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Silver-Catalyzed Decarboxylative Allylation of Aliphatic Carboxylic Acids in Aqueous Solution

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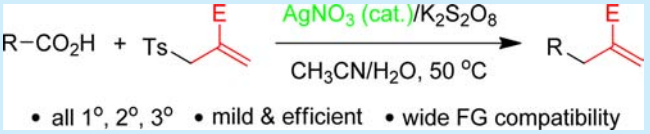
Supporting Information

ABSTRACT: Direct decarboxylative radical allylation of aliphatic carboxylic acids is described. With $K_2S_2O_8$ as the oxidant and $AgNO_3$ as the catalyst, the reactions of aliphatic carboxylic acids with allyl sulfones in aqueous CH_3CN solution gave the corresponding alkenes in satisfactory yields under mild conditions. This site-specific allylation method is applicable to all primary, secondary, and tertiary alkyl acids and exhibits wide functional group compatibility.



Radical allylation has been demonstrated to be a versatile method for the construction of C(sp^3)−allyl bonds. It generally takes place between a carbon-centered radical and a suitable allylic reagent via radical addition/fragmentation processes. A variety of allylating agents have been developed for this purpose, including allyl sulfides,[1] allyl sulfoxides,[2] allyl sulfones,[3] allyltrimethylsilanes,[4] allyltributylstannanes,[5] allyl halides/chalcolides,[6] and allylmetallic (Co, Zr, Ga) complexes.[7] Meanwhile, a number of organic compounds can be employed as radical precursors to participate in this type of transformation, such as alkyl halides/chalcolides, boronates,[8] xanthates,[9] enamines,[10] active methylene compounds,[11] and even aliphatic hydrocarbons.[12] However, many radical allylation reactions also suffer from either the use of toxic organotin initiators or the use of excess transition metals or limited substrate scopes. The discovery of general and efficient methods under mild and transition-metal-catalyzed conditions remains a challenging task. Herein we report the silver-catalyzed decarboxylative radical allylation of aliphatic carboxylic acids in aqueous solution, providing an efficient and convenient entry to site-specific C(sp^3)−C(sp^3) bond formations.

Aliphatic carboxylic acids are promising raw materials for chemical synthesis due to their high stability, ready availability, and low cost.[13] In particular, the Hunsdiecker-type reactions involving the cleavage of C(sp^3)−CO_2H bonds allow the introduction of various functional groups in a site-specific manner.[14] The decarboxylative allylation was first introduced by Barton and Crich in which carboxylic acids were converted into the corresponding pyridine-2-thione-*N*-oxycarbonyl esters followed by reaction with an allylating agent such as allyl phenyl selenide.[15] More recently, Chen and Hu reported the visible-light-induced, ruthenium-catalyzed decarboxylative allylation of *N*-acyloxyphthalimides with allyl sulfones.[16] However, these two methods require the prior conversion of carboxylic acids into esters and suffer from the low overall efficiency or limited scope of application (Figure 1). It is certainly highly desirable to develop a one-step method for this type of transformation,

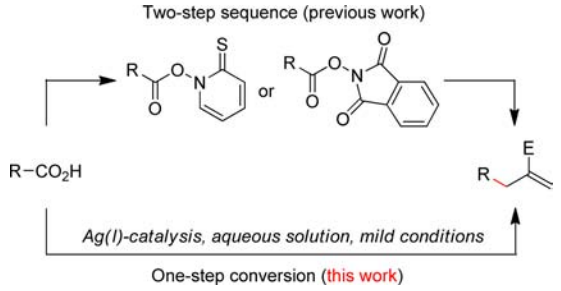


Figure 1. Decarboxylative allylation of aliphatic carboxylic acids.

especially in a catalytic manner. As a continuation of our interest in silver-catalyzed decarboxylative functionalization reactions,[17,18] we set out to explore this possibility (Figure 1).

Thus, 2-ethyltetradecanoic acid (**1a**) was used as the model substrate for the optimization of reaction conditions (Table 1). With $AgNO_3$ (20 mol %) as the catalyst and $K_2S_2O_8$ (1.5 equiv) as the oxidant, reaction of **1a** with ethyl 2-(tosylmethyl)acrylate (**2a**, 2 equiv) in aqueous CH_2Cl_2 solution at 40 °C for 24 h gave no expected product while all the acid **1a** was recovered (entry 1, Table 1). Changing the solvents to acetone/H_2O did not offer any product either (entry 2, Table 1). However, when the reaction was carried out in aqueous CH_3CN solution, we found that the expected product **3a** was obtained in 42% yield (entry 3, Table 1). Increasing the temperature increased the product yield (entries 4 and 5, Table 1). The highest yield (89%) was achieved when the reaction was performed at 50 °C for 12 h (entry 6,

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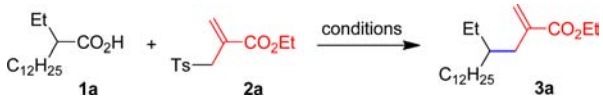
Table 1. Optimization of Reaction Conditions



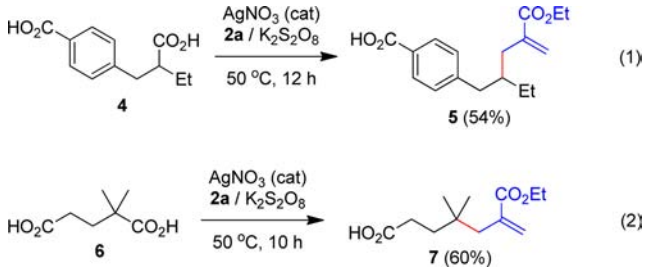
entry[a]	catalyst (mol %)	solvent	temp/time (°C/h)	yield (%)[b]
1	$AgNO_3$ (20)	CH_2Cl_2/H_2O (1:1)	40/24	0
2	$AgNO_3$ (20)	Me_2CO/H_2O (1:1)	40/24	0
3	$AgNO_3$ (20)	CH_3CN/H_2O (1:1)	40/24	42
4	$AgNO_3$ (20)	CH_3CN/H_2O (1:1)	50/24	73
5	$AgNO_3$ (20)	CH_3CN/H_2O (1:1)	60/24	62
6	**$AgNO_3$ (20)**	**CH_3CN/H_2O (1:1)**	**50/12**	**89**
7	$AgBF_4$ (20)	CH_3CN/H_2O (1:1)	50/12	78
8	AgOTf (20)	CH_3CN/H_2O (1:1)	50/12	64
9	AgOAc (20)	CH_3CN/H_2O (1:1)	50/12	67
10	none	CH_3CN/H_2O (1:1)	50/12	0
11[c]	$AgNO_3$ (20)	CH_3CN/H_2O (1:1)	50/12	0
12	$AgNO_3$ (20)	$CH_3CN/H_2O/CH_2Cl_2$ (2:4:1)	50/12	58

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $K_2S_2O_8$ (0.3 mmol), Ag(I) catalyst (0.04 mmol), solvent (2 mL). [b]Isolated yield based on **1a**. [c]No $K_2S_2O_8$ was added.

Table 1). The reaction was clean, and no radical−radical coupling byproduct (13,14-diethylhexacosane) could be detected. Switching the catalyst to other Ag(I) salts such as $AgBF_4$ or AgOTf resulted in a lower yield of **2a** (entries 7−9, Table 1). Control experiments indicated that Ag(I) and persulfate were necessary for the transformation (entries 10 and 11, Table 1). When $K_2S_2O_8$ was replaced by $(NH_4)_2S_2O_8$ as the oxidant, the product yield was decreased to 60%. However, only a trace amount of **3a** could be detected when either (diacetoxy)iodobenzene or [bis(trifluoroacetoxy)]iodobenzene was used as the oxidant (not shown in Table 1). It should be mentioned that the use of $CH_3CN/CH_2Cl_2/H_2O$ as the mixed solvents lowered the yield of **2a** (entry 12, Table 1). However, this biphasic solvent system turned out to be advantageous in some cases (vide infra) presumably because the addition of CH_2Cl_2 inhibited the decomposition of product alkenes.

With the optimized conditions in hand, we next examined the scope and imitation of this new decarboxylative allylation method with allyl sulfone **2a** as the allylating reagent. As shown in Scheme 1, secondary alkyl carboxylic acids underwent efficient decarboxylative allylation, furnishing the corresponding products **3a**−**3j** in high yields. Reactions of tertiary alkyl carboxylic acids also proceeded smoothly, leading to the formations of acrylates **3k**−**3q** in satisfactory yields. *α*-Oxy or *α*-amino acids could also be used as substrates, as exemplified by the synthesis of **3r**−**3t**. Allylation was also applicable to primary alkyl carboxylic acids, albeit in moderate efficiency (46% for **3u**). Interestingly, formation of acrylate **3v** as the mixture of two stereoisomers in an 85:15 ratio was observed if *trans*- (*trans*-**1v**) or *cis*-2-benzoylcyclohexanecarboxylic acids (*cis*-**1v**) was used as the starting material. The results in Scheme 1 also showed the excellent tolerance of the decarboxylation toward a variety of functional groups, including amide, sulfonamide, ester, ether, nitro, and alkyl or aryl halides. This should allow the late-stage allylation of complex molecules. For example, decarboxylative allylation of dehydrolithocholic acid (**1w**) under the above optimized conditions afforded the corresponding product **3w** in 80% yield.

Treatment of aromatic acids such as 4-chlorobenzoic acid under the above reaction conditions failed to give any decarboxylative allylation products, while all the acids remained unchanged. This phenomenon in combination with the results in Scheme 1 parallels our observations in other $AgNO_3$-catalyzed decarboxylative functionalization reactions,[17] which in turn clearly indicates that an oxidative radical decarboxylation mechanism is involved in the above reactions. Thus, chemoselective decarboxylative allylation reactions could be designed based on this assumption. Indeed, diacid **4** underwent chemoselective decarboxylation to afford exclusively the monoallylation product **5** in 54% yield (eq 1). Similarly, the tertiary alkylic



carboxyl group in 2,2-dimethylpentanedioic acid (**6**) was selectively removed, producing the acrylate **7** in 60% yield while the primary alkylic carboxyl group remained safe (eq 2).

We then examined the generality of this catalytic allylation toward different allylating agents. The above reaction conditions were directly used without further optimization, and the results are summarized in Scheme 2. With 2-cyanoallyl sulfone **2b** as the reagent, the decarboxylative allylation of acids **1a** and **1s** proceeded nicely to give the expected products **8** and **11**, respectively. Other than **2a** and **2b**, which are electron-deficient alkenes, electron-rich alkenes such as 2-methylallyl sulfone **2c** and allyl sulfone **2d** also served as good allylating agents in the decarboxylative allylation, as exemplified by the synthesis of electron-rich alkenes **9**, **10**, **12**, and **13** in moderate to high yields. These results significantly expand the scope of application of the new method. Nevertheless, our attempt to use 1-fluoroallyl sulfone **2e** as the allylating agent failed. Reaction of acid **1a** with **2e** did not offer the expected product **14**. Instead, vinyl fluoride **15** was obtained in 70% yield as the rearrangement product of **2e** (eq 3).

As indicated above, a radical mechanism can be drawn for this catalytic decarboxylative allylation. To provide further evidence,

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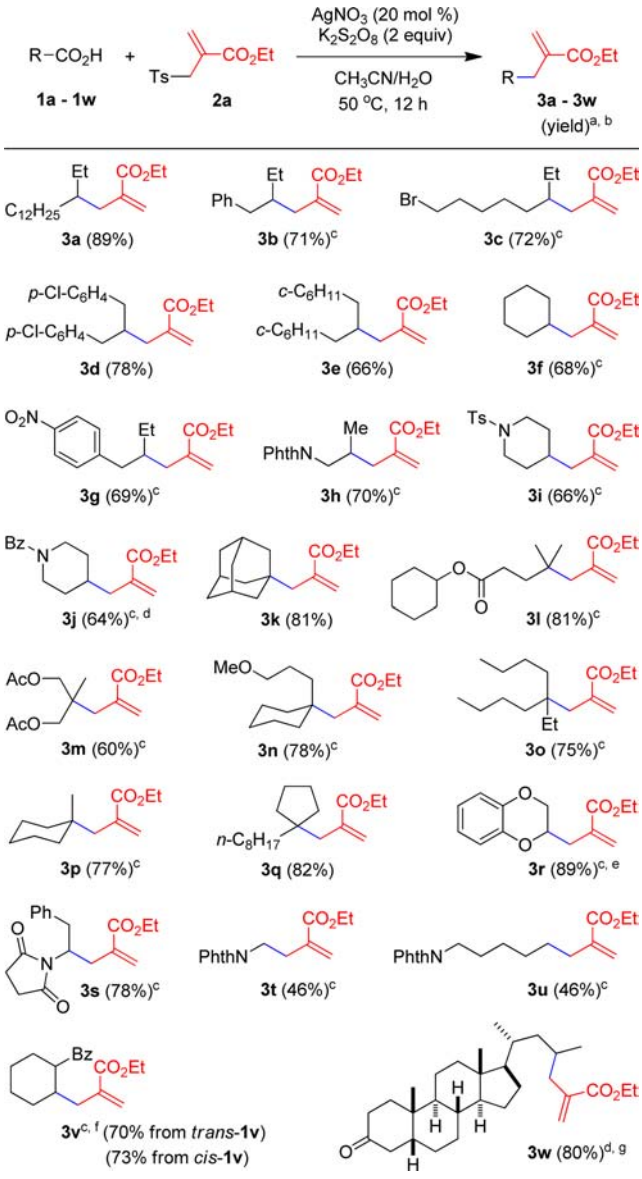
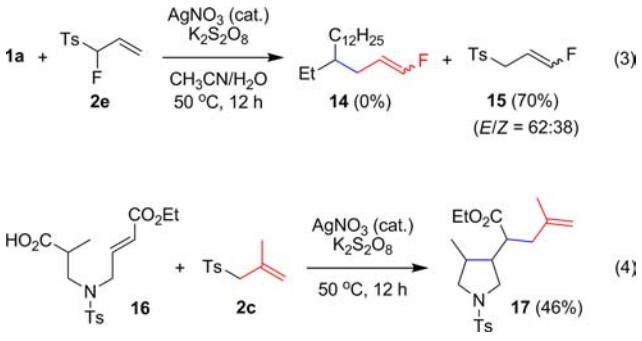
Scheme 1. Silver-Catalyzed Decarboxylative Allylation

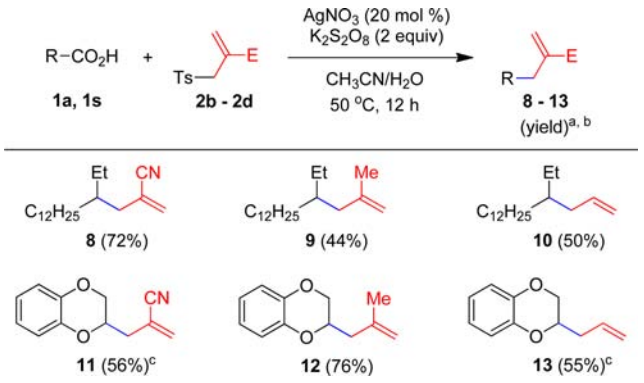


[a]Reaction conditions: carboxylic acid (0.2 mmol), **2a** (0.4 mmol), $K_2S_2O_8$ (0.3 mmol), $AgNO_3$ (0.04 mmol), CH_3CN (1 mL), H_2O (1 mL), 50 °C, 12 h. [b]Isolated yield based on the corresponding carboxylic acid. [c]Solvent: $CH_3CN/CH_2Cl_2/H_2O$ (2:4:1). [d]Reaction time: 5 h. [e]Reaction time: 10 h. [f]*trans*/*cis* = 85:15. [g]dr = 1:1.



substrate **16** was designed as the probe for the mechanism. Reaction of **16** with allylating agent **2c** underwent the decarboxylation/5-*exo* cyclization/allylation sequence to give

Scheme 2. Decarboxylative Allylation with Different Allylating Agents



[a]Reaction conditions: carboxylic acid (0.2 mmol), allylating agent (0.4 mmol), $K_2S_2O_8$ (0.3 mmol), $AgNO_3$ (0.04 mmol), CH_3CN (1 mL), H_2O (1 mL), 50 °C, 12 h. [b]Isolated yield based on the corresponding carboxylic acid. [c]Solvent: $CH_3CN/CH_2Cl_2/H_2O$ (2:4:1).

the cyclized product **17** in 46% yield as the mixture of four stereoisomers in 9:14:26:51 ratio determined by GC−MS (eq 4).

A plausible mechanism was thus proposed, as shown in Figure 2. The Ag(I) is first oxidized by persulfate to give the highly

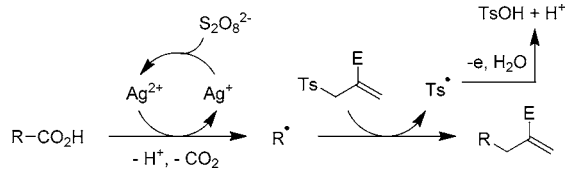


Figure 2. Proposed mechanism of decarboxylative allylation.

reactive Ag(II) intermediate, which in turn oxidizes a carboxylate to produce the carboxyl radical via single-electron transfer.[19] The carboxyl radical then undergoes fast decarboxylation to generate the alkyl radical. The addition of the alkyl radical onto an allyl sulfone followed by β-elimination leads to the product alkene and a tosyl radical. Finally, oxidation of the tosyl radical gives rise to TsOH.

In summary, we have successfully developed the one-step decarboxylative allylation of aliphatic carboxylic acids in aqueous solution. This transformation is not only efficient and chemoselective but also silver catalytic. In addition, it possesses a broad substrate scope and wide functional group compatibility. In view of its operational simplicity and mild experimental conditions, this method should find important applications in organic synthesis.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b00802.

Full experimental details, characterizations of new compounds, and copies of ^1H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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