



# Metal-catalyzed direct carboxylation of unactivated alkyl halides with CO<sub>2</sub>

Yu Liu and Ruben Martin\*

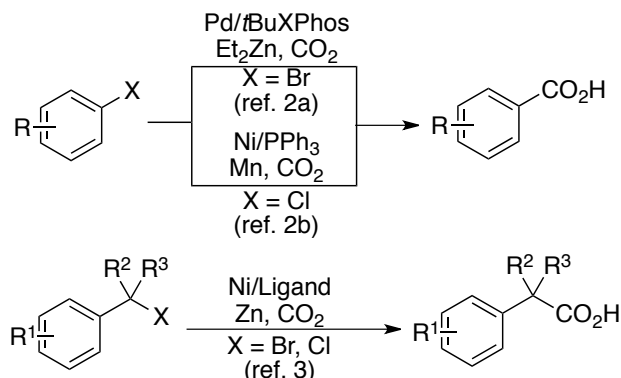
Av. Països Catalans 16, 43007 Tarragona, Spain

[rmartinromo@iciq.es](mailto:rmartinromo@iciq.es); [yuliu@iciq.es](mailto:yuliu@iciq.es)

carbon dioxide; alkyl halide; carboxylation

## INTRODUCTION

The exploitation of carbon dioxide as a C1 source has attracted much attention due to the fact that it is a renewable, inexpensive, nontoxic and environment-friendly carbon feedstock.<sup>1</sup> In recent years, the catalytic carboxylation of arylmetal species, alkynes and activated C-H bonds has been well documented in the literature.<sup>1</sup> We<sup>2a</sup> and others<sup>2b</sup> have also developed the carboxylation of aryl halides with CO<sub>2</sub> leading to benzoic acids. Recently, we described the first catalytic carboxylation of primary, secondary and tertiary benzyl halides with CO<sub>2</sub> en route to phenylacetic acids (Figure 1).<sup>3</sup> Despite the advances realized, to the best of our knowledge the direct carboxylation of unactivated alkyl halides<sup>4</sup> with CO<sub>2</sub> has not been reported.

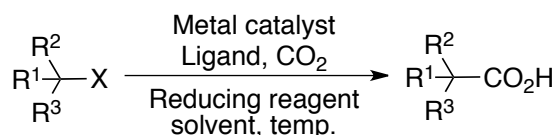


**Figure 1.** Metal-catalyzed carboxylation of aryl or benzyl halides with CO<sub>2</sub>.

## RESULTS AND DISCUSSION

We chose differently substituted unactivated alkyl halides to study a catalytic carboxylation event via dual activation of alkyl halides and CO<sub>2</sub>. Based on the experience of our laboratories in catalytic CO<sub>2</sub> activation,<sup>2,3</sup> the effect of catalysts, reducing agents, additives and solvents were systematically examined. After careful screening of the reaction conditions, we finally found appropriate conditions that allowed us to deliver the targeted aliphatic carboxylic acids in good yields. Importantly, the proclivity of the in situ formed alkyl metal species

towards reductive elimination was significantly retarded by ligand modulation. Likewise, the fine-tuning of the reaction conditions suppressed other side-reactions such as the reduction of the parent alkyl halide. Importantly, the protocol is distinguished by its wide substrate scope and mild conditions, allowing for the coupling of different alkyl halides in good to excellent yields in the presence of rather sensitive functional groups.



**Figure 2.** Metal-catalyzed carboxylation of unactivated alkyl halides with CO<sub>2</sub>.

## CONCLUSION

In conclusion, we have developed a novel and straightforward metal-catalyzed carboxylation reaction of unactivated alkyl halides with CO<sub>2</sub>, leading to a series of carboxylic acids in good yields. Further investigations are ongoing in our laboratories.

## ACKNOWLEDGEMENTS

We thank the ICIQ Foundation, the European Research Council (ERC-277883), and MICINN (CTQ2012-34054) for financial support.

## REFERENCES

- <sup>1</sup> For selected reviews, see: (a) Cokoja, M.; Bruckmeier, C.; Rieger, B.; Herrmann, W. A.; Kühn, F. E. *Angew. Chem. Int. Ed.* **2011**, *50*, 8510. (b) Correa, A.; Martin, R. *Angew. Chem. Int. Ed.* **2009**, *48*, 6201. (c) Sakakura, T.; Choi, J.-C.; Yasuda, H. *Chem. Rev.* **2007**, *107*, 2365.
- <sup>2</sup> (a) Correa, A.; Martin, R. *J. Am. Chem. Soc.* **2009**, *131*, 15974. (b) Fujihara, T.; Nogai, K.; Xu, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2012**, *134*, 9106.
- <sup>3</sup> Leon, T.; Correa, A.; Martin, R. *J. Am. Chem. Soc.* **2013**, *135*, 1221.
- <sup>4</sup> For selected reviews on the activation of alkyl halides, see: (a) Rudolph, A.; Lautens, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 2656. (b) Frish, A. C.; Beller, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 674.