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Zinc-mediated allylation of carbon dioxide—the LiOAc effect†

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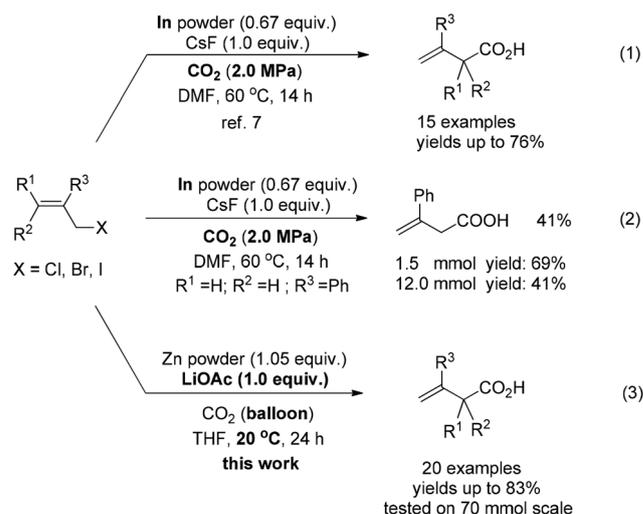
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A direct carboxylation reaction of allylic bromides mediated by zinc powder has been developed. The reaction occurred smoothly at room temperature with 1 atm of CO₂ provided by a balloon. The reaction was conducted in the presence of LiOAc giving excellent yields. An excellent branched regioselectivity was observed and the reaction was easily scaled-up to 10 gram-scale.

Introduction

With growing concern over the greenhouse effect, much attention has been paid to the different issues relating CO₂. For example, carbon dioxide itself is becoming a more and more popular C1 starting material in C–C bond formation reactions owing to its non-toxicity and abundance as well as its advantages for the syntheses of carbonyl compounds.¹ As we know the allylation reaction of carbon dioxide would be the most efficient approach for the synthesis of the not readily available 3-alkenoic acids. Early attempts with allylic lithium or Grignard reagents afforded the products with poor regioselectivity and functional group tolerance.² Transition metal-catalyzed reactions of pre-prepared toxic allylic stannanes and boranes, in some cases, yielded a mixture of 2- and 3-alkenoic acids.^{3–6} CO₂ allylation reactions starting directly from allylic halides in the presence of an appropriate metal is no doubt the most promising and straightforward approach. Early this year, we reported an indium-mediated allylation of carbon dioxide, which requires a 2.0 MPa pressure of CO₂ at 60 °C [Scheme 1, eqn (1)]; in addition, while it is a reaction with a very high regioselectivity, it is difficult to run the reaction on a synthetically practical scale: the yield dropped to 41% when the reaction was conducted on 12 mmol scale [Scheme 1, eqn (2)].⁷ Thus, we wish to further develop a protocol using atmospheric pressure of CO₂ with cheap metal, which may be easily run on a large scale for practical application. Here we report a room temperature zinc-mediated carboxylation reaction of



Scheme 1 Direct allylation of carbon dioxide in the presence of metal.

allylic bromides under a CO₂ balloon atmosphere with the help of LiOAc [Scheme 1, eqn (3)].

Results and discussion

To address the issue of high pressure, we run the reaction with the CO₂ provided by a balloon (1 atm) and screened all the commercially available metal powders at room temperature for the purpose of energy saving. Treatment of 2-phenylallyl bromide (**1a**) with indium in DMF led to a complicated mixture after 24 h (Table 1, entry 1). Screening of other metal powders including Al, Fe, Bi, Mn didn't give any better results (Table 1, entries 2–5). Interestingly, when Zn powder was used, the expected product **2a** was formed in 73% yield (Table 1, entry 6). Replacing DMF with THF gave the same yield but THF is beneficial in the workup for the reason of its low boiling point (entry 8). Other solvents led to poor results

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(Table 1, entries 7, 9 and 10). Then many additives were screened and it is exciting to observe that some lithium salts may accelerate the reaction with a much higher yield: When 1.0 equivalent of LiOAc was added, the yield reached 84% and C=C isomerization was not observed as judged by the NMR analysis of the crude product (Table 1, entry 14, see also entries 3 and 5 of Table 4; entry 3 of Table 5)!⁸

Table 1 Optimization of the reaction conditions^a

Entry	Metal powder (x equiv.)	Solvent	Additive	Yield of 2a ^b (%)	1a ^b (%)
1	In (0.70)	DMF	—	Complicated	—
2	Al (0.70)	DMF	—	—	76
3	Fe (0.70)	DMF	—	—	74
4	Bi (0.70)	DMF	—	Complicated	—
5	Mn (1.05)	DMF	—	—	68
6	Zn (1.05)	DMF	—	73	—
7	Zn (1.05)	DMSO	—	58	—
8	Zn (1.05)	THF	—	73	—
9	Zn (1.05)	Dioxane	—	25	—
10	Zn (1.05)	Et ₂ O	—	—	87
11	Zn (1.05)	THF	LiCl	81	5
12	Zn (1.05)	THF	LiBr	74	6
13	Zn (1.05)	THF	LiOCOCF ₃	34	1
14	Zn (1.05)	THF	LiOAc	84	—

^aThe reaction was conducted with 1.0 mmol of allylic halide and metal powder in 5 mL of an anhydrous solvent with a CO₂ balloon.
^bNMR yield.

In order to check whether any impurity in the zinc powder may have an impact on the yield of the reaction, zinc powders from different manufacturers with different purities were tested. The results in Table 2 show that different zinc powders gave the product in different yields.

Table 2 Reaction of zinc powder purchased from different sources^a

Entry	Zn Source	Purity (%)	Particle size (μm)	Yield of 2a ^b (%)
1	Sinopharm	>95	~20	84
2	J & K	98	~90	67
3	Acros	>98	~100	65
4	Alfa-Aesar	99.995	~140	58
5	Acros	99.999	>320	55

^aThe reaction was conducted with 1.0 mmol of **1a** and 1.05 mol of zinc powder in 5 mL of THF with a CO₂ balloon.
^bNMR yield.

However, we did consider that the difference was not caused by the purity but by the particle size of the zinc powder. The EDX (energy dispersive X-ray spectroscopy) results for the different zinc powders are shown in Fig. 1. It is obvious that the smaller the zinc powder size, the higher the yield.

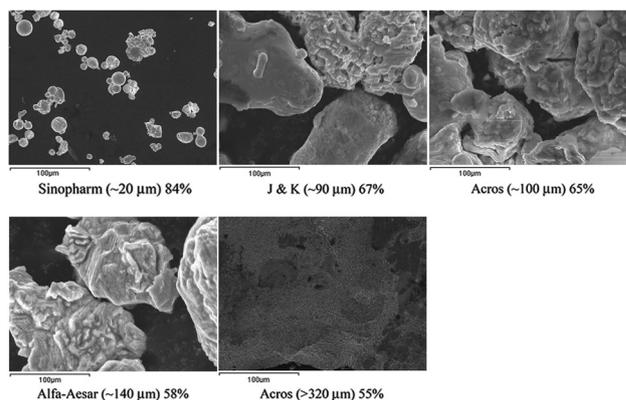


Fig. 1 EDX measurement of zinc powders from different suppliers and the corresponding yields of **2a**.

In order to further confirm the above conclusion, the purity of the zinc powder purchased from Sinopharm Chemical Reagent Co., Ltd was measured by XRF (X-ray fluorescence) after washing and drying sequentially with 3 M HCl, acetone and Et₂O (each 3 times). The purity was measured to be 99.94% and the confirmed impurities including Fe (0.03%) and Cr (0.03%) were caused by background information from the XRF studies. To further eliminate the possible catalytic effect of these impurities, 1 mol% each of these salts was added to the reactions with zinc powder purchased from J&K (purity: 98%) (Table 3). We didn't observe any obvious improvement in the yield.

Table 3 Study on the effect of impurities on the yield of **2a**^a

Entry	Additive (1 mol%)	Yield of 2a ^b (%)
1	—	68
2	Fe powder	61
3	FeCl ₂	54
4	FeCl ₃	53
5	Fe ₂ O ₃	70
6	Cr powder	65
7	CrCl ₃	41
8	Cr ₂ O ₃	68
9	CrCl ₃ -FeCl ₃ = 1 : 1	40

^aThe reaction was conducted with 0.01 mmol of additive, 1.0 mmol of **1a** and 1.05 mmol of zinc powder in 5 mL of THF with a CO₂ balloon.
^bNMR yield.

The scope of the reaction was then investigated under the optimized conditions with zinc powder from Sinopharm. Reactions with 2-aryl, 2-benzyl- and 2-alkyl-substituted allylic bromides **1a-g** were attempted and the corresponding acids were afforded in decent yields (Table 4, entries 1–5). Interestingly, substrates containing an enyne fragment **1f** and **1g** underwent

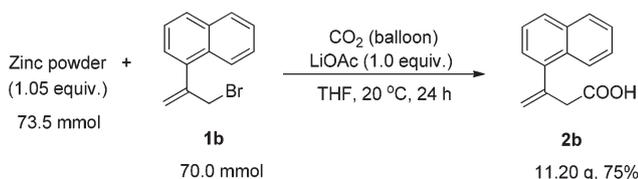
the reaction smoothly with no C=C bond isomerization observed although the yields were a little bit lower (Table 4, entries 6 and 7).

Table 4 Substrate scope of the reaction of 2-substituted allylic bromides^a

Entry	R	Yield ^b (%)
1	Ph (1a)	82 (2a)
2	α -naphthyl (1b)	79 (2b)
3	<i>p</i> -tol (1c)	80 (61) ^c (2c)
4	Bn (1d)	80 (2d)
5	ⁿ C ₆ H ₁₃ (1e)	83 (68) ^c (2e)
6	\equiv -Ph (1f)	49 (2f)
7	\equiv - ⁿ Bu (1g)	65 (2g)

^aThe reaction was conducted with 1.0 mmol of allylic halide and 1.05 mmol of zinc powder in 5 mL of anhydrous THF at room temperature with a CO₂ balloon. ^bIsolated yield. ^cThe reaction was conducted in the absence of LiOAc. ^dThe reaction was conducted in 5 mL of DMF.

The reaction was then conducted on a 70 mmol scale successfully to afford 11.20 g of **2b**, showing its practicality (Scheme 2).



Scheme 2 70 mmol scale reaction of **1b**.

To further investigate the generality of this reaction, the reaction of allylic bromides bearing halogen atoms at *ortho*-, *meta*- and *para*-positions of the 2-phenyl group was studied providing the corresponding carboxylic acids in good yields with an excellent chemoselectivity (Table 5, entries 1–5); a CF₃-group did not affect the reaction (Table 5, entry 6); gratifyingly, ester and cyano functionalities, which are not compatible with organolithium or Grignard reagents, have been preserved under the standard reaction conditions (Table 5, entries 7–8); although a ketone carbonyl group is not directly applicable, the reaction proceeded successfully after a simple protection with glycol (Table 5, entry 9).

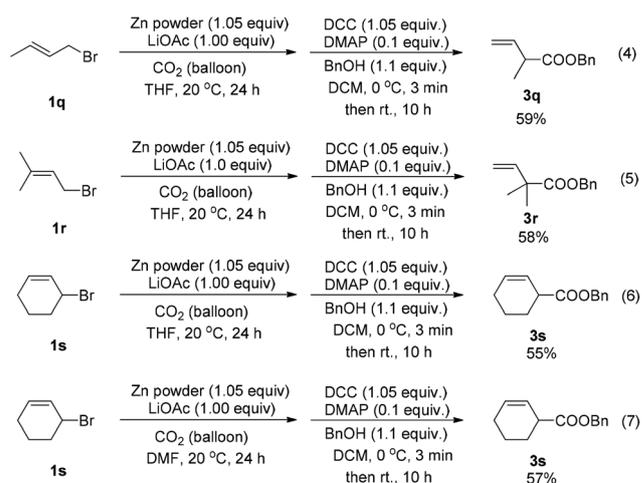
The reaction was attempted with several commercially available differently substituted allylic bromides followed by esterification with benzyl alcohol. For the 3-substituted allylic bromides such as crotyl bromide, the branched product **3q** was formed exclusively with no regioisomer detected as judged by ¹H NMR analysis of the crude reaction mixture [Scheme 3, eqn (4)]; an all-carbon quaternary center could even be formed in a moderate yield when starting from 3-methyl-2-butenyl

Table 5 Functional group tolerance of the zinc-mediated allylic carbonylation reaction^a

Entry	R	Yield ^b (%)
1	<i>o</i> -F (1h)	78 (2h)
2	<i>m</i> -F (1i)	74 (2i)
3	<i>p</i> -F (1j)	83 (45) ^c (2j)
4	<i>m</i> -Cl (1k)	73 (2k)
5	<i>p</i> -Cl (1l)	73 (2l)
6	<i>p</i> -CF ₃ (1m)	71 (2m)
7	<i>p</i> -COOEt (1n)	55 (2n) ^d
8	<i>m</i> -CN (1o)	55 (2o) ^d
9	<i>p</i> - (1p)	71 (2p)

^aThe reaction was conducted with 1.0 mmol of allylic halide and 1.05 mmol of zinc powder in 5 mL of anhydrous THF at room temperature with a CO₂ balloon. ^bIsolated yield. ^cThe reaction was conducted in the absence of LiOAc. ^dThe reaction was conducted in 5 mL of DMF.

bromide [Scheme 3, eqn (5)]; 2-cyclohexenyl bromide also worked [Scheme 3, eqn (6)]. Replacing THF with DMF as the solvent gave a similar yield [Scheme 3, eqn (7)].



Scheme 3 Reaction of commercially available allylic bromides.

Conclusions

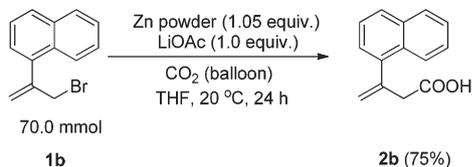
In summary, a direct carbonylation reaction of allylic bromides mediated by zinc powder with 1 atm of carbon dioxide provided by a balloon has been developed. A wide range of functional groups such as halogen, CF₃, ester, cyano, ketal are well tolerated and a specific regioselectivity for the formation of the branched products has been observed. The reaction could easily be conducted on 70 mmol scale, which indicates its

practicality. Further studies on the reaction mechanism and the role of LiOAc are still on-going in our group.⁸

reproducing the results of entry 6 in Table 2, entry 5 in Table 3 and eqn(5) in Scheme 3.

Experimental section

Synthesis of 3-(1-naphthyl)-3-butenic acid (**2b**)



To an oven-dried 1 L three-neck flask equipped with a magnetic stirring bar were added zinc powder (4.81 g, 73.5 mmol), LiOAc (4.62 g, 70.0 mmol), **1a** (17.30 g, 70.0 mmol) and 350 mL of THF under an argon atmosphere. The mixture was then frozen with a liquid nitrogen bath and the argon inside was completely replaced by a balloon of CO₂. The flask was then allowed to stand until the mixture thawed with the CO₂ balloon and was stirred at 20 °C for 24 h. The mixture was poured into 500 mL of 3 M aq. HCl and the aqueous layer was extracted with ethyl acetate (150 mL × 5). The combined organic layer was washed with 500 mL of brine, dried over anhydrous Na₂SO₄, filtrated and concentrated. The crude product was purified by column chromatography on silica gel to afford 11.20 g of **2b**⁷ (75%, eluent: petroleum ether–ethyl acetate = 5 : 1 → dichloromethane–methanol = 20 : 1) as a yellow solid: ¹H NMR (400 MHz, CDCl₃) δ 9.03 (bs, 1 H, COOH), 8.04–7.97 (m, 1 H, ArH) 7.87–7.80 (m, 1 H, ArH), 7.80–7.73 (m, 1 H, ArH), 7.50–7.32 (m, 4 H, ArH), 5.61 (s, 1 H, one proton of CH₂=), 5.34 (s, 1 H, one proton of CH₂=), 3.55 (s, 2 H, CH₂).

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Notes and references

- For recent reviews on CO₂ activation, see: (a) J. Louie, *Curr. Org. Chem.*, 2005, **9**, 605; (b) T. Sakakura, J. C. Choi and H. Yasuda, *Chem. Rev.*, 2007, **107**, 2365; (c) M. Aresta and A. Dibenedetto, *Dalton Trans.*, 2007, **36**, 2975; (d) A. Correa and R. Martin, *Angew. Chem., Int. Ed.*, 2009, **48**, 6201; (e) S. N. Riduan and Y. Zhang, *Dalton Trans.*, 2010, **39**, 3347; (f) C. Federsel, R. Jackstell and M. Beller, *Angew. Chem., Int. Ed.*, 2010, **49**, 6254; (g) K. Huang, C. Sun and Z. Shi, *Chem. Soc. Rev.*, 2011, **40**, 2435; (h) M. Cokoja, C. Bruckmeier, B. Rieger, W. A. Herrmann and F. E. Kuhn, *Angew. Chem., Int. Ed.*, 2011, **50**, 8510.
- (a) R. T. Sanderson, *J. Am. Chem. Soc.*, 1955, **77**, 4531; (b) L. E. Friedrich and R. Cormier, *J. Org. Chem.*, 1971, **36**, 3011; (c) G. Courtois and L. Miginiac, *J. Organomet. Chem.*, 1974, **69**, 1.
- M. Shi and K. M. Nicholas, *J. Am. Chem. Soc.*, 1997, **119**, 5057.
- (a) R. Johansson and O. F. Wendt, *Dalton Trans.*, 2007, **36**, 488; (b) M. T. Johnson, R. Johansson, M. V. Kondrashov, G. Steyl, M. S. G. Ahl-quist, A. Roodt and O. F. Wendt, *Organometallics*, 2010, **29**, 3521.
- (a) J. Wu, J. C. Green, N. Hazari, D. P. Hruszkewycz, C. D. Incarvito and T. J. Schmeier, *Organometallics*, 2010, **29**, 6369; (b) D. P. Hruszkewycz, J. Wu, N. Hazari and C. D. Incarvito, *J. Am. Chem. Soc.*, 2011, **133**, 3280; (c) J. Wu and N. Hazari, *Chem. Commun.*, 2011, **47**, 1069; (d) N. Hazari, D. P. Hruszkewycz and J. Wu, *Synlett*, 2011, **13**, 1793; (e) D. P. Hruszkewycz, J. Wu, J. C. Green, N. Hazari and T. J. Schmeier, *Organometallics*, 2012, **31**, 470.
- H. A. Duong, P. B. Huleatt, Q. Tan and E. L. Shuying, *Org. Lett.*, 2013, **15**, 4034.
- B. Miao and S. Ma, *Chem. Commun.*, 2014, **50**, 3285.
- For a brief discussion on the role of LiOAc, see ESI.†