ACS Catalysis

Copper-Catalyzed Carboxylation of Aryl Iodides with Carbon Dioxide

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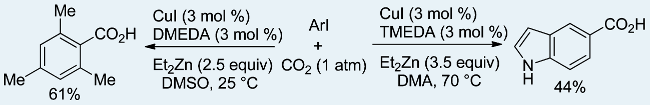
Supporting Information

ABSTRACT: A method for carboxylation of aryl iodides with carbon dioxide has been developed. The reaction employs low loadings of copper iodide/*N,N,N′,N′*-tetramethylethylenediamine (TMEDA) or *N,N′*-dimethylethylenediamine (DMEDA) catalyst, 1 atm of CO_2, dimethylsulfoxide (DMSO) or dimethylacetamide (DMA) solvent, and proceeds at 25−70 °C. Good functional group tolerance is observed, with ester, bromide, chloride, fluoride, ether, hydroxy, amino, and ketone functionalities tolerated. Additionally, hindered aryl iodides such as iodomesitylene can also be carboxylated



KEYWORDS: *carbon dioxide, copper catalysis, aryl halides, carboxylation, arenecarboxylic acids*

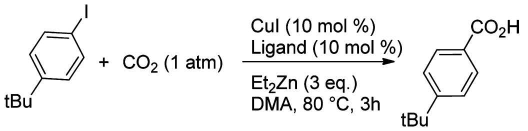
Carbon dioxide is a cheap and abundant C1-synthon.[1] Billions of tons of CO_2 have been released into Earths' atmosphere as a consequence of fossil fuel consumption. Consequently, there is substantial drive for the decrease of CO_2 emissions and sequestration of released carbon dioxide.[2] However, despite substantial interest in carbon dioxide utilization, relatively few chemical processes incorporate it in the final products. This may be caused by low reactivity of carbon dioxide. Thus, both fundamental investigations in CO_2 chemistry and development of new processes that utilize CO_2 are quite important.

Carbon dioxide has been utilized in the synthesis of aliphatic carboxylic acids since 1858, when Wanklyn showed that reaction of ethylsodium with CO_2 affords sodium propionate.[3a] In 1866, Kekulé reported that arylsodium reagents react with carbon dioxide.[3b] One of the earliest examples of transition-metal aryl reactions with carbon dioxide were reported by DePasquale and Tamborski who showed that pentafluorophenylcopper can be transformed into pentafluorobenzoic acid in DMA solvent.[4] Subsequently, rhodium, nickel, and other transition metal aryls and alkyls were shown to react with carbon dioxide.[5] More recently, the focus of research has shifted to development of transition-metal catalyzed carboxylation reactions. Specifically, boronic acid derivatives, alkenes, stannanes, and organozinc reagents have been carboxylated under nickel, rhodium, and copper catalysis.[6] A elegant paper by Martín describes a palladium-catalyzed aryl halide carboxylation by carbon dioxide at 40 °C.[7] Bulky phosphine ligand, diethylzinc reducing agent, and 10 atm of CO_2 were used. Two recent papers report catalytic aryl- and benzyl halide carboxylation by using the more accessible first-row transition metal nickel.[8] We report here a copper-catalyzed aryl iodide carboxylation by carbon dioxide.

Copper complexes have been used in aryl boronate carboxylation by CO_2.[6b,j] The reactions proceed via aryl copper reagents that are known to react with carbon dioxide.[4] Since aryl boronates are usually made from aryl halides,[9] it would be advantageous to directly carboxylate aryl halides. Rieke has shown that aryl halides react with copper clusters to form aryl copper reagents.[10] Consequently, it should be possible to carboxylate aryl halides if zerovalent copper species could be directly generated from copper carboxylates.

The initial optimization reactions were carried out by using a combination of 4-iodo-*t*-butylbenzene, diethyl zinc, ligand, and catalytic copper(I) iodide under 1 atm of CO_2 at 80 °C. Arylcopper reagents react with CO_2 in polar aprotic solvents.[4] Consequently, DMA solvent was chosen for reaction optimization. Reaction was efficient with bidentate nitrogen-based ligands, and *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) or *N,N′*-dimethylethylenediamine (DMEDA) ligands were chosen because of cost considerations (Table 1).

Table 1. Ligand Optimization



entry	ligand	yield (%)[a]
1	triphenylphosphine	44
2	tricyclohexylphosphine	43
3	DIPHOS[b]	23
4	1,10-phenanthroline	73
5	TMEDA[c]	79
6	*N,N′*-DMEDA[d]	82
7	2,2′-bipyridine	70
8	*trans*-1,2-diaminocyclohexane	67

[a] Yields determined by GC. Please see Supporting Information for details. [b] 1,2-bis(Diphenylphosphino)ethane. [c] *N,N,N′,N′*-Tetramethylethylenediamine. [d] *N, N′*-Dimethyl-ethylenediamine.

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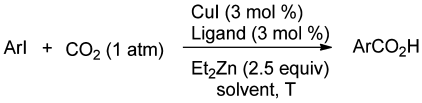
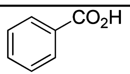
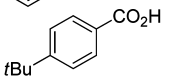
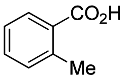
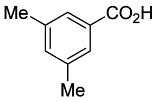
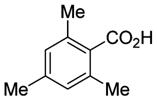
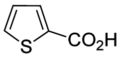
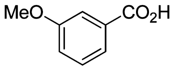
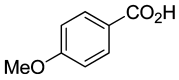
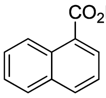
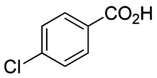
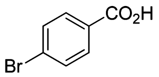
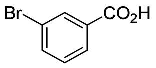
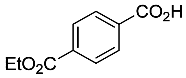
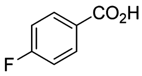
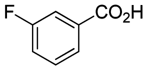
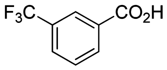
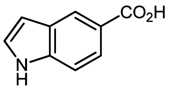
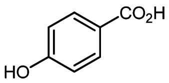
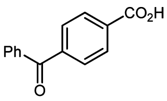
Table 2. Aryl Iodide Carboxylation[a]



entry	Ar–I	ArCO₂H	yield (%)
1	PhI		88
2	4-*t*BuC₆H₄I		81
3	2-MeC₆H₄I		86
4	3,5-Me₂C₆H₃I		80
5	2,4,6-Me₃C₆H₂I		61
6	2-Iodothiophene		63
7	3-MeOC₆H₄I		77
8	4-MeOC₆H₄I		60
9	1-Iodo-naphthalene		68
10	1-Cl-4-I-benzene		61
11	1-Br-4-I-benzene		59
12	1-Br-3-I-benzene		51
13	Ethyl-4-iodobenzoate		62
14	1-F-4-I-benzene		60
15	1-F-3-I-benzene		55
16	1-CF₃-3-I-benzene		56
17[b]	5-Iodoindole		44
18[b]	4-Iodophenol		40
19	4-Iodo-benzophenone		53

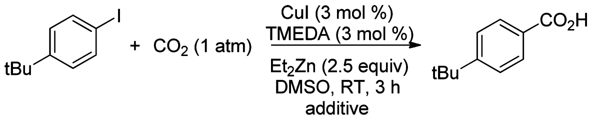
[a] Entries 1–9, DMSO (dimethyl sulfoxide) solvent; entries 10–19, DMA (dimethylacetamide) solvent. Entries 1–6, 25 °C; entries 7–19, 70 °C. Reaction time: 4–20 h. TMEDA ligand: entries 1–2, 6, 8, 10–19. DMEDA ligand: entries 3–5, 7, 9. Yields are isolated yields. Please see Supporting Information for details. [b] Et_2Zn (3.5 equiv).

The optimized reaction conditions for most electron-rich aryl iodide carboxylation involve 3 mol % CuI catalyst, 3 mol % TMEDA or DMEDA ligand, dimethylsulfoxide (DMSO) solvent, and 1 atm of CO_2. The carboxylation of electron-poor aryl iodides requires DMA solvent. The results are summarized in Table 2.

The carboxylation of electron-rich aryl iodides proceeds at 25–70 °C (entries 1–8). Hindered aryl iodides, such as 2-iodotoluene (entry 3), iodomesitylene (entry 5), and 1-iodonaphthalene (entry 9) are reactive. Heterocyclic 2-iodothiophene (entry 6) is carboxylated in a good yield. Alkoxy groups are tolerated and 3- and 4-iodoanisoles are reactive (entries 7 and 8). Carboxylation of electron-poor aryl iodides requires more forcing conditions. Reactions proceed at 70 °C and higher yields are obtained in DMA solvent. Selective carboxylation of iodide in presence of bromo- or chloro substituent, which could be used for further transformations, is possible (entries 10–12). Ethyl-4-iodobenzoate is carboxylated in good yield (entry 13). Fluoroiodobenzenes are also carboxylated in a good yields (entries 14–16). Moreover, the method allows for the carboxylation of aryl iodides that possess unprotected amino, hydroxy, and ketone functionalities (entries 17–19). Consequently, the procedure shows higher functional group tolerance compared with other direct carboxylation methods. Some reduction of ArI to ArH is observed. For entries 17–19, decreased yields are due to incomplete reactions, and substantial amounts of starting materials were recovered. No conversion was observed in the absence of either CuI or Et_2Zn.

The reaction may involve the generation of Cu(0) species which have been shown by Rieke to oxidatively add aryl halides.[10] The presence of colloidal metal was tested by using a mercury additive (Scheme 1).[11,12] With no mercury additive, the carboxylation of 4-iodo-*t*-butylbenzene afforded 79% yield of the corresponding acid. If 200 equiv of Hg with respect to Cu were added, the yield decreased to 24%. Addition of 500 equiv of Hg decreased the yield of product to 10%. Thus, it is

Scheme 1. Reaction in the Presence of Hg Additive

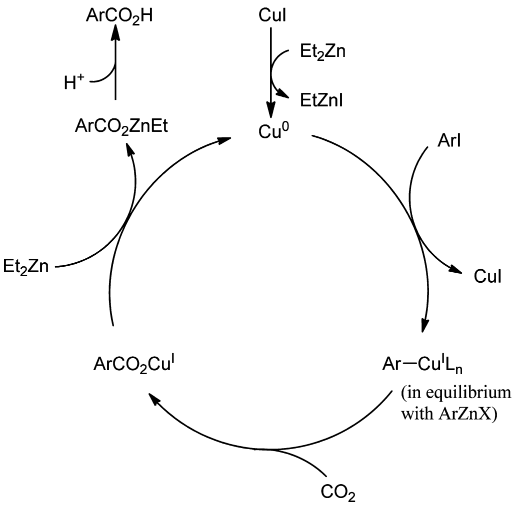


No additive: 79% (GC)
Additive: 200 equiv Hg (per Cu): 24%
500 equiv Hg (per Cu): 10%

highly likely that copper clusters are present in the reaction mixture.

The possible reaction mechanism is shown in Scheme 2.[13] Reduction of Cu(I) with diethylzinc affords Cu(0) via EtCu intermediate.[14] The Cu(0) species oxidatively adds ArI to give ArCu(I) complex. Insertion of CO_2 gives a copper carboxylate, which upon reaction with diethylzinc regenerates Cu(0) via EtCu and forms zinc carboxylate. The lower reactivity of electron-deficient aryl iodides is curious and may have implications with respect to the reaction mechanism. Oxidative additions are typically faster for electron-deficient aryl iodides.[15] Hence, the turnover-limiting step, at least for electron-poor aryl iodides, may be the carboxylation of arylcopper species. A reversible aryl transfer between copper and zinc is likely.[6i] However, reaction of CO_2 with carbon−zinc bonds is probably slow compared to insertion into copper−carbon bonds.[13] Propionic acid was not observed in crude reaction mixtures showing that lifetime of ethylcopper reagent is low.[14]

Scheme 2. Proposed Reaction Mechanism



In conclusion, we have developed a mild method for carboxylation of aryl iodides. The reaction employs low loadings of copper iodide/TMEDA or DMEDA catalyst, 1 atm of CO_2, DMSO or DMA solvent, and proceeds at 25−70 °C. Excellent functional group tolerance is observed, with ester, bromide, chloride, fluoride, ether, amino, hydroxy, and carbonyl functionalities tolerated. Hindered aryl iodides such as iodomesitylene can also be carboxylated. The mechanism likely involves intermediacy of copper clusters.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed experimental procedures and characterization data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(12) Analysis by TEM was inconclusive. Please see Supporting Information for TEM data.

(13) A reviewer suggested that Et_2Zn may react with ArI to generate ArZnR species. Acid quench of reaction run under standard conditions but omitting CuI catalyst and CO_2 does not give a measurable amount of ArH showing that non-catalyzed transmetallation does not occur to a measurable extent. However, CuI catalyzes transmetallation between

Et_2Zn and ArI affording ArZnR species. Please see Supporting Information (Table S4) for details. See also Kneisel, F. F.; Dochnahl, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 1017.

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