). Treating 1- or 2-halides (halide = Cl, Br) substituted naphthalene with CO_2 under the standard conditions furnished the corresponding acids **21** and **22** in moderate to good yields (55–73%). Furthermore, S-containing aryl chlorides and aryl bromides also worked in our reaction systems, providing the desired carboxylic acids **23**–**25** in 23–66% yields. It is noteworthy that this conversion could selectively realize the carboxylation of C(sp^2)–Br bond with C(sp^2)–Cl bond remained via conditions control (**26**–**28**). To our delight, the carboxylation procedure of aryl chlorides was also suitable for the vinyl chlorides, furnishing the α,β-unsaturated carboxylic acids in moderate to good yield (**29**–**35**). Subsequently, the scope with respect to vinyl chlorides was examined. By treating chloro-substituted cyclohexene with CO_2 under the optimal conditions, the corresponding acids were obtained in good yields (**29**–**31**, 74–83%). The vinyl chlorides conjugated with a benzene ring also proceeded smoothly affording the corresponding carboxylic acid in moderate yields (**32**–**33**). Notably, the endocyclic vinyl chlorides derived from camphor also worked well giving the desired product in 70% yield (**34**). Moreover, our carboxylation protocol was also suitable for the chain vinyl chloride, as exemplified by methacrylic acid (**35**, 68%). Benzyl chloride was also tested as a substrate under the standard conditions but no desired product was obtained.



Scheme 2 Synthetic applications.

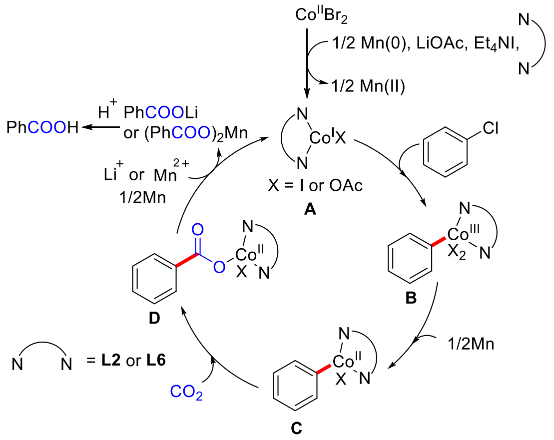
The cobalt-catalyzed carboxylation reaction was further demonstrated by its applicability in the amplified scale experiment and late-stage carboxylation of complicated compounds (Scheme 2). The carboxylation of 1-chloro-3,5-dimethylbenzene was amplified to 5 mmol scale using a 500 mL Schlenk flask affording the corresponding carboxylic acid 19 in 78% yield (0.59 g) under the standard conditions. Furthermore, the complex vinyl chloride compounds derived from Testosterone and Dehydroepiandrosterone could proceed smoothly in this catalytic system giving the desired products in 72% (**36**) and 58% (**37**) yields, respectively. This indicated that this protocol offers a potential synthetic route for the carboxylation of some complicated molecules.

To probe the catalytic mechanism, a control experiment was carried out. Aryl manganese species may be involved in the carboxylation procedure. Therefore, phenyl manganese chloride was prepared from $MnCl_2$, LiCl, and Grignard reagent according to the literature (For details, see the ESI).[10] Treatemnt of phenyl manganese chloride with CO_2 under the standard conditions gave no the desired product (Scheme 3). This result indicated that the arylmanganese species may not behave as an intermediates in this carboxylation reaction. The formation and reaction of ArMnCl species could be excluded from the possibility.



Scheme 3 An control experiment.

On the basis of the results of experiments and literature reports,[2-4,6] a possible mechanism is proposed for the present catalytic reaction (Scheme 4). Initially, $Co^{II}Br_2$ is reduced to the $Co^{I}XL$ (X = I or OAc) species (**A**) with Mn powder in the presence of ligand. Then, oxidative addition of aryl halide takes place via C–Cl or C–Br bond cleavage, giving an aryl Co^{III} intermediate (**B**). Subsequently, reduction of aryl Co^{III} gives the aryl Co^{II} species (**C**). Then CO_2 is inserted into the C–Co^{II} bond assisted by Lewis acid (Li^+) to produce Co^{II} carboxylate intermediate (**D**).[2e] Finally, the reduction of **D** with manganese affords the corresponding manganese or lithium carboxylate and regenerates the Co^{I} catalytic species (**A**) for the next catalytic cycle. LiOAc plays a double rule in this reaction, offering lithium salt and serving as base.



Scheme 4 Proposed mechanistic pathway.

In conclusion, we have developed cobalt-catalyzed carboxylation of aryl halides (halides = Cl, Br) and vinyl chlorides

View Article Online
DOI: 10.1039/D0CC06451C

with carbon dioxide under mild conditions. A broad scope of substrates has been established in this conversion, furnishing the corresponding carboxylic acids in good to high yields. The applicability was demonstrated in the late-stage carboxylation of Testosterone and Dehydroepiandrosterone derivatives. Further investigations on the reaction mechanism and applications of this method are in progress in our laboratory.

The authors wish to thank the National Natural Science Foundation of China for financial support (No. 21871151 and 21672108).

Conflicts of interest

There are no conflicts to declare.

Notes and references

(1) For selected reviews: (*a*) M. Cokoja, C. Bruckmeier, B. Rieger, W. A. Herrmann and F. E. Kuhn, *Angew. Chem. Int. Ed.,* 2011, **50**, 8510; (*b*) K. Huang, C.- L. Sun and Z.- J. Shi, *Chem. Soc. Rev.,* 2011, **40**, 2435; (*c*) Y. Tsuji and T. Fujihara, *Chem. Commun.,* 2012, **48**, 9956; (*d*) M. Börjesson, T. Moragas, D. Gallego and R. Martin, *ACS Catal.,* 2016, **6**, 6739; (*e*) S. Wang, G. Du and C. Xi, *Org. Biomol. Chem.*, 2016, **14**, 3666; (*f*) X.-F. Wu and F. Zheng, *Top. Curr. Chem.,* 2017, **375**, 4; (*g*) A. Tortajada, F. Juliá-Hernándeẓ, M. Börjesson, T. Moragas and R. Martin, *Angew. Chem. Int. Ed.,* 2018, **57**, 15948; (*h*) T. Fujihara and Y. Tsuji, *Beilstein J. Org. Chem.,* 2018, **14**, 2435; (*i*) Y. Zhang, J. Cen, W. Xiong, C. Qi and H. Jiang, *Prog. Chem.,* 2018, **30**, 547; (*j*) Y.-G. Chen, X.-T. Xu, K. Zhang, Y.-Q. Li, L.-P. Zhang, P. Fang and T.-S. Mei, *Synthesis,* 2018, **50**, 35; (*k*) J. Hong, M. Li, J. Zhang, B. Sun and F. Mo, *ChemSusChem,* 2019, **12**, 6; (*l*) T. Fujihara and Y. Tsuji, *Front. Chem.,* 2019, **7**, 430; (*m*) L. Zhang, Z. Li, M. Takimoto and Z. Hou, *Chem. Rec.,* 2020, **20**, 494; (*n*) R. Shang, Y. Fu, J. -B. Li, S. -L. Zhang, Q. -X. Guo and L. Liu, *J. Am. Chem. Soc.,* 2009, **131**, 5738; (*o*) Y.-N. Wu, M. -C. Fu, R. Shang and Y. Fu, *Chem. Commun.,* 2020, **56**, 4067.

(2) (*a*) T. Fujihara, K. Nogi, T. Xu, J. Terao and Y. Tsuji, *J. Am. Chem. Soc.,* 2012, **134**, 9106; (*b*) F. B. Sayyed, Y. Tsujib and S. Sakaki, *Chem. Commun.,* 2013, **49**, 10715; (*c*) F. Rebih, M. Andreini, A. Moncomble, A. Harrison-Marchand, J. Maddaluno and M. Durandetti, *Chem. - Eur. J.,*. 2016, **22**, 3758; (*d*) Q.-Y. Meng, S. Wang and B. König, *Angew. Chem. Int. Ed.,* 2017, **56**, 13426; (*e*) D. J. Charboneau, G. W. Brudvig, N. Hazari, H. M. C. Lant and A. K. Saydjari, *ACS Catal.,* 2019, **9**, 3228; (*f*) A. Tortajada, Y. Duan, B. Sahoo, F. Cong, G. Toupalas, A. Sallustrau, O. Loreau, D. Audisio and R. Martin, *ACS Catal.,* 2019, **9**, 5897; (*g*) S. Saini, H. Singh, P. K. Prajapati, A. K. Sinha and S. L. Jain, *ACS Sustainable Chem. Eng.,* 2019, **7**, 11313.

(3) (*a*) A. Correa and R. Martin, *J. Am. Chem. Soc.,* 2009, **131**, 15974; (*b*) K. Shimomaki, K. Murata, R. Martin and N. Iwasawa, *J. Am. Chem. Soc.,* 2017, **139**, 9467.

(4) (*a*) W. Hang, Y. Yi and C. Xi, *Adv. Synth. Catal.,* 2020, **362**, 2337; (*b*) K. Nogi, T. Fujihara, J. Terao and Y. Tsuji, *J. Org. Chem.,* 2015, **80**, 11618.

(5) (*a*) H. Tran-Vu and O. Daugulis, *ACS Catal.,* 2013, **3**, 2417; (*b*) S.-S. Yan, D.-S. Wu, J.-H. Ye, L. Gong, X. Zeng, C.-K. Ran, Y.-Y. Gui, J. Li and D.-G. Yu, *ACS Catal.,* 2019, **9**, 6987; (*c*) S.-L. Xie, X.-Y. Cui, X.-T. Gao, F. Zhou, H.-H. Wu and J. Zhou, *Org. Chem. Front.,* 2019, **6**, 3678.

(6) For selected works: (*a*) P. Gomes, C. Gosmini and J. Périchon, *Org. Lett.,* 2003, **5**, 1043; (*b*) M. Amatore, C. Gosmini and J. Périchon, *Eur. J. Org. Chem.,* 2005, 989; (*c*) M. Amatore, C. Gosmini and J. Périchon, *J. Org. Chem.,* 2006, **71**, 6130; (*d*) M. Amatore and C. Gosmini, *Angew. Chem. Int. Ed.,* 2008, **47**, 2089; (*e*) C. Gosmini, J. M. Bégouin and A. Moncomble, *Chem. Commun.,* 2008, 3221; (*f*) M. Amatore and C. Gosmini, *Synlett,* 2009, 1073; (*g*) A. Moncomble, P. Le Floch and C. Gosmini, *Chem. - Eur. J.,* 2009, **15**, 4770; (*h*) M. Amatore and C. Gosmini, *Chem. - Eur. J.,* 2010, **16**, 5848; (*i*) A. Moncomble, P. Le Floch, A. Lledos and C. Gosmini, *J. Org. Chem.,* 2012, **77**, 5056; (*j*) K. Nogi, T. Fujihara, J. Terao and Y. Tsuji, *Chem. Commun.*, 2014, **50**, 13052.

(7) (*a*) K. -C. Lau, B. J. Petro, S. Bontemps and R. F. Jordan, *Organometallics*, 2013, **32**, 6895; (*b*) J. E. Heimann, W. H. Bernskoetter, N. Hazari and J. M. Mayer, *Chem. Sci.*, 2018, **9**, 6629.

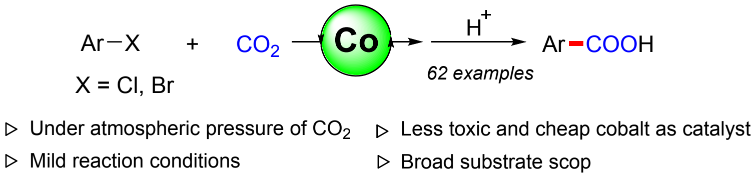
(8) E. Richmond and J. Moran, *Synthesis*, 2018, **50**, 499.

(9) A. A. Isse, C. Y. Lin, M. L. Coote and A. Gennaro, *J. Phys. Chem. B,* 2011, **115**, 678.

(10) (*a*) A. Leleu, Y. Fort and R. Schneider, *Adv. Synth. Catal.,* 2006, **348**, 1086; (*b*) G. Cahiez and E.Metais, *Tetrahedron Lett.,* 1995, **36**, 6449.

View Article Online
DOI: 10.1039/D0CC06451C

Yanwei Wang, Xiaomei Jiang, and Baiquan Wang*



Cobalt-Catalyzed Carboxylation of Aryl and Vinyl Chlorides with CO_2

Cobalt-catalyzed carboxylation of aryl and vinyl chlorides and bromides with CO_2 has been developed. These transformations proceed under mild conditions and exhibit a broad substrate scope, affording the corresponding carboxylic acids in good to high yields.