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Silver-Mediated Decarboxylative C−S Cross-Coupling of Aliphatic Carboxylic Acids under Mild Conditions

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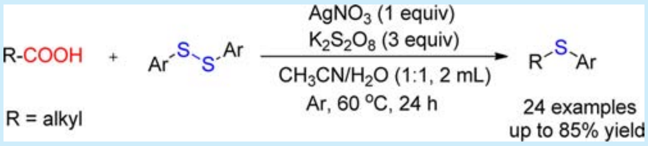
Supporting Information

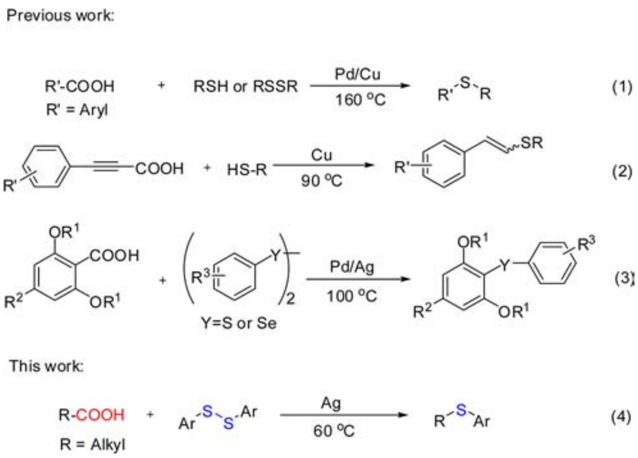
ABSTRACT: A silver-mediated decarboxylative C−S cross-coupling reaction of aliphatic carboxylic acid is described. This reaction occurs smoothly under mild conditions and shows good tolerance of functional groups. It provides an alternative approach for the synthesis of alkyl aryl sulfides.



Organic molecules containing C−S bonds widely exist in many biologically active compounds.[1,2] They are also frequently used as building blocks of many functional polymer materials.[3] Although the methods for C−N[4] and C−O[5] bonds formation receive extensive attention in the field of traditional metal-catalyzed cross-couplings, efficient construction of a C−S bond through transition-metal catalysis still needs more studies. Recent progress has been made in C−S cross-couplings catalyzed by Pd,[6] Cu,[7] and Ni,[2d,8] but many of these methods depend on harsh reaction conditions such as high reaction temperature, the necessity of strong base, and use of expensive ligand, and they suffer from limited substrate scope. Moreover, catalyst poisoning by the sulfide is one of the limiting factors in these approaches. Consequently, it remains important to explore new approaches for efficient construction of the C−S bonds.

In recent years, a new method for the C−S bond formation has emerged that relies on decarboxylative C−S couplings of aryl carboxylic acids.[9] For instance, Liu et al. developed a method to synthesize aryl sulfides by decarboxylative C−S cross-coupling of aryl carboxylic acids and thiols (Scheme 1, eq 1).[9a] More recently, they developed a synthesis of vinyl sulfides by the decarboxylative cross-coupling of arylpropiolic acids with thiols using copper(I) salts as catalysts (Scheme 1, eq 2).[9b] Afterward, Becht et al. reported a simple route to diaryl sulfides using a decarboxylative palladium-catalyzed reaction between electron-rich 2,6-dialkoxybenzoic acid derivatives and diaryl disulfides (Scheme 1, eq 3).[9c] In 2012, Li et al. reported the silver-catalyzed decarboxylative chlorination, fluorination, and alkynylation of aliphatic carboxylic acids under mild reaction conditions.[10] These studies greatly promoted the chemistry of decarboxylative coupling.[11] The related decarboxylative reactions involving the cleavage of C(sp3)−COOH bonds were reported by others[12,13] and our group.[14] Such reactions are synthetically useful for preparing aliphatic compounds and therefore need more studies. Moreover, aliphatic carboxylic acids are cheap and available substrates. Herein, we reported a silver-mediated decarboxylative C−S cross-coupling reaction of aliphatic carboxylic acids (Scheme 1, eq 4).

Scheme 1. Decarboxylative C−S Coupling Reactions



We began our investigation by exploring the reaction between 1,4-benzodioxane-2-carboxylic acid (**1e**) and diphenyl disulfide (**II**) (Table 1). Unfortunately, no desired product could be obtained in different solvents such as THF, CH_3CN, CH_2Cl_2, H_2O, CH_2Cl_2/H_2O, and acetone/H_2O at 50 °C in the presence of $AgNO_3$ (30 mol %) and 3 equiv of $K_2S_2O_8$ (the results are not shown in Table 1). We were delighted to find that when CH_3CN/H_2O was used as the solvent, the desired product **3e** was obtained in 49% yield at 50 °C under an argon atmosphere (entry 1). Then various silver salts such as Ag_2CO_3, $AgBF_4$, AgOAc, AgOTf were further examined. It turned out that less than 44% yield of **3e** was detected (entries 2−5). With regard to the influence of reaction temperature, it was found that the yield of **3e** increased to 54% at 60 °C, whereas the yield

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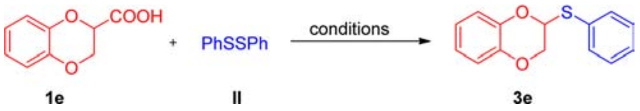
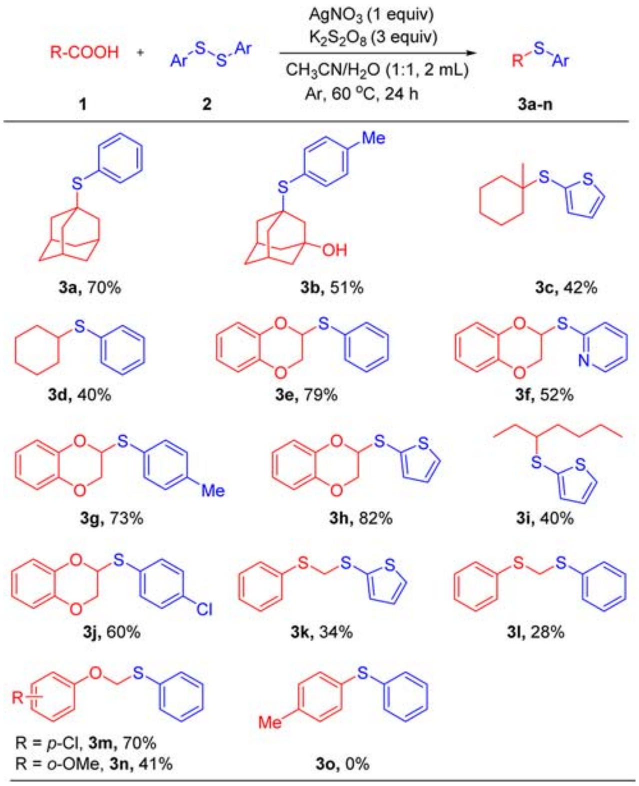
Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst (equiv)	oxidant (equiv)	temp (°C)	time (h)	yield[b] (%)
1	$AgNO_3$ (0.3)	$K_2S_2O_8$ (3)	50	24	49
2	Ag_2CO_3 (0.3)	$K_2S_2O_8$ (3)	50	24	41
3	$AgBF_4$ (0.3)	$K_2S_2O_8$ (3)	50	24	37
4	AgOAc (0.3)	$K_2S_2O_8$ (3)	50	24	43
5	AgOTf[e] (0.3)	$K_2S_2O_8$(3)	50	24	34
6	$AgNO_3$ (0.3)	$K_2S_2O_8$ (3)	60	24	54
7	$AgNO_3$ (0.3)	$K_2S_2O_8$ (3)	70	24	52
8	$AgNO_3$ (0.5)	$K_2S_2O_8$ (3)	60	24	60
9	$AgNO_3$ (0.8)	$K_2S_2O_8$ (3)	60	24	69
10	**$AgNO_3$ (1)**	**$K_2S_2O_8$(3)**	**60**	**24**	**79**
11	$AgNO_3$ (1.2)	$K_2S_2O_8$ (3)	60	24	78
12	$AgNO_3$ (1)	$K_2S_2O_8$ (2)	60	24	70
13	$AgNO_3$ (1)	$K_2S_2O_8$ (4)	60	24	75
14	$AgNO_3$ (1)	$K_2S_2O_8$ (3)	60	18	67
15	$AgNO_3$ (1)	$K_2S_2O_8$ (3)	60	30	74
16[c]	$AgNO_3$ (1)	$K_2S_2O_8$ (3)	60	24	77
17	$AgNO_3$ (1)		60	24	
18		$K_2S_2O_8$ (3)	60	24	
19[d]	$AgNO_3$ (1)	$AgNO_3$ (1)	60	24	77

[a] Unless otherwise stated, all reactions were carried out with **1e** (0.25 mmol), **II** (1.5 equiv), and MeCN/H_2O (1:1, 2 mL) under an argon atmosphere. [b] Isolated yields based on **1e**. [c] The amount of diphenyl disulfide was increased to 2.5 equiv. [d] SDS (20 mol %) was added to the reaction (SDS = sodium dodecyl sulfate). [e] AgOTf = silver trifluoromethanesulfonate.

Scheme 2. Scope of Aliphatic Carboxylic Acids[a,b]



[a] Reaction conditions: **1** (0.25 mmol), **2** (1.5 equiv), $AgNO_3$ (1 equiv), $K_2S_2O_8$ (3 equiv), CH_3CN/H_2O (1:1, 2 mL), 60 °C, 24 h. [b] Isolated yield based on **1**.

had a slight reduction when the reaction was conducted at 70 °C (entries 6 and 7). By changing the amount of $AgNO_3$, we further improved the yield of **3e** to 79% (entries 8−11). Furthermore, the amount of $K_2S_2O_8$, diphenyl disulfide, and reaction time were investigated, but an elevated yield was not obtained (entries 12−16). It should be mentioned that no product was detected when the reaction was performed in the absence of $AgNO_3$ or $K_2S_2O_8$ (entries 17−18). The results proved that both $AgNO_3$ and $K_2S_2O_8$ were essential for the reaction. While our study was in progress, Shen et al. reported silver-catalyzed decarboxylative trifluoromethylthiolation of aliphatic carboxylic acids in aqueous emulsion.[15] Inspired by their works, we also tried to add SDS to our reaction, but it failed to improve the reaction (entry 19).

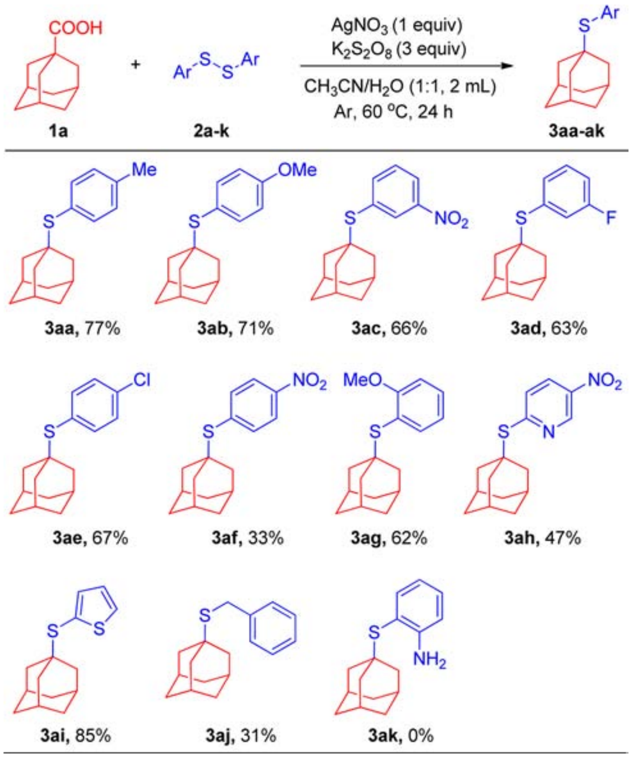
With the optimal reaction conditions in hand, we then explored the scope of this method with various aliphatic carboxylic acids (Scheme 2). It was found that various aliphatic carboxylic acids could successfully decarboxylate to give the desired products in modest to good yields. For example, the reactions of 1,4-benzodioxane-2-carboxylic acid (**1e**) achieved the desired products in good yields (**3e**,**g**,**h**), whereas modest yields were obtained when 1,2-di(pyridin-2-yl)disulfane and 1,2-bis(4-chlorophenyl)disulfane were used to react with the acid (**3f**,**j**). Tertiary alkyl carboxylic acids underwent decarboxylation to give alkyl aryl sulfides in modest to good yields (**3a**−**c**). Other secondary alkyl acids were employed as the substrates to produce the corresponding products in 40% yield (**3d**,**i**). It should be noted that primary aliphatic carboxylic acids could also undergo decarboxylation to generate the desired products in yields of 28−70% (**3k**−**n**). Using 2-(phenylthio)acetic acid as a coupling partner could give low yields of 34% and 28%, respectively (**3k**,**l**).

The lower yields indicated that the reactivity of primary aliphatic carboxylic acids was very low. On the other hand, aromatic acids such as 4-methylbenzoic acid under the above conditions failed to produce the expected product (**3o**).

Under the optimal conditions, we further explored the scope of diaryl disulfides (Scheme 3). Both the electron-rich and -deficient diaryl disulfides gave the desired products in modest to good yields (**3aa**−**aj**). The diaryl disulfide bearing an *ortho*-substitutent also worked well to produce the desired product (**3ag**). It should be pointed out that the reaction was compatible with heterocyclic aromatic disulfides, such as thiophene and pyridine (**3ah**,**ai**). It is interesting to note that the corresponding product was obtained in 31% yield when benzyl disulfide, a dialkyl disulfide, was used as a substrate (**3aj**). However, the reaction did not tolerate an unprotected amino group (**3ak**).

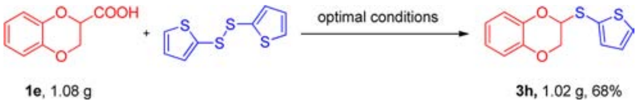
Next, we conducted a gram-scale experiment using 1,4-benzodioxane-2-carboxylic acid and 2-thienyl disulfide as the substrates. We found that the corresponding alkyl aryl sulfide was obtained in 68% yield (Scheme 4). Stoichimetric silver nitrate was used in the reaction, whereas a catalytic amount of silver nitrate was used for decarboxylation of aliphatic carboxylic acids according to previous reports.[10] Thus, we studied the possible reason for using stoichimetric silver nitrate. We isolated the main byproducts in some reactions, and it was found that diaryl disulfides were oxidized into the arylthiosulfonates in the presence of silver nitrate through NMR and HRMS analysis. When 1-adamantanecarboxylic acid (**1a**) and

Scheme 3. Scope of Diaryl Disulfides[a,b]

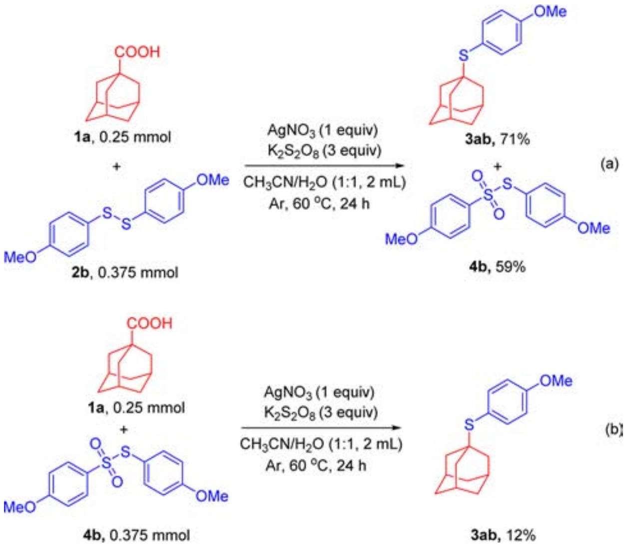


[a]Reaction conditions: **1a** (0.25 mmol), **2** (1.5 equiv), AgNO$_3$ (1 equiv), K$_2$S$_2$O$_8$ (3 equiv), CH$_3$CN/H$_2$O (1:1, 2 mL), 60 °C, 24 h. [b]Isolated yield based on **1a**.

Scheme 4. Gram-Scale Reaction

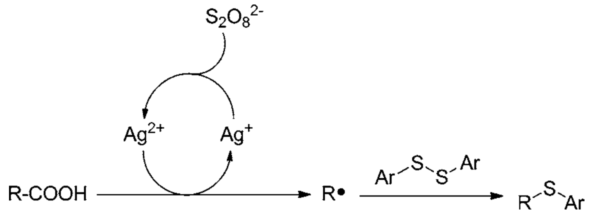


Scheme 5. Study on the Side Reactions[a]



[a]Isolated yield of **3ab** based on **1a** and isolated yield of **4b** based on **2b**.

Scheme 6. Proposed Reaction Mechanism



1,2-bis(4-methoxyphenyl)disulfane (**2b**) were used as the substrates, the corresponding product (**3ab**) was obtained in 71% yield. In this case, we also isolated the main byproduct, *S*-(4-methoxyphenyl)-4-methoxybenzensulfinothioate (**4b**) in 59% yield (Scheme 5a). The results indicated that silver nitrate was not only used for the decarboxylation of aliphatic carboxylic acids but also used for oxidation of diaryl disulfides to arylthiosulfonates, and thus, it helped to explain the possible reason for using stoichimetric silver nitrate. To explore whether the side products could react with aliphatic carboxylic acids to produce the same thiolation products, another experiment was carried out by using **1a** and **4b** as coupling partners. It was found that alkyl aryl sulfide **3ab** was obtained in 12% yield (Scheme 5b).

According to the previous studies,[10,16] we proposed that the reaction may proceed through the mechanism presented in Scheme 6. First, Ag(I) is oxidized to Ag(II) in the presence of persulfate, and subsequently, Ag(II) combines with aliphatic carboxylic acid to produce the alkyl radical via decarboxylation pathway. Then, the alkyl radical attacks diaryl disulfide to generate the desired product.

In conclusion, we developed a silver-mediated decarboxylative C–S cross-coupling reaction of aliphatic carboxylic acids using K$_2$S$_2$O$_8$ as the oxidant and diaryl disulfides as the sulfur source. The new reaction tolerated many functional groups and could be performed under mild reaction conditions. Furthermore, the reaction provided a new approach to the synthesis of alkyl aryl sulfides.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed experimental procedures and spectra data for all 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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