Chemistry Letters

Copper-Catalyzed Carboxylation of Unactivated Aryl- and Alkenylsilanes with Carbon Dioxide

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doi:10.1246/cl.190577

Copper-Catalyzed Carboxylation of Unactivated Aryl- and Alkenylsilanes with Carbon Dioxide

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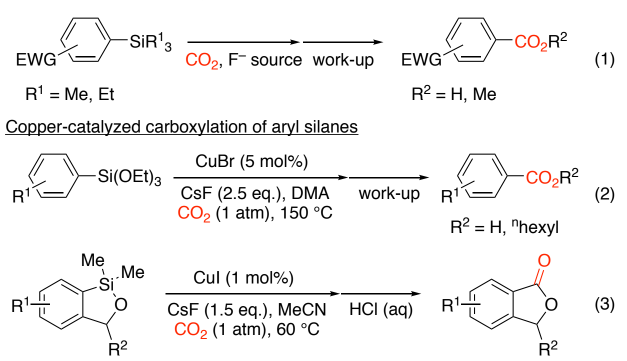
A mild synthetic protocol for the preparation of aryl and alkenyl carboxylic acids was developed through a copper-catalyzed carboxylation reaction of organosilanes with carbon dioxide. The key to this process was the fine-tuning of the reactivity and selectivity of the organometallic nucleophile through structural modifications of the silane.

Keywords: Carbon dioxide, Organosilanes, Copper

The synthetic applications of carbon dioxide (CO_2) has gain much attention in recent years as chemists seek renewable carbon feedstocks in organic chemistry.[1] A well-known carboxylation reaction is the nucleophilic addition reactions of organometallic reagents with CO_2 to generate carboxylic acids. While initial reports focused on highly reactive substrates, such as organolithium and Grignard reagents, they are considered to be unattractive coupling partners due to their moisture and air sensitivity, and poor functional group tolerance.[2] To address these issues, catalytic carboxylation reactions of less reactive, but stable organometallic nucleophiles (Zn,[3] Al,[4] B,[5] Si[6]) have been developed. However, a major limitation in this field is the carboxylation reaction of arylsilanes.

Prior to our efforts, carboxylation of these organometallic nucleophiles was limited to those bearing electron-withdrawing groups (Scheme 1, eq. 1).[6e-h] We found that by employing CuBr as a catalyst, the carboxylation reaction of unactivated aryl- and alkenyltrialkoxysilanes could be achieved, although a reaction temperature of 150 °C was required (Scheme 1, eq. 2).[6i] On the other hand, when we investigated the copper-catalyzed carboxylation reaction of benzoxasiloles, the desired phthalides could be prepared in good yields under a mild reaction temperature of 60 °C (Scheme 1, eq. 3).[6j] Based on the results of the catalytic carboxylation reaction of benzoxasiloles, it was believed that simple arylsilanes could be employed for the synthesis of benzoic acids under a mild reaction temperature. By considering the structure of the assumed intermediates in the copper-catalyzed carboxylation reaction of benzoxasiloles, we hypothesized that a hypervalent silicate, derived from HOMSi (dimethyl(*o*-hydroxymethylphenyl)silane) reagents[7] **1**, could undergo catalytic carboxylation reactions under mild reaction conditions (Figure 1). Herein, we describe the development of a copper-catalyzed carboxylation reaction of HOMSi reagents that can overcome the previously reported limitations to prepare various aryl- and alkenyl carboxylic acids in good yields.



Scheme 1. Carboxylation reactions of arylsilanes.

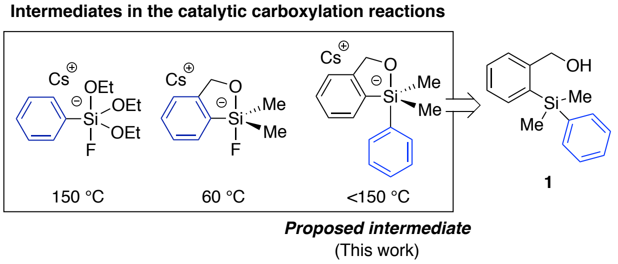
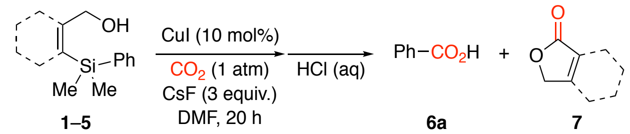
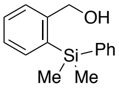
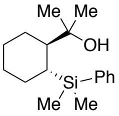
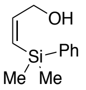
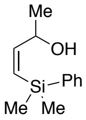
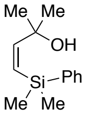


Figure 1. Assumed intermediates in the copper-catalyzed carboxylation reactions of arylsilanes.

To test this hypothesis, the copper-catalyzed carboxylation of HOMSi reagent **1a** with CO_2 was examined. After optimization of the reaction conditions,[8] it was found that benzoic acid (**6a**), along with an undesired side product phthalide (**7a**) could be obtained with yields of 81% and 9% respectively at a reaction temperature of 30 °C (Table 1, entry 1). Since the formation of **7a** is derived from selectivity issues arising from the transmetallation step, efforts to minimize the cleavage of the unwanted C–Si bond was undertaken by modifying the structure of the aryl silane. For instance, we examined a highly chemoselective aryl(trialkyl)silane **2**[7g] for the copper-catalyzed carboxylation reaction and found that while the undesired side-product was not observed, the yield of **6a** was only 13% even at an elevated temperature of 80 °C (entry 2). In order to achieve a balance between the promoting the desired carboxylation of the aryl moiety and preventing the formation of the side-product, vinyl silane **3** was examined,

Table 1. Investigations into the effect of the structure of arylsilanes for the copper-catalyzed carboxylation reaction.[a]



Entry	Silane	Temp. (°C)	**6a** (%)[b]	**7** (%)[b]
1	 **1a**	30	81	9
2	 **2**	80	13	N.D.
3	 **3**	80	79	N.D.
4	 **4**	80	87	8
5	 **5**	30	70	32

[a] Reaction conditions: **1**–**5** (0.25 mmol), CuI (0.025 mmol), CsF (0.75 mmol), DMF (1.5 mL), CO_2 (balloon). [b] Yield was determined by ^1H NMR analysis using 1,1,2,2-dichloroethane as an internal standard.

and it was found that at 80 °C, **6a** could be obtained in 79% yield without any by-product formation (entry 3). To improve the reactivity of the vinyl organosilane, methyl substituents were introduced to the α-position, and organosilane **4** was found to be a slightly more reactive substrate that provided 87% of **6a** with 8% of **7b** at 80 °C (entry 4). On the other hand, when *gem*-dimethyl substituted silane **5** was employed, the reactivity was greatly enhanced and a significant amount of **7b** was observed even when the reaction was conducted at 30 °C (entry 5).

Although it was shown that the modification of the structure of the arylsilanes controlled the reactivity and selectivity of the copper-catalyzed carboxylation reaction with CO_2, we opted to employ HOMSi reagents for the substrate scope since these organometallic nucleophiles could be employed at room temperature (Table 2). It was found that neutral and electron-deficient arylsilanes **1a**–**d** could be utilized to provide various carboxylic acids in moderate to good yields (entries 1-5). However, when electron-rich arylsilane **1e** was examined for the carboxylation process, only 36% of benzoic acid **6e** was obtained. Furthermore, arylsilane **1f** did not undergo the catalytic carboxylation reaction. To solve the low reactivity of these unactivated silanes, the reaction temperature was increased from 30 to 60 °C and this led an improvement in the yields of carboxylic acids **1e** and **1f** (entries 5-6). The effect of the substitution pattern of the arylsilanes was examined, and no significant changes were observed (entries 7-8). Finally, alkenylsilane **1i** was subjected to the carboxylation conditions and the expected α,β-unsaturated carboxylic acid **6i** was obtained in good yield (entry 9).

Table 2. Substrate scope for the copper-catalyzed carboxylation of HOMSi reagents **1a**–**i**.[a]

Entry	R	Temp. (°C)	Yield (%)[b]
1	Ph (**1a**)	30	79
2	4-Cl-C_6H_4 (**1b**)	30	67
3	4-CF_3-C_6H_4 (**1c**)	30	65
4	1-naphthyl (**1d**)	30	43
5	4-Me-C_6H_4 (**1e**)	60	72
6	4-MeO-C_6H_4 (**1f**)	60	64
7	3-Me-C_6H_4 (**1g**)	60	67
8	2-Me-C_6H_4 (**1h**)	60	72
9	(*Z*)-Ph-CH=CH (**1i**)	60	78

[a] Reaction conditions: **1a**–**i** (0.50 mmol), CuI (0.05 mmol), CsF (1.5 mmol), DMF (3.0 mL), CO_2 (balloon). [b] Yield of isolated products **6a**–**i** was based on **1a**–**i** as the limiting reagent.

In conclusion, we developed a copper-catalyzed carboxylation reaction of HOMSi reagents using CO_2 that could be conducted under mild reaction conditions to generate a wide range of aryl and alkenyl carboxylic acids in moderate to good yields. The key for this reaction was the structural modification of the organosilane reagents, which modulated the reactivity and selectivity of the organometallic species for the carboxylation process.

This work was partially supported by Grant-in-Aid for Science Research from the Japan Society for the Promotion of Science (JSPS), Global COE Program, The University of Tokyo, MEXT, Japan, the Japan Science and Technology Agency (JST), and the Japan Agency for Medical Research and Development (AMED).

Supporting Information is available on http://dx.doi.org/10.1246/cl.******.

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8 Please see the Supporting Information for details of the optimization studies.