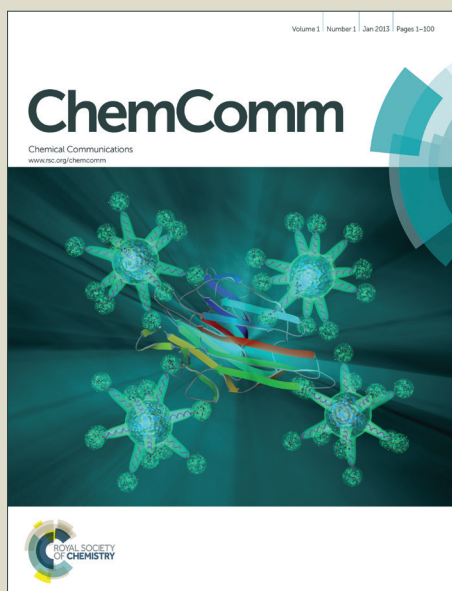


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Nickel-Catalysed Carboxylation of Organoboronates

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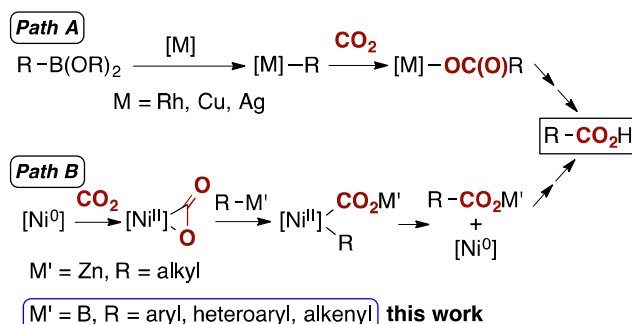
A nickel/*N*-heterocyclic carbene (NHC) catalysed carboxylation of aryl-, heteroaryl- and alkenylboronates, affording the corresponding carboxylic acids, has been developed. This transformation proceeds under one atmosphere of CO₂ with a broad range of substrates and exhibits good functional group compatibility.

Carbon dioxide (CO₂) is one of the most promising carbon sources for the production of fine chemicals as it is abundant, non-toxic, cheap and renewable.¹ Amongst the numerous reports regarding CO₂ fixation mediated by metal centres, significant efforts have targeted the development of efficient and direct carboxylation protocols.² Highly reactive organometallic reagents, such as organolithium and Grignard reagents, are the historical, yet still typical starting materials for nucleophilic carboxylation, since they are reactive enough to overcome the inherent thermodynamic stability of CO₂. However, their narrow functional group compatibility hampers their general and practical use. Consequently, carboxylation using a widely adaptable reagent is highly desirable.^{3–9} In the last decade, the transition metal catalysed carboxylation of organoboronates with CO₂ has been achieved using Rh,³ Cu⁴ and Ag⁵ catalysts (Scheme 1, path A).

Yorimitsu, Oshima and Dong have described a nickel-catalysed carboxylation employing organozinc reagents with CO₂, and proposed that an Aresta-type complex was involved in the catalytic cycle (Scheme 1, path B, M'=Zn).^{7,10} While these reactions were restricted mostly to alkylzinc reagents,¹¹ nickel-based systems offer fascinating possibilities in terms of adopting a mechanism distinct from those reported with other transition metals (Scheme 1). Nickel catalysis typically proceeds through oxidative cyclization of CO₂ by zero-valent nickel, followed by a transmetalation and reductive elimination (Scheme 1, path B). Other transition metal catalysts normally involve transmetalation followed by insertion of CO₂ into a

metal–carbon bond without a change in metal oxidation state (Scheme 1, path A).

Herein, we report a methodology for the carboxylation of organoboronates under one atmosphere of CO₂ catalysed by a well-defined nickel pre-catalyst having a specific *N*-heterocyclic carbene ligand (Scheme 1, path B, M'=B). This reaction presents broad functional group compatibility and simple reaction conditions. Moreover, to the best of our knowledge, the nickel-catalysed coupling of organoboron reagents with CO₂ has not been reported to date.



Scheme 1. Two distinct pathways for the metal-catalysed carboxylation of less-nucleophilic organometallic reagents.

Very recently, we reported the synthesis and characterization of novel [Ni(NHC)(allyl)Cl] complexes, bearing the flexible yet bulky NHC ligands IPr* and IPr*^{OMe}; these complexes are useful catalysts for C–N and C–S coupling reactions.¹² Although they generate Ni(0) active species easily with the assistance of the steric pressure of the bulky NHC ligand and the labile η³-allyl moiety, these complexes possess good stability. In this context, we began to explore the possibility of an efficient carboxylation methodology using this catalytic nickel system in conjunction with organoboron reagents and CO₂ as the reaction partners.

We began our survey by screening the reactivity of nickel precatalysts **1a-g**, as depicted in Table 1. [Ni(NHC)(allyl)Cl] complexes bearing less sterically demanding NHCs (IPr, SIPr, IMes and SIMes, see Figure 1 for key structural features of NHC used in this study) showed poor to moderate reactivities (entries 1–4). For example, the reaction of boronate **2a** using [Ni(IPr)(allyl)Cl] as precatalyst gave the carboxylation product **3a** in only 7% NMR conversion.¹³ The catalytic activity was drastically shifted by a judicious selection of the NHC ligand. Indeed, the reactions using the bulkier IPr*-based ligands (IPr* and IPr*^{OMe}) afforded the corresponding carboxylic acids quantitatively (entries 5 and 9). At 80 °C, the IPr* ligand showed higher reactivity than IPr*^{OMe} (entries 6 and 10). The effect of the steric hindrance may very well result in an improvement of the stability of the active species or in the acceleration of one of the catalytic steps. Other observations concerning the optimized reaction conditions are to be noted: a 5 mol % catalyst loading is required for excellent conversion (entry 5 vs. 7); the analogous nickel complex with a Cp moiety, instead of an allyl group, showed no activity (entry 8)^{12a}, a catalytic species prepared *in situ* from [Ni(cod)₂] and IPr* led to high conversion (entry 11),¹⁴ ethers could be used but polar or chlorinated solvents gave no conversion (entries 12–15); despite its ability to activate boron reagents, CsF displays no reactivity as a base, (entry 16).^{3,4a} The use of hydroxides and carbonates also gave no conversion (entries 19 and 20). When a sub-stoichiometric amount of KO^tBu was used, the product was formed sub-stoichiometrically (entry 17) and carboxylation did not proceed in the absence of the nickel pre-catalyst (entry 18).

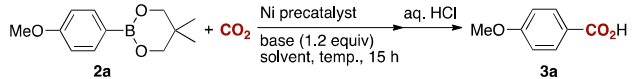
Importantly, possible side-reactions such as homocoupling or protodeborylation were not observed and the starting boronate was the only recovered material when reactions did not proceed efficiently to product. Other arylboron reagents such as boronic acids, pinacolates, and potassium trifluoroborates were tested but resulted in almost no reaction.^{13,15} Thus, conditions employed in entry 5 were selected as the optimum reaction settings.

We next evaluated the carboxylation of a range of aryl- and heteroarylboronates with CO₂ under these optimized conditions. As shown in Table 2, *p*-anisic acid (**3a**), benzoic acid (**3b**) and *p*-toluic acid (**3c**) were obtained in excellent yields (entries 1–3). In addition, this nickel-catalysed carboxylation tolerated a variety of functional groups at the *para* position of the arylboronate reagent: examples include silyl ether, CF₃ and tertiary amino groups, as well as halides (entries 4–8).

Notably, electrophilic and base-sensitive functionalities were also compatible, giving the corresponding benzoic acid derivatives **3i** (90%) and **3j** (97%), respectively, while leaving the ester and nitrile moieties untouched (entries 9 and 10). This transformation was also applicable to both electron-rich and electron-deficient substituents in the *meta* position (entries 11–14). The current limitation of the method lies with the poor tolerance of *ortho*-substituted arylboronates. For example, the reaction of the neopentylglycolate of *o*-tolylboronic acid

resulted in no reaction. Although the reaction proved to be sensitive to proximal steric bulk, *o*-anisic acid (**3o**) and 2-fluorobenzoic acid (**3p**) could be synthesised (92% and 81% respectively) (entries 15 and 16). Heteroaromatic boronate **2q** reacted with CO₂ to provide 3-thenoic acid (**3q**) in 88% yield with 10 mol % catalyst (entry 17). Boronate **2r** was more reactive, affording 2-furoic acid (**3r**) in 93% yield (entry 18). The protocol was successfully extended to alkenylboron reagents (Scheme 2).¹⁶ Boronates having a conjugated π -system **4a** and non-conjugated **4b** reacted efficiently to afford the corresponding α,β -unsaturated carboxylic acids **5a** and **5b** in 85% and 92% yield, respectively. *Exo*-olefinic boronate **4c** also showed good reactivity (75%).

Table 1. Nickel-Catalysed Carboxylation of **2a**.^a



entry	Ni pre-catalyst	T(°C)	Solvent	y ^b (%)
1	[Ni(IPr)(all)Cl] (1a)	100	toluene	7
2	[Ni(SIPr)(all)Cl] (1b)	100	toluene	45
3	[Ni(IMes)(all)Cl] (1c)	100	toluene	15
4	[Ni(SIMes)(all)Cl] (1d)	100	toluene	10
5	[Ni(IPr*)(all)Cl] (1e)	100	toluene	quant.
6	1e	80	toluene	56
7 ^c	1e	100	toluene	15
8	[Ni(IPr*)(Cp)Cl] (1f)	100	toluene	0
9	[Ni(IPr* ^{OMe})(all)Cl] (1g)	100	toluene	quant.
10	1g	80	toluene	26
11 ^d	[Ni(cod) ₂]/IPr*	100	toluene	quant.
12	1e	80	dioxane	37
13	1e	80	CPME	47
14	1e	80	DMA	0
15	1e	80	DCE	0
16 ^e	1e	100	toluene	0
17 ^f	1e	100	toluene	10
18 ^g	–	100	toluene	0
19 ^h	1e	100	toluene	0
20 ⁱ	1e	100	toluene	0

^aReaction conditions: **2a** (0.2 mmol, 1.0 equiv), CO₂ (1 atm), Ni precatalyst (5 mol %), KO^tBu (0.24 mmol), solvent (1.0 mL), 15 h. ^bYield determined by ¹H NMR spectroscopic analysis of crude product after acidic work up using 1,2-diphenylethane as an internal standard; average of two runs. ^cwith 1.0 mol % of **1e**. ^dwith 5.0 mol % of [Ni(cod)₂] and 6.0 mol % of IPr*. ^ewith 0.24 mmol of CsF instead of KO^tBu. ^fwith 0.03 mmol of KO^tBu. ^gwithout Ni precatalyst. ^h0.24 mmol of KOH used instead of KO^tBu. ⁱ0.24 mmol of K₂CO₃ used instead of KO^tBu.

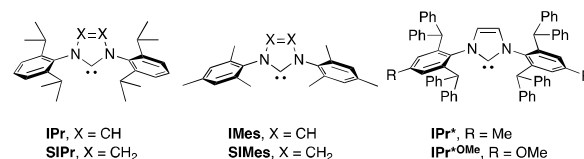


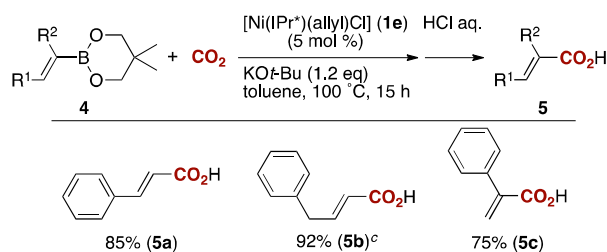


Figure 1. Structures of NHC ligands used in this study.

Table 2. Substrate Scope of the Nickel-Catalysed Carboxylation.^a

entry	product	Yield (%) ^b
$\text{R-B} \begin{array}{c} \diagup \text{O} \\ \text{O} \\ \diagdown \text{O} \end{array} + \text{CO}_2 \xrightarrow[\text{KO}^t\text{Bu (1.2 eq), toluene, 100 }^\circ\text{C, 15 h}]{[\text{Ni}(\text{IPr}^*)(\text{allyl})\text{Cl}] \text{ (1e) (5 mol \%), HCl aq.}} \text{R-CO}_2\text{H} \text{ (3)}$		
1	R = OMe (3a)	96
2	R = H (3b)	99
3	R = Me (3c)	99
4	R = OTBDMS (3d)	90
5	R = NMe ₂ (3e)	84
6	R = F (3f)	96
7	R = Cl (3g)	83
8	R = CF ₃ (3h)	97
9 ^c	R = CO ₂ Me (3i)	90
10	R = CN (3j)	97
11	R = OMe (3k)	96
12	R = F (3l)	78
13	R = CF ₃ (3m)	96
14	R = CO ₂ Me (3n)	90
15	R = OMe (3o)	92
16	R = F (3p)	81
17 ^c	R =  (3q)	88
18	R =  (3r)	93

^a Reaction conditions: **2** (0.4 mmol), CO₂ (1 atm), **1e** (5 mol %), and KO^tBu (0.48 mmol) in toluene (2.0 mL) at 100 °C for 15 hours. ^bYield of isolated product; average of two runs. ^c10 mol % **1e**.

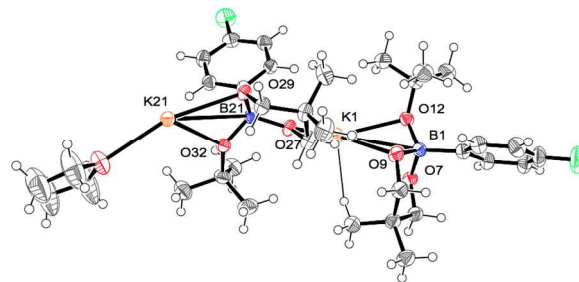
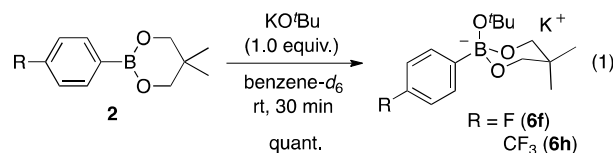
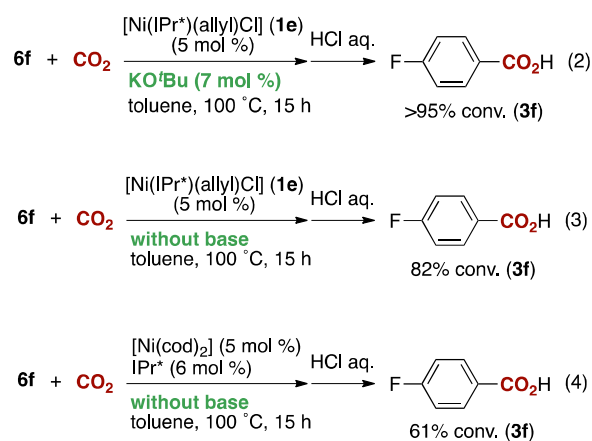
Table 2. Nickel-Catalysed Carboxylation of Alkenylboronates **4**.^{a,b}

^aReaction conditions: **4** (0.4 mmol), CO₂ (1 atm), **1e** (5 mol %), and KO^tBu (0.48 mmol) in toluene (2.0 mL) at 100 °C for 15 hours unless otherwise noted. ^bYield of isolated product; average of two runs. ^c10 mol % **1e**.

As there is such a profound influence of the boron reagents, initial studies focused on the alkoxide base and how it could modify the boron reagent. It was originally thought that the role of KO^tBu was to activate the boronates for transmetalation. Indeed, the reaction between **2** and KO^tBu gave the corresponding aryltrialkoxoborate **6**, quantitatively (eq. 1, see ESI for more details). This boron quaternization proceeds smoothly at room temperature and reached completion within 30 minutes as monitored by NMR spectroscopy.^{13,17} The atom connectivity in **6f** was unambiguously confirmed by X-ray analysis on single crystals (Figure 2).

The reactivity of the borate **6f** with CO₂ under nickel catalysis was then examined. Isolated **6f** was treated with CO₂ in the

presence of 5 mol % of **1e** and 7 mol % of KO^tBu (eq 2), and the reaction afforded >95% conversion to **3f**. In addition, the reaction proceeds with slightly lower reactivity in the absence of KO^tBu (eq 3). If a nickel(0) precursor is used, entirely base-free conditions can be achieved (61% conversion, eq 4).

**Figure 2.** Molecular structure of **6f**: (**6f**)₂·THF.

These results support our hypothesis that organoborates **6** are the reactive species in this reaction.

Conclusions

In summary, we have developed a novel Ni-catalysed strategy for CO₂ incorporation using organoboron reagents. IPr^{*}-based ligands show exceptional reactivity for this transformation. Substituted boronates with various functionalities are easily accessible and can be coupled with CO₂ using nickel catalysis. The substrate scope is complementary to the reaction of organozinc reagents, which is mainly suitable for alkylzinc reagents. Ongoing mechanistic and catalytic studies are aimed

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at understanding the critical role of the ligand in this and related catalytic transformations.

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†Electronic Supplementary Information (ESI) available: experimental details and characterization data for all new compounds and all products (PDF) See DOI: 10.1039/c000000x/

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