COMMUNICATION

Direct carboxylation of simple arenes with CO_2 through a rhodium-catalyzed C–H bond activation†
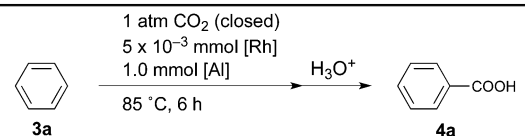
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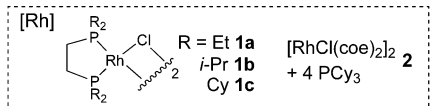
Direct carboxylation of simple arenes under atmospheric pressure of CO_2 is achieved through a rhodium-catalyzed C–H bond activation without the assistance of a directing group. Various arenes such as benzene, toluene, xylene, electron-rich or electron-deficient benzene derivatives, and heteroaromatics are directly carboxylated with high TONs.

The direct carboxylation reaction of simple arenes with carbon dioxide (CO_2), which is an abundant and potentially renewable carbon source, has still remained a great challenge due to low reactivity of CO_2.[1–3] Recently several groups developed gold(I) or copper(I) hydroxide-catalyzed carboxylation of arenes without a directing group; however, the substrates were limited to electron-deficient arenes having a rather acidic C–H bond since the key arylmetal intermediates were generated through deprotonation by the basic metal hydroxides.[4] On the other hand, we reported rhodium(I)-catalyzed direct carboxylation of phenylpyridine derivatives via chelation-assisted C–H bond activation. Although this reaction showed no limitation concerning the acidity of the C–H bond, a pyridine moiety was required to promote the reaction effectively.[5] Additionally, the two representative stoichiometric reactions for carboxylation of simple arenes with CO_2, that is, the base-promoted Kolbe–Schmitt reaction of phenol derivatives and the aluminum-promoted Friedel–Crafts type carboxylation, also have some drawbacks of substrate limitation and necessity of high pressure of CO_2.[6–8] Therefore, development of a new direct carboxylation reaction of simple arenes with wide generality is highly desired. Herein we report a direct carboxylation of simple arenes under atmospheric pressure of CO_2 through a rhodium-catalyzed C–H bond activation without the assistance of a directing group.[9] The reaction is applicable to both electron-rich and -deficient arenes, demonstrating promising utility as a new CO_2-fixation reaction.

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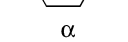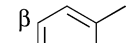
To realize the direct carboxylation of simple arenes, we started investigations utilizing the combination of a rhodium catalyst and a methylaluminum reagent as a stoichiometric reductant based on our previous success in the chelation-assisted carboxylation of phenylpyridine derivatives.[5] However, the rhodium catalyst with a bulky monodentate phosphine ligand, which was the active catalyst in our previous report, was totally ineffective for the direct carboxylation of benzene under various conditions. Extensive screening of the ligand and reaction conditions revealed that isolated 1,2-bis(dialkylphosphino)ethane–rhodium(I) chloride complexes **1** showed catalytic activity for the carboxylation of benzene in the presence of $AlMe_3$ as a stoichiometric reductant. A small amount of benzoic acid was obtained with a catalyst turnover number (TON) of 2.8 by treatment of rhodium complex **1c** bearing 1,2-bis(dicyclohexylphosphino)ethane (dcype) with an excess amount of $AlMe_3$ (100 equiv. to Rh) in a mixture of benzene and DMA (*N,N*-dimethylacetamide) (20 : 1) as the solvent

Table 1 Optimization of reaction conditions

Entry	[Rh]	[Al]	Cosolvent	TON[d]
1	**1a**	$AlMe_3$	DMA[b]	0
2	**1b**	$AlMe_3$	DMA[b]	1.0
3	**1c**	$AlMe_3$	DMA[b]	2.8
4	**2**	$AlMe_3$	DMA[b]	0
5	**1c**	$AlMe_{1.5}(OEt)_{1.5}$[a]	DMA[b]	29
6	**1c**	$AlMe_{1.5}(OEt)_{1.5}$[a]	DMA + TMU[c]	40
7	**1c**	$AlMe_2(OEt)$	DMA + TMU[c]	34
8	**1c**	$AlMe_{1.5}(OEt)_{1.5}$[a]	—	3.2

[a] 1.1 mmol of the Al reagent was used. See also ref. 10. [b] 0.1 mL. [c] 0.1 mL DMA + 6 μL TMU. [d] Calculated based on NMR yield. Effects of other factors (other co-solvents, concentrations) are summarized in the ESI.

at 85 °C for 6 h (entry 3, Table 1). The TON decreased when analogous complexes **1a** and **1b** bearing 1,2-bis(diethyl- or diisopropylphosphino)ethane (depe or dippe) were employed as catalysts (entries 1 and 2), suggesting the critical effect of bulkiness of alkyl substituents probably on stabilization of catalytically active, coordinatively unsaturated rhodium species. The bidentate structure was also essential as two molar bulky monodentate phosphine, PCy$_3$, was not effective at all (entry 4). Furthermore, use of AlMe$_{1.5}$(OEt)$_{1.5}$ instead of AlMe$_3$ dramatically improved the efficiency of the reaction,[10] achieving a TON of 29 in benzene–DMA and of 40 by further addition of TMU (1,1,3,3-tetramethylurea), which is believed to stabilize coordinatively unsaturated Rh(I) species through coordination, as a second cosolvent (entries 5 and 6).[11] AlMe$_2$(OEt) was slightly less effective than AlMe$_{1.5}$(OEt)$_{1.5}$ (entry 7). It should be noted that the reaction in the absence of DMA gave poor results (TON = 3.2, entry 8), indicating that polar cosolvents play important roles.[12]

Direct carboxylation of various simple arenes proceeded successfully under the optimized reaction conditions (Table 2). Simple monosubstituted arenes such as toluene **3b** and cumene **3c** were carboxylated to give toluic acid **4b** and cumic acid **4c** as a mixture of regioisomers with good TONs (TON = 18 for **4b** and 22 for **4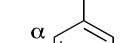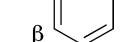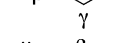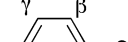c**) at 120 and 145 °C (entries 2 and 3). The steric repulsion of the bulky isopropyl group suppressed the carboxylation at the *ortho*-position. Among three isomers of xylene, the TON of *o*-xylene **3d** was the highest (TON = 46) while that of *m*- and *p*-xylenes decreased to 33 and 22, also indicating the importance of steric accessibility for efficient C–H activation (entries 4–6). The regioselectivities in these reactions are clearly different from those in aluminum-mediated Friedel–Crafts type carboxylation of arenes (*e.g.* α:β:γ = 7:3:90 for **3b** and 0:100:0 for **3e**, as shown in Olah's report[7a]), ruling out the possibility of the electrophilic substitution pathway promoted by aluminum species. Importantly, the reaction was also applicable to a solid arene such as naphthalene **3h** by using cyclooctane as an inert solvent to give a mixture of 1- and 2-naphthoic acids **4h** with a TON of 16 (entry 8).

Furthermore, good compatibility of this reaction with various functional groups was demonstrated. Arenes having fluorine (**3i**), chlorine (**3p**), silicon (**3k**), and trifluoromethyl (**3j** and **3n**) substituents were successfully carboxylated to afford the corresponding benzoic acid derivatives with a high TON of up to 48 (entries 9–11, 14, and 16).[13] Regioselective formation of 3,5-bis(trifluoromethyl)benzoic acid **4n** with a high TON is noteworthy in the reaction of **3n** (entry 14). The reactions of electron-rich arenes such as anisole **3l**, *N,N*-dimethylaniline **3m**, and benzo-1,4-dioxane **3o** also proceeded successfully (entries 12, 13, and 15), although the TON slightly decreased probably due to partial inhibition by coordination of the oxygen and nitrogen atoms to the catalyst.[14] Moreover, this reaction is applicable not only to benzene derivatives but also to heteroaromatic compounds. Carboxylation of benzofuran **3q** and 1-methylindole **3r** proceeded at 2-positions selectively, which are hardly carboxylated by Lewis acid- or base-promoted carboxylation protocols (entries 17 and 18).[7,8,15] Interestingly, ferrocene **3s** showed exceptionally high reactivity, and the TON reached 60 (entry 19). These results clearly demonstrate several advantages and characteristics of this reaction as follows. (1) The reaction is

Table 2 Carboxylation of benzene derivatives

Entry	Arene		Temp./°C	TON[a]	Regio[b] (α:β:γ)
1		R = H **3a**	85	**4a** 37	—
2		R = Me **3b**	120	**4b** 18	17:57:26
3		R = ^{i}Pr **3c**	145	**4c** 22	0.67:33
4		**3d**	145	**4d** 46	12:88:–
5		**3e**	145	**4e** 33	0:33:67
6		**3f**	145	**4f** 22	—
7		**3g**	145	**4g** 25	23:77:–
8[c]		**3h**	145	**4h** 16	46:54:–
9		R = F **3i**	85	**4i** 39	59:29:12
10		R = CF$_3$ **3j**	120	**4j** 44	0:77:23
11		R = SiMe$_3$ **3k**	145	**4k** 39	0:64:36
12		R = OMe **3l**	145	**4l** 15	23:54:23
13		R = NMe$_2$ **3m**	145	**4m** 9	0:56:44
14		**3n**	145	**4n** 48	0:0:100
15[d]		**3o**	145	**5o** 22	55:45:–
16		**3p**	145	**4p** 15	49:51:–
17[d]		**3q**	145	**5q** 12	100:0:–
18[d]		**3r**	145	**5r** 21[e]	86:14:–
19[c,d]		**3s**	145	**5s** 60[f]	—

[a] Calculated based on the isolated yield of products. [b] Determined by ^{1}H NMR. [c] 5.0 mmol of an arene was used in 2.0 mL of cyclooctane. [d] Isolated after Me-esterification. [e] Small amounts of other regioisomers were detected by GC-MS. The TON was calculated based on the yield of α- and β-isomers. [f] Small amounts of dicarboxylated products were detected.
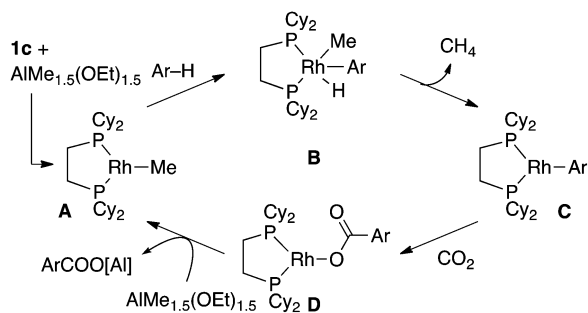
Scheme 1 Proposed mechanism.
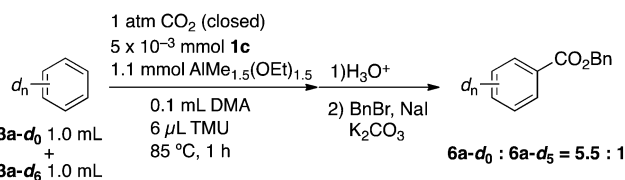
Scheme 2 KIE experiment.

applicable to both electron-rich and -deficient arenes whereas previously reported acid- or base-promoted reactions are limited to either one of them. (2) Preferential carboxylation with regio-selectivities different from those previously reported is possible. (3) The reaction proceeds under atmospheric pressure of CO_2 whereas Al-mediated electrophilic carboxylation requires high pressure. Therefore, this rhodium-catalyzed protocol demonstrates a new approach toward direct carboxylation of simple arenes utilizing CO_2 as a C1 source.

A tentatively proposed reaction mechanism is shown in Scheme 1. The reaction starts with generation of a methyl-rhodium(I) complex **A** from **1c** and $AlMe_{1.5}(OEt)_{1.5}$ followed by oxidative addition of an sp^2 C–H bond of a simple arene to **A**, giving an aryl(hydride)(methyl)rhodium(III) intermediate **B**. Reductive elimination of methane from **B** affords a highly reactive arylrhodium(I) complex **C**.[16] Nucleophilic addition of **C** to CO_2 gives a rhodium(I) benzoate complex **D**,[17] which is converted to methylrhodium(I) **A** through transmetallation with $AlMe_{1.5}(OEt)_{1.5}$.[18]

To obtain mechanistic insights, competitive reactions of C_6H_6 and C_6D_6 were examined in the same vessel. After esterification with benzyl bromide, the KIE value ([6a-d_0]/[6a-d_5]) at the point of 1 h reaction time was estimated to be 5.5, which suggests that the C–H bond activation step is the rate-determining step (Scheme 2).[19]

In conclusion, we have developed a novel method for direct carboxylation of simple arenes with 1 atm CO_2 through a rhodium-catalyzed C–H bond activation without the assistance of a directing group. This reaction demonstrates wide generality and intriguing regioselectivity, which were not achieved by using previous acid- or base-promoted protocols. These findings are highly promising to expand synthetic utility of the direct carboxylation of simple arenes even though a stoichiometric amount of aluminum reagent is required at present. Further studies on improvement of the efficiency of the reaction and investigations on the reaction mechanism are in progress.

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