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A Strained Disilane-Promoted Carboxylation of Organic Halides with CO_2 under Transition-Metal-Free Conditions

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Supporting Information

ABSTRACT: By using a strained four-membered ring disilane (3,4-benzo-1,1,2,2-tetraethyldisilacyclobutene) and CsF, a wide range of aryl, alkenyl, alkynyl, benzyl, allyl, and alkyl halides was successfully carboxylated under an ambient CO_2 atmosphere (CO_2 balloon) at room temperature within 2 h. In this carboxylation, a highly reactive silyl anion, which is generated from the disilane and CsF, is a key to facilitating the formation of a carbanion equivalent. The resulting anionic species can be trapped with CO_2 to produce carboxylic acids with high efficiency.

Carbon dioxide (CO_2) is an abundant, inexpensive, and relatively nontoxic C1 feedstock in organic synthesis and is, therefore, an ideal source for preparing carboxylic acid derivatives.[1] The preparation of these derivatives from halide compounds and CO_2 is very attractive since most of the fundamental halocarbons, especially aryl halides, are now commercially available and/or easily prepared. Organolithium and organomagnesium species[2] derived from halocarbons are known to react with CO_2 to afford the corresponding carboxylic acids, but these methods lack functional group tolerability due to their strongly basic and nucleophilic nature (Figure 1, eq 1). Additionally, these reactions should be performed under strictly anhydrous conditions at a low temperature since these reagents are water-sensitive and inherently thermodynamically unstable.

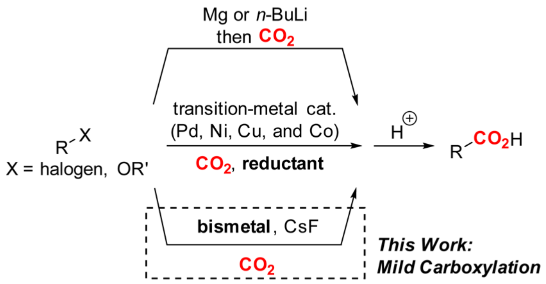

Figure 1. Synthetic strategy of carboxylic acid derivatives from organic halides.

To overcome these limitations, transition-metal catalysts such as Pd,[3a] Ni,[3b,c,4−6,8] Cu,[3d] and Co[7] possessing a phosphine or an amine ligand have been reported to promote reductive carboxylations of aryl halides[3]/pivalates,[4] benzyl halides[5]/pivalates,[4] allyl acetates,[6] propargyl acetates,[7] and alkyl halides/sulfonates[8] in combination with excess amounts of metal reductants (Et_2Zn,[3a,d] Mn,[3b,c,6−8] and Zn[5,6]) (eq 2).[9] Although these catalytic systems are prominent examples in this field, there is still room for the development of mild carboxylation of organic halides with simple operation.

Our research group has already reported the use of stannyl and silyl anion equivalents, which were derived from a bismetal and CsF, for the synthesis of α-amino acids from CO_2.[10] We next considered the use of these species for carbanion generation from halide compounds. Mori and Shibasaki reported intramolecular cyclization of haloketones[11] using $Me_3Si{-}SnBu_3$ and an appropriate activator such as CsF,[11b−e] in which a stannyl anion generated *in situ* attacks an aryl or a vinyl halide to generate a carbanion equivalent, which is then added to the ketone carbonyl group intramolecularly. If this anionic species can be trapped by CO_2, it would afford carboxylic acid derivatives. In addition, Ito[12] and Uchiyama[13] independently reported the formation of an aryl anion equivalent from an aryl halide in combination with a bismetal reagent ($PhMe_2Si$-Bpin or pinB-Bpin) and an appropriate Lewis basic activator without transition metals. However, it has not been reported that these intermediates can be trapped by carbonyl compounds including CO_2. We disclose herein a very mild carboxylation of halocarbons with CO_2 using a strained four-membered ring disilane and CsF under transition-metal-free conditions (eq 3).

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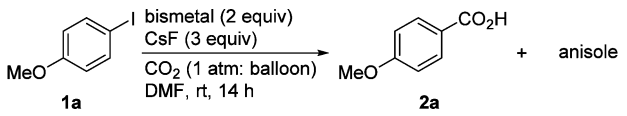
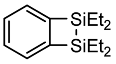
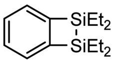
First, taking into account the reported strategies,[11−13] we examined several bismetal reagents, including silyl stannane, silyl boron, diboron, and disilane, for the carboxylation of 4-iodoanisole (**1a**) in the presence of CsF at room temperature for 14 h under 1 atm of CO_2 (CO_2 balloon) (Table 1). When $Me_3Si{-}SnBu_3$ was used under Mori and Shibasaki's conditions,[11b] *p*-anisic acid (**2a**) was obtained in 83% yield together with a protonated compound, anisole, in 15% yield (entry 1). The use of $PhMe_2Si$-Bpin also promoted carboxylation, albeit with a lower yield (entry 2). In contrast, pinB-Bpin was totally inactive in this carboxylation (entry 3). Interestingly, $Me_3Si{-}SiMe_3$ slightly mediated carboxylation (entry 4),[14] and potential disilanes were therefore tested. As a result, the use of phenyl-substituted disilanes resulted in better yields, but the starting iodide **1a** remained to some extent in each case (entries 5−9).

Table 1. Condition Screening



entry	bismetal	**2a** (%)[a]	anisole (%)[a]	rec **1a** (%)[a]
1	Me_3Si-$SnBu_3$	83	15	-
2	$PhMe_2Si$-Bpin	40	8	52
3	pinB-Bpin	-	-	quant
4	Me_3Si-$SiMe_3$	7	-	93
5	Me_3Si-$SiMe_2Ph$	30	-	69
6	$PhMe_2Si$-$SiMe_2Ph$	52	-	48
7	$PhMe_2Si$-$SiPh_3$	57	-	43
8[b]	Ph_3Si-$SiPh_3$	27	6	61
9	Me_3Si-$SiPh_3$	61	-	39
10[c]		quant (99)	-	-
11[c,d]		83	5	-

[a]Yields were determined by ^1H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard. The isolated yield is given in parentheses. [b]The reaction was performed at 60 °C because the disilane was not dissolved in DMF at rt. [c]Reaction time: 2 h. [d]3 equiv of KF were used instead of CsF.

We then turned our attention to the use of a strained four-membered ring disilane[15] such as 3,4-benzo-1,1,2,2-tetraethyl-disilacyclobutene.[15b] This disilane was originally prepared by Ishikawa for use in thermal generation of *o*-quinodisilane, which smoothly reacted with various unsaturated bonds via [4 + 2] cycloaddition,[15b] but it has not been used under fluoride-mediated conditions. If an appropriate fluoride source exists, the Si−Si bond seems to be readily cleaved by its ring strain to immediately generate the corresponding silyl anion. In fact, the desired carboxylation was completed within 2 h at room temperature and the target carboxylic acid was obtained quantitatively (entry 10).[16] KF was also found to be an effective fluoride source, but a small amount of anisole (5%) was obtained as a byproduct (entry 11).

The substrate scope of carboxylation using this strained four-membered ring disilane and CsF was performed under the optimized conditions (DMF, rt, and 2 h) (Figure 2). The products were basically isolated as carboxylic acid forms, but when carboxylic acids were difficult to isolate as pure forms, they were isolated as methyl ester by treatment with CH_2N_2. Electron-rich, -neutral, and -deficient as well as heteroaromatic substrates were all carboxylated in moderate to high yields

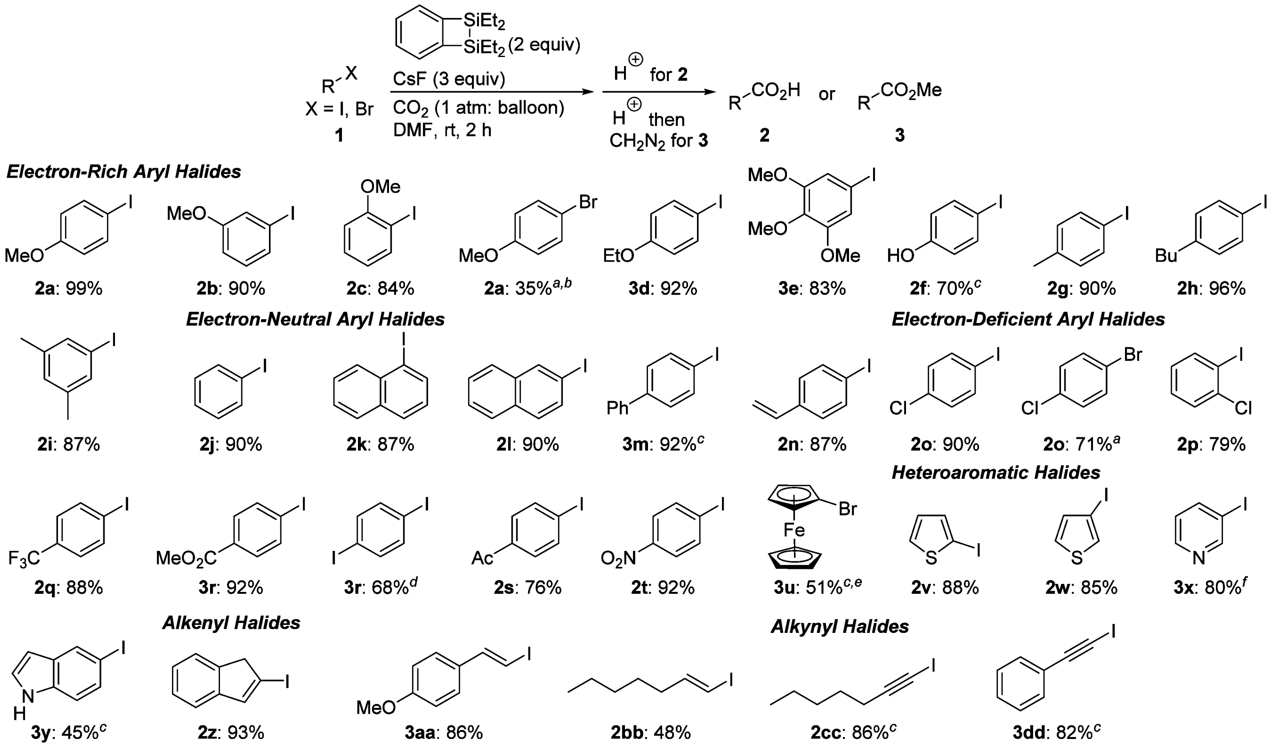
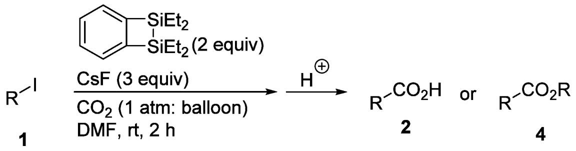


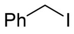
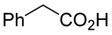
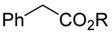
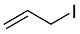
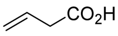
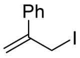
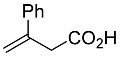
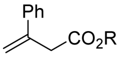
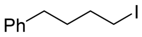
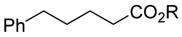
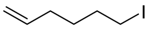
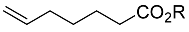
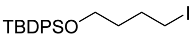
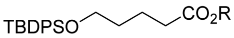
Figure 2. Substrate scope for the carboxylation. Isolated yields are shown unless otherwise noted. [a] Yields were determined by ^1H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard. [b] 4-Bromoanisole was recovered in 63% yield. [c] Disilane (3 equiv) was used. [d] Disilane (4 equiv) and CsF (6 equiv) were used. [e] **1u** was recovered in 40% yield. [f] MeI (1.2 equiv) and Cs_2CO_3 (2 equiv) were employed for esterification.

(**1a**−**1y**). Not only aryl iodides but also aryl bromides underwent carboxylation, albeit with lower yields (4-bromoanisole, 4-bromochlorobenzene, and **1u**). All positions of the methoxy group at the aromatic ring (*ortho*-, *meta*-, and *para*-positions) were equally active (**1a**, **1b**, and **1c**). Notably, 4-iodophenol was successfully carboxylated even though it has an acidic phenolic proton (**1f**). An ester, a ketone, and a nitro group, which are incompatible under conditions using Grignard and *n*-BuLi, were all tolerated (**1r**, **1s**, and **1t**). In addition, alkenyl and alkynyl iodides could undergo carboxylation efficiently without any problem (**1z**−**1dd**).

Next, the scope of further substrates including benzyl, allyl, and alkyl halides was examined. Benzyl iodide (**1ee**) was carboxylated to afford **2ee** in 37% yield together with carboxydimerization product **4ee** and the dimerization product in 20% and 43% yield, respectively (Table 2, entry 1). Allyl iodide (**1ff**) also underwent carboxylation to afford **2ff** in moderate yield (entry 2). Allylic iodide **1gg** was also a reactive substrate, affording both **2gg** and **4gg** (entry 3). Interestingly, alkyl iodides **1hh**−**1kk** underwent carboxydimerization exclusively to afford **4hh**−**4kk** in 40−53% yields (entries 4−7). Notably, the TBDPS group in **1kk** could survive under the fluoride-mediated conditions.

Table 2. Substrate Scope for Benzyl, Allyl, and Alkyl Iodides

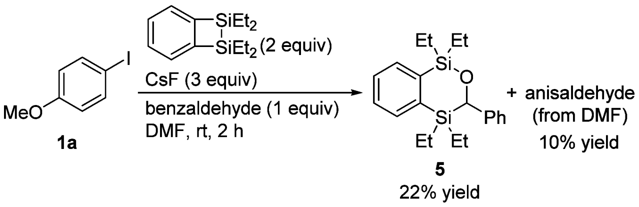


entry	halide	product(s) and their yields (%)[a]		
1	 **1ee**	 **2ee**: 37%	 **4ee**: 20%	 43%[b]
2	 **1ff**	 **2ff:** 34%[c] (54%[b])		
3	 **1gg**	 **2gg**: 30%	 **4gg**: 15%[b]	 47%[b]
4	$C_6H_{13}I$ **1hh**	$C_6H_{13}CO_2C_6H_{13}$ **4hh**: 42%[b]		
5	 **1ii**	 **4ii**: 53%		
6	 **1jj**	 **4jj**: 49%		
7	 **1kk**	 **4kk**: 40%		

[a] Isolated yields are shown unless otherwise noted. [b] Yields were determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard. [c] The isolated yield was diminished due to the volatility.

The four-membered ring disilane was totally ineffective for the addition of 4-iodoanisole to benzaldehyde because the silyl addition to the aldehyde would be faster than the addition to the halide (Scheme 1). The six-membered ring byproduct **5**[15b] derived from benzaldehyde was obtained in 22% yield along with anisaldehyde produced by the reaction of **1a** with DMF. An inert character of this disilane over CO_2 resulted in the selective activation of halocarbons to generate reactive carbanions under a CO_2 atmosphere.

Scheme 1. Addition to an Aldehyde



Based on these phenomena, a tentative reaction mechanism is shown in Figure 3.[17] First, a fluoride anion attacks one of the silicone atoms to produce silyl anion species **I**. Then its nucleophilic attack to the halide would produce either Si−X⁻−R ate complex **II** or a carbanion **III** with the generation of **IV**. Finally, the nucleophilic addition of the resultant species to CO_2 would afford the cesium carboxylate, which is hydrolyzed by an acid workup to afford carboxylic acid **2** and/or alkylated with **1** (in the case benzyl, allyl, and alkyl iodides) to afford **4**. The released **IV** was decomposed by an acid workup to produce a thermodynamically stable siloxane **V**, the structure of which was umambiguously determined by ^{1}H, ^{13}C NMR, and APCI-MS analyses.

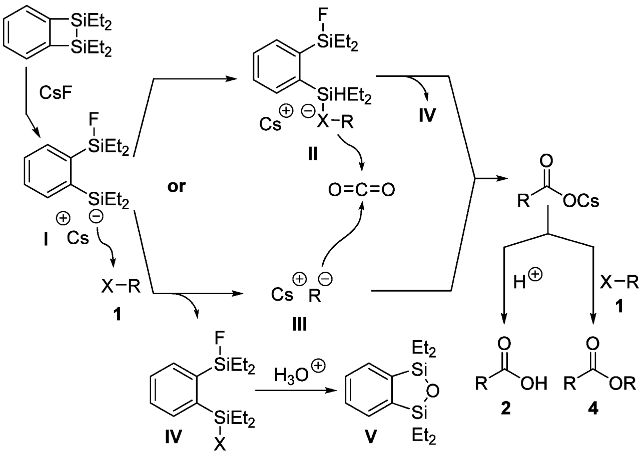


Figure 3. Proposed reaction mechanism.

In summary, we have developed carboxylation of organic halides with CO_2 using a four-membered ring disilane and CsF under very mild conditions. Carboxylation can be conducted at room temperature under 1 atm of CO_2, and a wide range of halocarbons including aryl, heteroaryl, alkenyl, alkynyl, benzyl, allyl, and alkyl halides can be successfully carboxylated within 2 h (40 examples).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02645.

Details of experimental procedures and physical properties of new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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(16) The use of 1.2 equiv of disilane with 1.8 equiv of CsF produced **2a** in 78% yield along with the recovery of **1a** in 21% yield.

(17) The addition of a radical scavenger (BHT or TEMPO) did not shut down the desired carboxylation, and **2a** was obtained in 86% and 82% yield, respectively under the optimal conditions (Table 1, entry 10), which indicates exclusion of the radical process.