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Nickel-Catalyzed Carboxylation of Organozinc Reagents with CO_2

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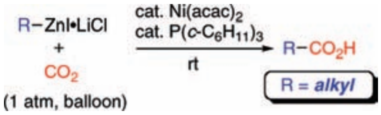
ABSTRACT



An efficient nickel catalyst system for the carboxylation of organozinc reagents with CO_2 under very mild conditions has been developed. The catalyst system complements the conventional methods and enables the direct synthesis of various saturated carboxylic acid derivatives from the corresponding alkylzinc reagents and CO_2.

Fixation of carbon dioxide has received significant attention from the viewpoint of organic synthesis as well as C1 chemistry that utilizes compounds containing only one carbon since CO_2 is a cheap and abundant source of carbon.[1] Reaction of carbon nucleophiles with CO_2 is one of the most fundamental processes for CO_2 fixation and is an attractive way to synthesize carboxylic acids. Highly reactive organometallic reagents such as organolithiums and Grignard reagents can react with the relatively unreactive CO_2. Organocopper and -manganese reagents are known to react with CO_2.[2] The reactions mentioned above are restricted in scope and generality, and the development of new methods for carboxylation of much milder organometallic reagents with CO_2 is strongly desired. In 2006, Iwasawa succeeded in rhodium-catalyzed carboxylation of aryl- and alkenylboronic esters with CO_2.[3] While the catalytic reaction provided an efficient route to a variety of benzoic and cinnamic acid derivatives, the corresponding alkylboronic esters could not participate in the reaction. Catalytic synthesis of saturated aliphatic carboxylic acids under mild conditions has still remained a challenge. Herein, we report nickel-catalyzed carboxylation of organozinc reagents with CO_2. The catalyst system allows alkylzinc reagents to serve as carbon nucleophiles toward CO_2, providing an efficient synthesis of various saturated carboxylic acid derivatives directly from CO_2 and the corresponding alkylmetals of mild reactivity.[4]

Treatment of a solution of hexylzinc iodide−lithium chloride complex (**1a**) in THF[5,6] with CO_2 (1 atm, balloon) in the presence of 5 mol % of $Ni(acac)_2$ and 10 mol % of $P(c\text{-}C_6H_{11})_3$ in THF at room temperature for 3 h afforded heptanoic acid (**2a**) in 70% yield (Table 1, entry 1).[7] The procedure was so simple that the catalytic reaction was practical. Interestingly, the addition of lithium chloride was

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[1] Reviews: (a) Behr, A. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 661–678. (b) Braunstein, P.; Matt, D.; Nobel, D. *Chem. Rev.* **1988**, *88*, 747–764. (c) Aresta, M.; Armor, J. N.; Barteau, M. A.; Beckman, E. J.; Bell, A. T.; Bercaw, J. E.; Creutz, C.; Dinjus, E.; Dixon, D. A.; Domen, K.; Dubois, D. L.; Eckert, J.; Fujita, E.; Gibson, D. H.; Goddard, W. A.; Goodman, D. W.; Keller, J.; Kubas, G. J.; Kung, H. H.; Lyons, J. E.; Manzer, L. E.; Marks, T. J.; Morokuma, K.; Nicholas, K. M.; Periana, R.; Que, L.; Rostrup-Nielson, J.; Sachtler, W. M. H.; Schmidt, L. D.; Sen, A.; Somorjai, G. A.; Stair, P. C.; Stults, B. R.; Tumas, W. *Chem. Rev.* **2001**, *101*, 953–996.

[2] Reactions of organocopper with CO_2: (a) Normant, J. F.; Cahiez, G.; Chuit, C.; Villieras, J. *J. Organomet. Chem.* **1973**, *54*, C53–C56. Reactions of organomanganese with CO_2: (b) Friour, G.; Cahiez, G.; Alexakis, A.; Normant, J. F. *Bull. Soc. Chim. Fr. II* **1979**, 515–517.

[3] Ukai, K.; Aoki, M.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2006**, *128*, 8706–8707.

[4] CO_2 fixation through oxidative cyclization of CO_2 and carbon−carbon unsaturated molecules on Ni: (a) Mori, M.; Takimoto, M. In *Modern Organonickel Chemistry*; Tamaru, Y., Ed.; Wiley-VCH: Weinheim, 2005; Chapter 7, pp 205−223. (b) Mori, M. *Eur. J. Org. Chem.* **2007**, 4981–4993. (c) Louie, J.; Gibby, J. E.; Farnworth, M. V.; Tekavec, T. N. *J. Am. Chem. Soc.* **2002**, *124*, 15188–15189. (d) Murakami, M.; Ishida, N.; Miura, T. *Chem. Commun.* **2006**, 643–645. (e) Murakami, M.; Ishida, N.; Miura, T. *Chem. Lett.* **2007**, 476–477. (f) Aoki, M.; Izumi, S.; Kaneko, M.; Ukai, K.; Iwasawa, N. *Org. Lett.* **2007**, *9*, 1251–1253.

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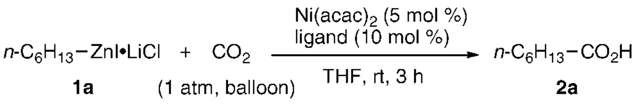
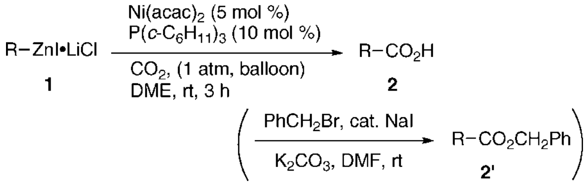
Table 1. Optimization Studies of Nickel-Catalyzed Carboxylation of Hexylzinc Iodide−Lithium Chloride Complex (**1a**) with CO_2[a]

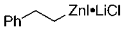
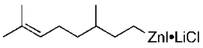
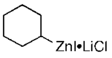
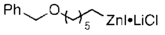
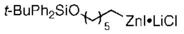
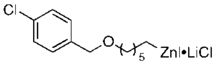
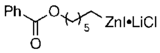
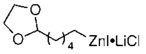
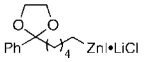


entry	ligand	^{1}H NMR yield of **2a** (%)
1	$P(c\text{-}C_6H_{11})_3$	70
2[b]	$P(c\text{-}C_6H_{11})_3$	5
3	P(*t*-Bu)$_3$	38
4	P(*n*-Bu)$_3$	31
5	DBU	27
6[c]	dtbpy	44
7[d]	$P(c\text{-}C_6H_{11})_3$	58

[a] A mixture of Ni(acac)$_2$ (0.025 mmol), ligand (0.050 mmol), and **1a** (0.70 M in THF solution, 0.71 mL, 0.50 mmol) was stirred in THF (5.0 mL) for 3 h under CO_2 atmosphere (1 atm, balloon). [b] With LiCl-free hexylzinc iodide instead of hexylzinc iodide−lithium chloride complex (**1a**). [c] In the presence of 5 mol % of dtbpy. [d] Ni(cod)$_2$ was used istead of Ni(acac)$_2$.

Table 2. Nickel-Catalyzed Carboxylation of Organozinc Reagents **1** with CO_2[a]



entry	1		isolated yield of **2** or **2'** (%)[b]
1[c]	*n*-C_6H_{13}−ZnI•LiCl	**1a**	**2a'**, 62 (70)
2		**1b**	**2b**, 60 (74)
3		**1c**	**2c'**, 62 (69)
4		**1d**	**2d**, 50 (69)
5[d]		**1e**	**2e'**, 63 (75)
6[e]		**1f**	**2f'**, 41 (51)
7		**1g**	**2g'**, 68 (69)
8		**1h**	**2h'**, 67 (76)
9[e,f]		**1i**	**2i**, (79)[g]
10[h]		**1j**	**2j'**, 36 (50)

[a] A mixture of Ni(acac)$_2$ (0.025 mmol), $P(c\text{-}C_6H_{11})_3$ (0.050 mmol), and **1** (ca. 0.7 M in THF solution, 0.50 mmol) was stirred in DME (5.0 mL) for 3 h under CO_2 atmosphere (1 atm, balloon). [b] Yields of **2** determined by ^{1}H NMR analysis are in parentheses. [c] In THF. [d] Reaction time was 8 h. [e] Reaction time was 6 h. [f] At 50 °C. [g] The product was too unstable to isolate. [h] The acetal protection was removed upon work up with 1.0 M aq HCl.

essential for the carboxylation. Without lithium chloride, the desired carboxylic acid was obtained in only 5% yield (entry 2).[8] The effects of other ligands were also examined. The use of P(*t*-Bu)$_3$ and P(*n*-Bu)$_3$ instead of $P(c\text{-}C_6H_{11})_3$ failed to furnish **2a** in satisfactory yield (entries 3 and 4). Amine ligands such as 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) and 4,4′-di(*tert*-butyl)-2,2′-bipyridine (dtbpy), which were frequently employed as supported ligands in nickel-mediated CO_2 fixation,[4] also showed lower activities (entries 5 and 6). In the absence of the nickel catalyst, no reaction took place. We could use Ni(cod)$_2$ as the precursor of the catalyst, albeit with a lower yield (entry 7).

With the optimized conditions in hand, we performed the carboxylation of an array of alkylzinc reagents (Table 2).[9] Isolation of highly polar carboxylic acids **2** often resulted in significantly lower yields than those determined by ^{1}H NMR analysis of the crude products, and most of the products were isolated as the corresponding benzyl esters **2′**. The larger phenylethylzinc reagent **1b** reacted with CO_2 smoothly to furnish **2b** in good yields (entry 2). The olefin moiety of **1c** did not interfere with the reaction (entry 3). To our delight, the reactions of not only primary alkylzincs but also secondary ones were carried out. Cyclohexylzinc iodide−lithium chloride complex (**1d**) was converted to cyclohexanecarboxylic acid (**2d**) in 69% yield (entry 4). By taking advantage of high functional group compatibility of organozinc reagents, alkylzincs bearing various functional groups were prepared and subjected to the carboxylation reaction. The silyl and benzyl ether moieties were tolerated under the reaction conditions (entries 5 and 6). The carbon−chloride bond of **1g** did not suppress the formation of **2g** despite its conceivable oxidative addition to the zerovalent nickel (entry 7). It is noteworthy that the reaction of **1h** with CO_2 gave **2h** in good yield, leaving the ester linkage untouched (entry 8). Although preparation of alkylzinc reagents having aldehyde and ketone groups was quite difficult, the corresponding acetal-protected reagents were readily accessible and reacted with CO_2 without any difficulties (entries 9 and 10).

We are tempted to assume the reaction mechanism as follows (Scheme 1). A zero-valent nickel species **3** is initially formed by reduction of Ni(acac)$_2$ with organozinc reagent **1**. The active Ni(0) **3** reacts with CO_2 to produce η^2-coordinated complex **4**.[10] The subsequent transmetalation with **1**[11] followed by rapid reductive elimination yields **6** along with the starting nickel complex **3** to complete the catalytic cycle. Protonolysis of **6** upon workup furnishes

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(5) (a) Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 6040–6044. (b) Ren, H.; Dunet, G.; Mayer, P.; Knochel, P. *J. Am. Chem. Soc.* **2007**, *129*, 5376–5377. (c) Boudet, N.; Sase, S.; Sinha, P.; Liu, C.-Y.; Krasovskiy, A.; Knochel, P. *J. Am. Chem. Soc.* **2007**, *129*, 12358–12359.

(6) LiBr worked as well (70% yield), but LiI was inferior (41% yield).

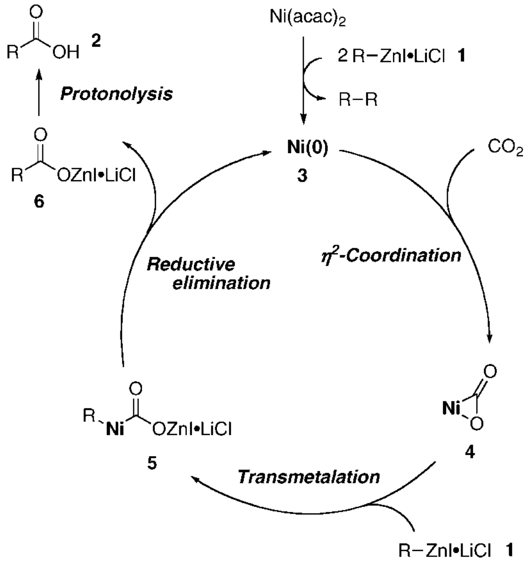
(7) An addition of TMEDA completely inhibited the reaction.

(8) Preparation of LiCl-free alkylzinc iodide: (a) Knochel, P.; Yen, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390–2392.

(9) Except for the reaction of **1a**, the use of DME as a solvent gave better results.

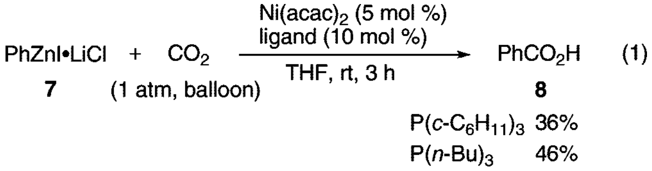
(10) Aresta, M.; Nobile, C. F.; Albano, V. G.; Forni, E.; Manassero, M. *J. Chem. Soc., Chem. Commun.* **1975**, 636–637.

Scheme 1. Plausible Reaction Mechanism



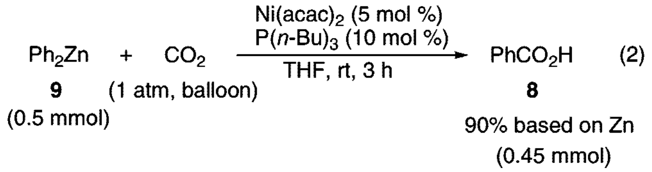
carboxylic acid **2**. Strongly electron-donating tricyclohexylphosphine increased the electron density of the oxygens of **4**, which would allow for the following transmetalation. The bulky tricyclohexylphosphine would also promote the reductive elimination without suffering from β-hydride elimination. Although further investigation is required for the clarification of the exact role of lithium chloride, it could change the association state of organozinc iodide via its coordination to the zinc center, leading to the monomeric species, which could more readily undergo the transmetalation.[12]

Finally, we applied the nickel catalyst system to the carboxylation of phenylzinc iodide−lithium chloride complex (**7**)[5a] with CO_2 (eq 1). On exposure of **7** to the standard reaction conditions, benzoic acid (**8**) was obtained in 36% yield. The use of P(n-Bu)$_3$ instead of P(c-C_6H_{11})$_3$ was found to improve the yield to 46%. However, any changes of reaction parameters such as solvent, temperature, and additive gave no positive effect on yield. We then turned our attention to diphenylzinc (**9**) (eq 2). Gratifyingly, the reaction of **9** with CO_2 proceeded smoothly to form the desired carboxylic acid in 90% yield based on zinc.[13] The result shows the high potential of the catalyst system, although further modifications are essential.



$$\underset{\mathbf{7}}{\mathrm{PhZnI{\bullet}LiCl}} + \underset{\text{(1 atm, balloon)}}{\mathrm{CO_2}} \xrightarrow[\text{THF, rt, 3 h}]{\text{Ni(acac)}_2\text{ (5 mol \%)}\\ \text{ligand (10 mol \%)}} \underset{\mathbf{8}}{\mathrm{PhCO_2H}} \quad (1)$$

P(c-C_6H_{11})$_3$ 36%
P(n-Bu)$_3$ 46%



$$\underset{\substack{\mathbf{9}\\ \text{(0.5 mmol)}}}{\mathrm{Ph_2Zn}} + \underset{\text{(1 atm, balloon)}}{\mathrm{CO_2}} \xrightarrow[\text{THF, rt, 3 h}]{\text{Ni(acac)}_2\text{ (5 mol \%)}\\ \text{P(}n\text{-Bu)}_3\text{ (10 mol \%)}} \underset{\mathbf{8}}{\mathrm{PhCO_2H}} \quad (2)$$

90% based on Zn
(0.45 mmol)

In conclusion, we have found an efficient nickel catalyst system for the carboxylation of organozinc reagents, in particular alkylzincs, with CO_2. The catalyst system complements the rhodium-catalyzed process[3] and provides a new access to highly functionalized saturated carboxylic acid derivatives from CO_2 under mild conditions.

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Supporting Information Available: Experimental details and characterization data of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Similar transmetalations between η^2-coordinated nickel complexes with aldehyde and organometallic reagents were suggested. (a) Biswas, K.; Prieto, O.; Goldsmith, P. J.; Woodward, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 2232–2234. (b) Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2005**, *7*, 4689–4691. (c) Hirano, K.; Yorimitsu, H.; Oshima, K. *Adv. Synth. Catal.* **2006**, *348*, 1543–1546. (d) Arao, T.; Kondo, K.; Aoyama, T. *Tetrahedron Lett.* **2007**, *48*, 4115–4117.

(12) Knochel proposed a similar effect of lithium chloride in a halogen/magnesium exchange reaction. (a) Krasovskiy, A.; Knochel, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 3333–3336.

(13) In the case of the reaction of phenylzinc iodide-lithium chloride complex (**7**), diphenylzinc (**9**) would be generated in situ through Schlenk equilibrium and participate in the reaction.