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A Copper-Catalyzed Three-Component Reaction of Triethoxysilanes, Sulfur Dioxide, and Hydrazines

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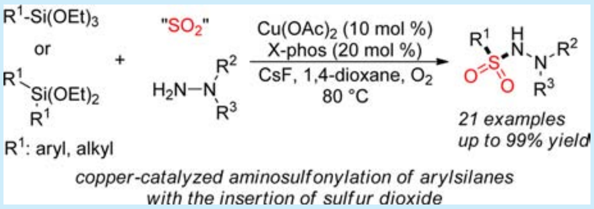
Supporting Information

ABSTRACT: A three-component reaction of triethoxysilanes, sulfur dioxide, and hydrazines catalyzed by copper(II) acetate is reported, leading to *N*-aminosulfonamides in good yields. Not only triethoxy(aryl)silanes but also triethoxy(alkyl)silanes are compatible during the process of insertion of sulfur dioxide. Additionally, diethoxydiarylsilanes are suitable under the conditions as well.

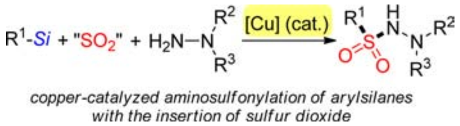


Palladium-catalyzed cross-coupling reactions employing silylated molecules have been well developed,[1−3] which provide an efficient and powerful method for the formation of a new C−C bond in organic synthesis. Among the couplings, the Hiyama[2a] and Hiyama−Denmark[2b] reactions are well-known. Recently, copper-catalyzed coupling reactions of silylated compounds have been developed.[4,5] For instance, Riant described the synthesis of enynes via a copper-catalyzed cross-coupling reaction of vinylsiloxanes with bromoalkynes.[5a] Giri reported the copper-catalyzed reaction of arylsilanes with aryl iodides.[5c] Due to the advantages of copper catalysts in organic transformations, broadening the applications of copper-catalyzed couplings of silylated compounds would be attractive and highly desirable.

Recently, the insertion of sulfur dioxide into small organic molecules has attracted growing interest.[6−9] So far, continuous efforts have been made in this area, especially in the aminosulfonylation process. DABCO-bis(sulfur dioxide) and inorganic metal sulfides have been utilized as a source of sulfur dioxide in the aminosulfonylation reaction. The electrophiles include aryl halides,[7] arylboronic acids,[8] aryldiazonium tetrafluoroborates,[9] etc. For example, Willis described the utilization of DABCO-bis(sulfur dioxide) in a palladium-catalyzed coupling reaction of aryl iodides and hydrazines.[7a] Mascitti and Toste reported the synthesis of sulfinates from a gold-catalyzed reaction of boronic acids and potassium metabisulfite.[8b] Wu also provided an efficient route to *N*-aminosulfonamides through an insertion reaction of sulfur dioxide with aryldiazonium salt and hydrazines under extremely mild conditions.[9a]

Due to the importance of sulfonylamide[10] as a pharmacophore in drug discovery as well as our interest in Hiyama couplings, we envisioned that a copper-catalyzed coupling reaction of silylated molecules could be developed combined with the insertion of sulfur dioxide (Scheme 1). It is known that sulfur dioxide is produced enormously annually in industry. It will be attractive if this approach is feasible. Herein, we disclose the first example of a copper-catalyzed aminosulfonylation of arylsilanes, which proceeds through an insertion reaction of sulfur dioxide in the presence of hydrazines.

Scheme 1. A Copper-Catalyzed Aminosulfonylation of Arylsilanes with the Insertion of Sulfur Dioxide



A model reaction of triethoxy(phenyl)silane **1a**, sulfur dioxide, and morpholin-4-amine **2a** was selected. The studies were initially performed in the presence of CuF_2 (10 mol %) in DCE at 80 °C with a balloon of oxygen. Different fluorides were screened first. It was found that the reaction worked efficiently when CsF was employed, leading to the desired product **3a** in 20% yield (TBAF: 10%; NaF: trace; KF: 13%; LiF: trace; data not shown in Table 1). No reaction occurred without the addition of a copper catalyst. We also examined other oxidants; however, no better results were observed (Table 1, entries 2−5). Further exploration of copper catalysts revealed that the reaction worked efficiently in the presence of copper(II) acetate, producing the corresponding product **3a** in 27% yield (Table 1, entries 6−12). Different solvents were then screened (Table 1, entries 13−18), which indicated that 1,4-dioxane was the best choice (46% yield). The yield was lower when the reaction temperature was changed (data not shown in Table 1). We also explored the reaction in the presence of various ligands (including phosphine ligands and nitrogen ligands; see Supporting Information (SI)). Gratifyingly, the transformation afforded the desired product **3a** in 71% yield when X-Phos was employed (Table 1, entry 19; for other results, see SI).

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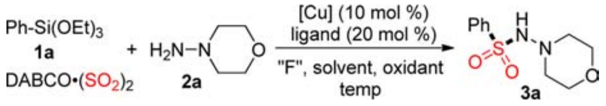
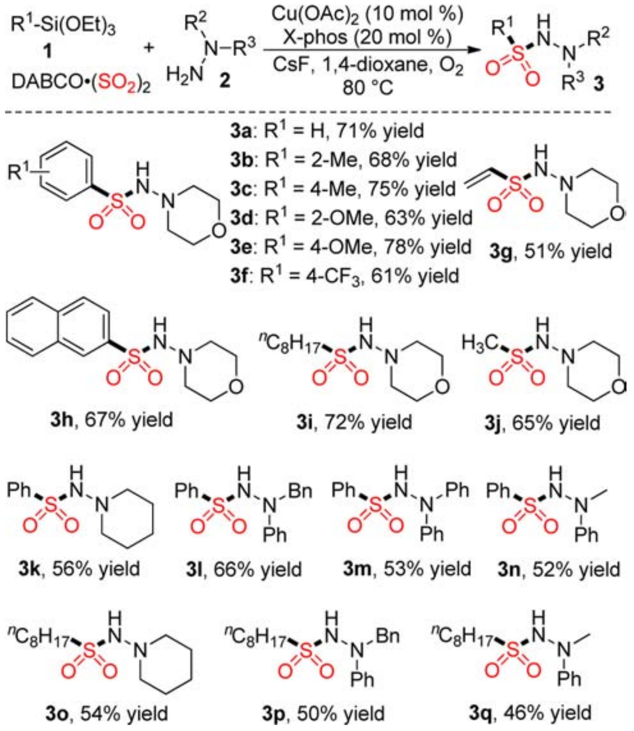
Table 1. Initial Studies for the Copper-Catalyzed Three-Component Reaction of Triethoxyphenylsilane 1a, Sulfur Dioxide, and Morpholin-4-amine 2a[a]



entry	[Cu]	oxidant	solvent	yield (%)[b]
1	CuF_2	O_2	DCE	20
2	CuF_2	Ag_2CO_3	DCE	trace
3	CuF_2	$PhI(OAc)_2$	DCE	8
4	CuF_2	oxone	DCE	10
5	CuF_2	$K_2S_2O_8$	DCE	15
6	$Cu(OAC)_2$	O_2	DCE	27
7	CuI	O_2	DCE	8
8	CuSCN	O_2	DCE	10
9	$CuBr_2$	O_2	DCE	14
10	$CuCl_2$	O_2	DCE	17
11	Cu_2O	O_2	DCE	16
12	$Cu(OTf)_2$	O_2	DCE	19
13	$Cu(OAC)_2$	O_2	^{t}BuOH	11
14	$Cu(OAC)_2$	O_2	1,4-dioxane	46
15	$Cu(OAC)_2$	O_2	toluene	21
16	$Cu(OAC)_2$	O_2	DMF	9
17	$Cu(OAC)_2$	O_2	MeCN	38
18	$Cu(OAC)_2$	O_2	THF	32
19[c]	$Cu(OAC)_2$	O_2	1,4-dioxane	71

[a] Reaction conditions: [Cu] (0.03 mmol), ligand (0.06 mmol), triethoxyphenylsilane **1a** (0.30 mmol), DABCO·$(SO_2)_2$ (0.60 mmol), morpholin-4-amine **2a** (0.60 mmol), "F" (0.60 mmol), oxidant, solvent (2.0 mL), 80 °C. [b] Isolated yield based on triethoxyphenylsilane **1a**. [c] In the presence of X-Phos. For the result by employing other ligands, please see Supporting Information.

Scheme 2. A Copper-Catalyzed Three-Component Reaction of Triethoxysilanes, Sulfur Dioxide, and Hydrazines[a]

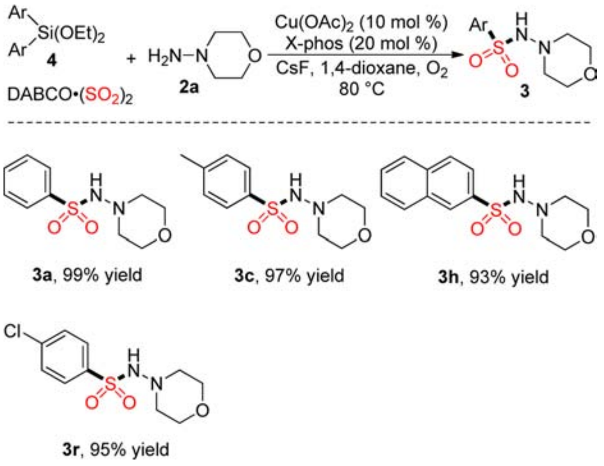


[a] Reaction conditions: $Cu(OAc)_2$ (0.03 mmol), X-Phos (0.06 mmol), triethoxysilanes **1** (0.30 mmol), DABCO·$(SO_2)_2$ (0.60 mmol), hydrazines **2** (0.60 mmol), CsF (0.60 mmol), O_2, 1,4-dioxane (2.0 mL), 80 °C. Isolated yield based on triethoxysilane **1**.

After establishing the optimal conditions, the copper-catalyzed three-component reaction of triethoxysilanes, sulfur dioxide, and hydrazines was then explored. The result is summarized in Scheme 2. It was found that all reactions worked well to give rise to the corresponding *N*-aminosulfonamides in moderate to good yields: (1) Different functional groups including electron-donating and -withdrawing groups attached on the aromatic ring of triethoxy(aryl)silanes were all compatible under the standard conditions (products **3a**–**3f**). (2) The reaction employing triethoxy(vinyl)silane proceeded smoothly as well to generate the desired product **3g**. (3) Not only triethoxy(aryl)silanes but also triethoxy(alkyl)silanes are suitable during the process of insertion of sulfur dioxide. For the reactions of triethoxy(octyl)silane, it is noteworthy that the *β*-elimination of hydrogen is minimized during the transformation. For example, coupling of triethoxy(octyl)silane, sulfur dioxide, and morpholin-4-amine **2a** afforded the expected product **3i** in 72% yield. Additionally, triethoxy(methyl)silane reacted with DABCO-bis(sulfur dioxide) and morpholin-4-amine well, leading to *N*-morpholinomethanesulfonamide **3j** in 65% yield. These results are interesting, since it is the first example with the insertion of sulfur dioxide for the preparation of *N*-aminoalkylsulfonamides. (4) Other hydrazines were all good partners in this three-component reaction (compounds **3k**–**3q**). (5) No reaction occurred when amines or anilines were utilized as the replacement for hydrazines (data not shown in Scheme 2), which was similar to previous reports.

Furthermore, reactions of diethoxydiarylsilanes with sulfur dioxide and hydrazines under the above conditions are investigated. The result is presented in Scheme 3. Excellent yields were obtained for these cases. For instance, diethoxydiphenylsilane **4a** reacted with DABCO-bis(sulfur dioxide) and morpholin-4-amine **2a**, producing the corresponding product **3a** in almost quantitative yield. The reaction proceeded well

Scheme 3. A Copper-Catalyzed Three-Component Reaction of Diethoxydiarylsilanes, Sulfur Dioxide, and Hydrazines[a]



[a] Reaction conditions: $Cu(OAc)_2$ (0.03 mmol), X-Phos (0.06 mmol), diethoxydiarylsilane **4** (0.30 mmol), DABCO·$(SO_2)_2$ (0.60 mmol), morpholin-4-amine **2a** (0.60 mmol), CsF (0.60 mmol), O_2, 1,4-dioxane (2.0 mL), 80 °C. Isolated yield based on diethoxydiarylsilane **4**.

when diethoxydi(4-methyl)phenylsilane or diethoxydi(4-chloro)phenylsilane was employed. A good yield for product **3h** was observed also when diethoxydi(naphthalen-2-yl)silane was utilized in the reaction.

In conclusion, we have discovered a copper-catalyzed three-component reaction of triethoxysilanes, sulfur dioxide, and hydrazines, leading to *N*-aminosulfonamides in moderate to good yields. Not only triethoxy(aryl)silanes but also triethoxy(alkyl)silanes are compatible during the process of insertion of sulfur dioxide. Additionally, diethoxydiarylsilanes are suitable under the conditions as well. This method provides an excellent alternative to *N*-aminosulfonamides. Moreover, employing triethoxysilanes or diethoxydiarylsilanes in the insertion of sulfur dioxide would broaden the copper-catalyzed coupling reactions.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details, compound characterization, and spectra. 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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