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Ruthenium-catalyzed decarboxylative C–S cross-coupling of carbonothioate: synthesis of allyl(aryl) sulfide†

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A novel ruthenium-catalyzed decarboxylative cross-coupling of carbonothioate is disclosed. This method provides straightforward access to the corresponding allyl(aryl)sulfide derivatives in generally good to excellent yields under mild conditions and features a broad substrate scope, wide group tolerance and in particular, no need to use halocarbon precursors.

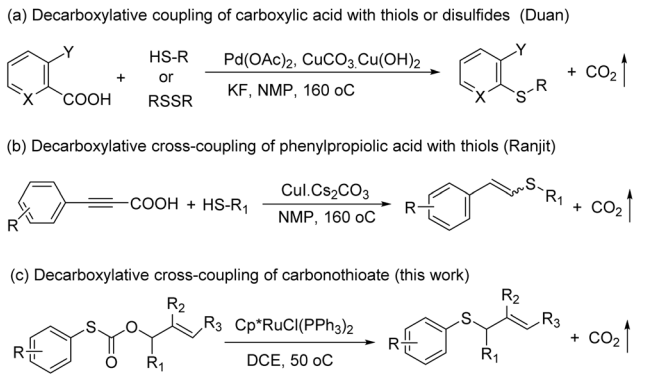
1. Introduction

Sulfur-containing molecules such as thioethers are commonly found in chemical biology, organic synthesis, and materials chemistry.[1] The development of mild and general methods for C–S bond formation has received significant attention; among them, the transition metals have been applied in this field, and the palladium-catalyzed coupling of thiols with aryl halides is one of the most important methods in the synthesis of thioethers.[2] Other metals have also been used for the same purpose.[3] Despite the phenomenal growth in diverse synthetic methodologies, the synthesis of C–S bonds is generally limited to the condensation reaction between a metal thiolate and an organic halide.[4] Organohalides have potential environmental and human health effects, and their wastes require costly remediation, particularly on an industrial scale.

Recently, transition metal-catalyzed decarboxylative allylation reactions are a powerful method for the allylation of a wide variety of nucleophiles under neutral conditions.[5] In particular, as one of the most efficient ways to capture the ketone enolates, palladium-catalyzed decarboxylative allylation of β-ketoesters[6] has attracted considerable attention since the early discoveries reported by Tsuji[7] and Saegusa.[8] In contrast with C–H bond activation reactions, decarboxylative cross-coupling reactions through loss of CO_2 generally do not need expensive organometallic reagents, while maintaining the advantage of regioselectivity offered by traditional cross-coupling reactions. Compared with a great wealth of studies on the decarboxylative allylation of C–C and C–N bond-forming transformations,[9] the corresponding C–S bond-forming reactions were much less investigated and more challenging, mainly due to catalyst poisoning by the mercapto group. In 2009, Duan and co-workers reported the first decarboxylative coupling of *ortho*-substituted aryl carboxylic acids with thiols as an unprecedented synthetic entry to aryl sulfides (Scheme 1a).[10] In a follow-up study, Ranjit and co-workers developed a versatile protocol, in which a CuI catalyst was used to initiate the decarboxylation of arylpropiolic acids, for the synthesis of vinyl sulfides (Scheme 1b)[11] by the cross-coupling of the arylpropiolic acids with thiols. In 2018, Ichiishi[12] and Ishitobi[13] reported the decarbonylative C–S coupling of thioesters into thioethers respectively.

We reasoned that the direct decarboxylative C–S coupling of carbonothioate, if possible, would provide an alternative access to aryl sulfides without the need for halocarbon precursors (Scheme 1c). Herein, we describe the integration of these concepts into the transition-metal-catalyzed synthesis of a broad range of aryl sulfides.

To test our hypothesis and also to identify an effective catalyst system, the decarboxylative allylation of *O*-allyl *S*-(*p*-tolyl) carbonothioate was selected as a model reaction and performed under different conditions (Table 1). To begin, we compared



Scheme 1 Synthesis of thioethers through the decarboxylative coupling reaction.

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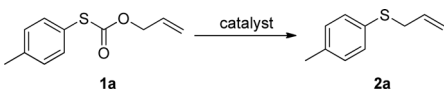
Table 1 Optimization of reaction conditions[a]



Entry	Catalyst/mol%	Solvent	T/°C	T/h	Yield[b] (%)
1	$Ni(acac)_2$(10)/PPh_3(10)	DCE	50	24	nr
2	$Fe(acac)_3$(10)/PPh_3(10)	DCE	50	24	nr
3	Ph_3PAuCl(5)/$NaBArF_4$(10)	DCE	50	24	nr
4	$Pd(PPh_3)_4$(5)	DCE	50	2	92
5	**Cp*RuCl(PPh$_3$)$_2$(3)**	**DCE**	**50**	**1**	**96**
6	$RuCl_3$(3)	DCE	50	24	nr
7	$Ru(PPh_3)_3Cl_2$(3)	DCE	50	5	<5
8	Cp*RuCl$(PPh_3)_2$(3)	DCE	rt	12	56
9	Cp*RuCl$(PPh_3)_2$(3)	THF	50	1	87
10	Cp*RuCl$(PPh_3)_2$(3)	CH_3CN	50	1	88
11	Cp*RuCl$(PPh_3)_2$(3)	Toluene	50	1	82

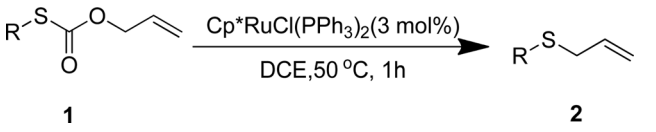
[a] Reactions run in vials; [**1a**] = 0.05 M. [b] Estimated by ^{1}H NMR using diethyl phthalate as an internal reference.

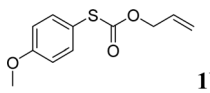
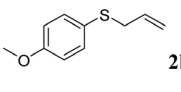
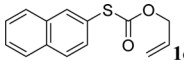
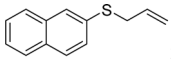
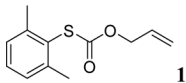
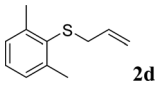
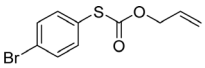
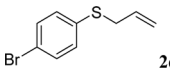
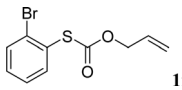
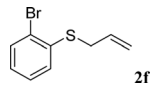
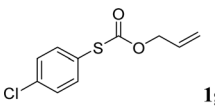
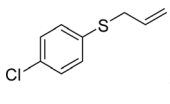
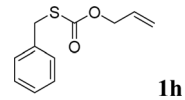
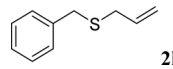
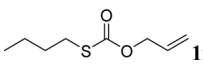
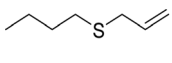
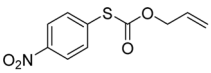
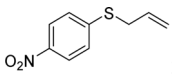
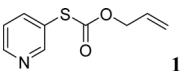
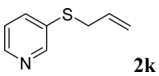
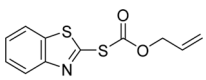
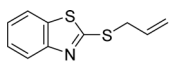
a variety of catalysts for their ability to effect the decarboxylative allylation of carbonothioate. Among them, nearly qualitative rate of decarboxylative allylation catalyzed by Pd and Ru catalysts (Table 1, entries 4–5), and that Fe, Ni and Au catalysts did not work with the reaction (entries 1–3). Different Ru catalysts was screened and the results showed that Cp*RuCl$(PPh_3)_2$ is the best catalyst (entries 5–7). A low yield was also resulted when the reaction was run at room temperature (entry 8). A series of solvents were examined (Table 1, entries 5, 9–11) and the desired product **2a** was observed in 96% yield when DCE was utilized, whereas all the other solvents investigated afforded lower yields.

With the optimal reaction conditions in hand (Table 1, entry 5), the scope of the reaction was then examined. As summarized in Table 2, a variety of carbonothioate undergo decarboxylative allylation in high yield. In particular, the reaction is effective for nearly any substitution pattern about the carbonothioate; even sterically demanding *ortho*-substituted carbonothioates undergo allylation, albeit at a reduced rate (entries 3 and 5). Gratifyingly, halogen atoms (Cl and Br) could be tolerated well (entries 4–6), which have the potential to interfere with the analogous palladium-catalyzed reactions. Notably, a 4-NO_2 group led to a significant decrease in the yield (entry 9). Replacing the phenyl group of **1** with a naphthyl (entry 2), a benzyl (entry 7), a butyl (entry 8), a pyridyl (entry 10), or a benzothiazolyl (entry 11) were all readily allowed and the corresponding products were isolated in good yields.

Next, the regioselectivity of the substituted allyl carbonothioates was investigated (Table 3). In all cases, the cinnamyl carbonothioates preferentially formed the linear allylic ethers in good yield (entries 3–5). As can be seen, cinnamyl carbonothioate substrates provided the linear product exclusively as judged by ^{1}H NMR spectroscopy. Thus, the reaction with aryl-substituted allylic carbonothioates is regioselective. Next, we investigated the coupling of crotyl alcohol, which provided the branched and linear allylation product with the ratio nearly of 1 : 1 and high yield (entry 6–7). The isomeric branched

Table 2 Reaction scope of unsubstituted allyl carbonothioates[a]



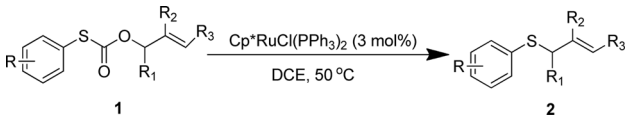
Entry	Allylthiocarbonate substrate	Products	Yield[b]/%
1	 **1b**	 **2b**	94
2	 **1c**	 **2c**	96
3	 **1d**	 **2d**	88
4	 **1e**	 **2e**	90
5	 **1f**	 **2f**	86
6	 **1g**	 **2g**	89
7	 **1h**	 **2h**	91
8	 **1i**	 **2i**	87
9	 **1j**	 **2j**	83
10	 **1k**	 **2k**	86
11	 **1l**	 **2l**	87

[a] Reactions run in vials; [**1**] = 0.05 M. [b] Isolated yields are reported.

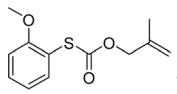
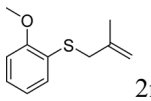
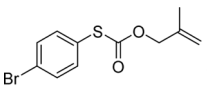
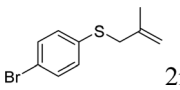
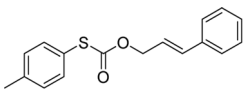
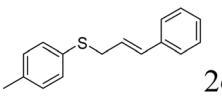
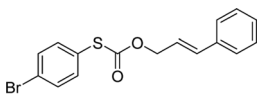
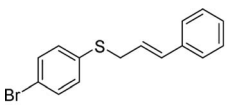
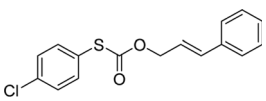
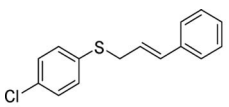
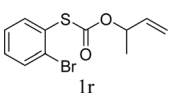
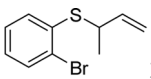
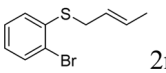
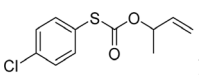
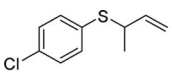
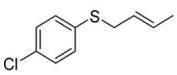
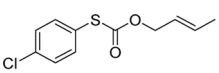
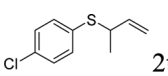
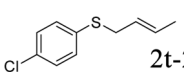
carbonothioate also produced the branched and linear allylation product with the ratio nearly of 1 : 1 (entry 8). While the regiochemical outcome slightly depends on the regiochemistry of the starting allyl ester, the reaction is not strongly regiospecific. In general, ruthenium catalyst favors the branched products in allylic substitution,[14] the higher reaction temperature maybe the main reason for the more stable linear product was obtained in our study.

In conclusion, a ruthenium-catalyzed decarboxylative allylation of carbonothioates was developed. The yields of the reaction are generally high and the Ru catalyst often provides chemo- and regioselectivities that complement those of more standard palladium catalysts. This method is important not only for expanding our understanding of the decarboxylative reaction but also for providing a convenient synthetic pathway

Table 3 Reaction scope of substituted allyl carbonothioates[a]



1 2

Entry	Substrate	Product	Time	Yield[b]/%
1	 1m	 2m	24 h	91
2	 1n	 2n	12 h	94
3	 1o	 2o	5 h	93 (>95 : 5)
4	 1p	 2p	24 h	89 (>95 : 5)
5	 1q	 2q	24 h	87 (>95 : 5)
6	 1r	 2r-1  2r-2	10 h	90 (50 : 50)
7	 1s	 2s-1  2s-2	4 h	91 (50 : 50)
8	 1t	 2t-1  2t-2	12 h	93 (50 : 50)

[a] Reactions run in vials; [3] = 0.05 M. [b] Isolated yields are reported.

for facile synthesis of biologically or pharmaceutically relevant compounds. Further investigations of the substrate scope of this transformation and the reaction mechanism are currently in progress in our laboratory.

Conflicts of interest

There are no conflicts to declare.

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