# Palladium-Catalyzed Visible-Light-Driven Carboxylation of Aryl and Alkenyl Triflates by Using Photoredox Catalysts

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Ⓢ *Supporting Information*

ABSTRACT: A visible-light-driven carboxylation of aryl and alkenyl triflates with CO_2 is developed by using a combination of Pd and photoredox catalysts. This reaction proceeds under mild conditions and can be applied to a wide range of substrates including acyclic alkenyl triflates.
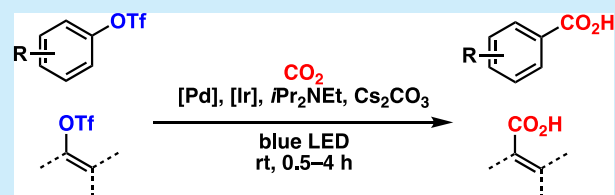
Carboxylation reactions utilizing carbon dioxide (CO_2) as a C1 source have attracted significant attention from many synthetic chemists for a long time. Highly nucleophilic metallic reagents such as Grignard reagents, which are directly generated from organic halides, are traditionally employed for carboxylation. Transition-metal-catalyzed carboxylation of organic halides has also been achieved by using a stoichiometric amount of metallic reductants such as Et_2Zn and Mn.[1] More recently, visible-light-driven carboxylation of aryl and alkyl halides was realized by using a Pd–Ir or Ni–organic dye dual catalyst system without the necessity of using a stoichiometric amount of strong metallic reductants.[2,3]

Aryl and alkenyl trifluoromethanesulfonates (triflates) are considered as an equivalent to the corresponding halides and are highly useful as they are easily available from the corresponding phenols and carbonyl or alkynyl compounds.[4] However, to the best of our knowledge, there have been only two reports on carboxylation of aryl or alkenyl triflates with transition-metal catalysts except for electrochemical methods.[5,6] In 2015, Tsuji et al. reported Co- and Ni-catalyzed carboxylation of aryl and alkenyl triflates using a stoichiometric amount of Mn as a reductant (Scheme 1a).[7] Later, König et al. reported carboxylation of aryl and alkyl bromides and aryl triflates using Ni and organic photoredox catalysts, where only three aryl triflates were employed as substrate (Scheme 1b).[2b] These two reactions proceeded smoothly at room temperature, but there are some drawbacks such as use of metallic reductants, long reaction time (>20 h), and limited substrate scopes, i.e., no examples of acyclic alkenyl triflates. Thus, development of more general methods is desirable for carboxylation of aryl and alkenyl triflates.

We here report a facile method for carboxylation of aryl and alkenyl triflates with a combination of Pd and photoredox catalysts using amine as a reductant (Scheme 1c). These reactions are completed within 4 h, much faster than the previously reported carboxylations of triflates, and a broad scope of triflates is applicable including acyclic alkenyl triflates.
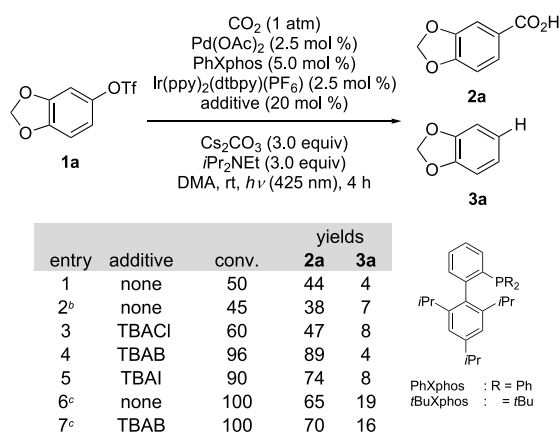
To initiate our study, the reaction of aryl triflates was examined on the basis of our photocatalytic carboxylation

Scheme 1. Direct Carboxylation of Aryl or Alkenyl Triflates with CO_2
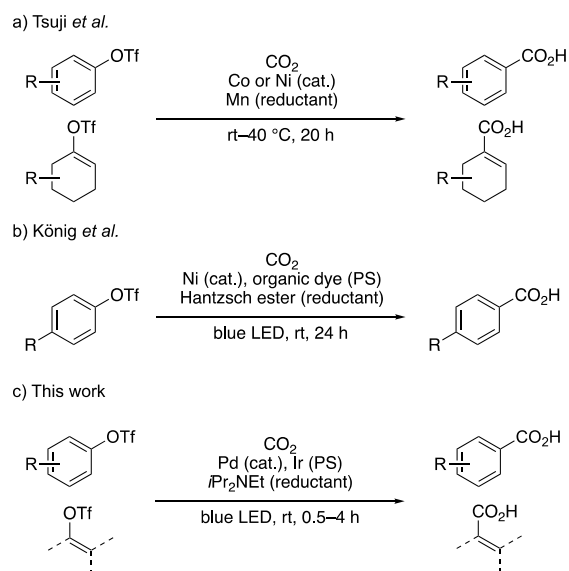
conditions of aryl halides (Table 1).[2a] First, we conducted the carboxylation of 3,4-(methylenedioxy)phenyl triflate (**1a**) using catalytic amounts of $Pd(OAc)_2$, 2-diphenylphosphino-2′,4′,6′-triisopropylbiphenyl (PhXphos),[8] and Ir-(ppy)$_2$(dtbpy)(PF$_6$) under irradiation with blue light emitting diodes (LEDs) in the presence of an excess amount of iPr$_2$NEt as an electron donor under a CO_2 atmosphere at room temperature (entry 1). Though this is the optimized condition for aryl bromides, the conversion of **1a** and the yield of the desired carboxylic acid **2a** were moderate, and a small amount of the hydrogenated product **3a** was obtained. Extension of the reaction time from 4 to 12 h did not improve the yield, suggesting the deactivation of the Pd catalyst (entry 2). As the
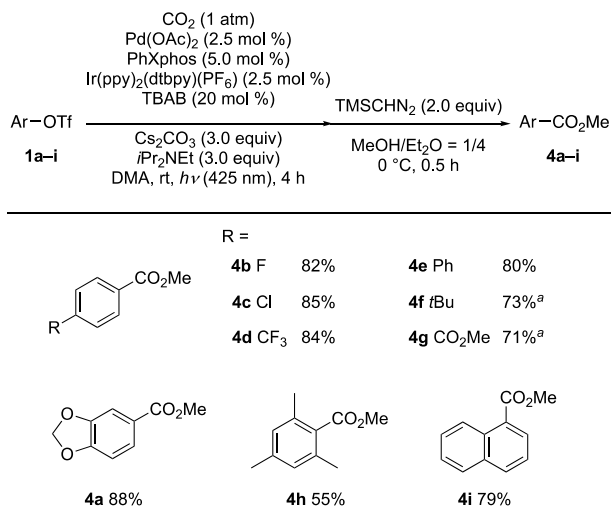
Table 1. Screening of Reaction Conditions for Aryl Triflates[a]

entry	additive	conv.	yields 2a	3a
1	none	50	44	4
2[b]	none	45	38	7
3	TBACl	60	47	8
4	TBAB	96	89	4
5	TBAI	90	74	8
6[c]	none	100	65	19
7[c]	TBAB	100	70	16

PhXphos : R = Ph
tBuXphos : = tBu

[a]Determined by ^{1}H NMR spectra. [b]12 h. [c]Using tBuXphos instead of PhXphos.

cationic [ArPd(PhXphos)]OTf[9] species generated in situ was supposed to be less stable than halide-containing neutral ArPdX(PhXphos) species, catalytic amounts of tetrabutylammonium (TBA) halides were added to the reaction mixture in order to convert the cationic Pd complex into the neutral one (entries 3−5). As expected, all of the halides improved the yields of **2a**, and quite pleasingly, **2a** was obtained in 89% yield with 20 mol % of TBA bromide (TBAB). The use of more electron-donating 2-(di-*tert*-butylphosphino)-2′,4′,6′-triisopropylbiphenyl (*t*BuXphos),[10] which is also effective for carboxylation of aryl halides,[2a] led to the full conversion of **1a**, but the yield of **2a** was not significantly increased upon addition of TBAB (entries 6 and 7).

With the optimized conditions in hand, we investigated the substrate scope of aryl triflates (Scheme 2). To facilitate the purification, the obtained carboxylic acids were converted into the corresponding methyl esters by treatment with (trimethylsilyl)diazomethane (TMSCHN$_2$). Aryl triflates **1b**−**1e** with electron-withdrawing substituents at the *para* position

Scheme 2. Substrate Scope of Aryl Triflates

R =
4b F 82%   **4e** Ph 80%
4c Cl 85%   **4f** *t*Bu 73%[a]
4d CF$_3$ 84%   **4g** CO$_2$Me 71%[a]

4a 88%   **4h** 55%   **4i** 79%

[a]Using *t*BuXphos instead of PhXphos.

gave the desired methyl esters **4b**−**4e** in good yields. Notably, the carboxylation of *p*-chlorophenyl triflate **1c** proceeded at the triflate group selectively while the chloride functionality remained inert, which can be employed for further transformations. For the aryl triflate **1f** with an electron-donating *tert*-butyl group, the conversion and yield were low with PhXphos (39% and 32% by NMR, respectively) probably due to the slower oxidative addition of the triflate. The use of more electron-donating *t*BuXphos as a ligand increased the yield of **4f** to 73%. Aryl triflate **1g** with a methoxycarbonyl substituent suffered from low NMR yield of **4g** (40%) with PhXphos due to generation of the corresponding phenol (29%), which was thought to be formed via direct one-electron reduction of the triflate by the Ir photocatalyst.[11] In this case also, employing *t*BuXphos was effective, affording **4g** in 71% yield with a trace amount of the phenol. Bulky 2,4,6-trimethylphenyl triflate **1h** was also applicable to the carboxylation although the yield of **4h** was slightly lower. Naphthyl triflate **1i** gave the methyl ester **4i** in 79% yield.

As the carboxylation of aryl triflates was found to be widely applicable based on the Pd−Ir dual catalyst system, the carboxylation of alkenyl triflates, which has never been achieved under photocatalytic conditions with organic reductants, was examined next (Table 2). Piperidone-derived

**Table 2. Screening of Reaction Conditions for Alkenyl Triflates**
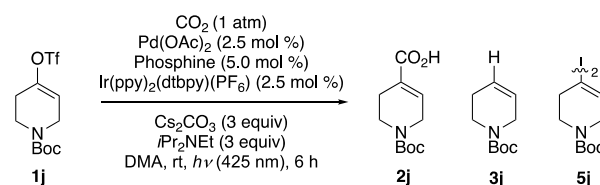
entry	phosphine	conv[a] (%)	yields[a] (%) 2j	3j	5j
1	PhXphos	100	37	31	14
2	*t*BuXphos	100	7	35	43
3	Ar[(CF3)2]Xphos	100	71	12	2
4[b]	Ar[(CF3)2]Xphos	100	62	11	4
5[c]	Ar[(CF3)2]Xphos	99	69	9	1

[a]Determined by ^{1}H NMR spectra. [b]With TBAB (20 mol %). [c]15 min.

triflate **1j** was chosen as a model cyclic substrate. Using PhXphos in the absence of TBAB, the desired ester **2j** was obtained in moderate yield with considerable amounts of the reduced product **3j** and the homodimer **5j** (entry 1). We examined more and less electron-donating Xphos-type ligands to find that 2-(3,5-bis(trifluoromethyl)phenyl)phosphino-2′,4′,6′-triisopropylbiphenyl (Ar[(CF3)2]Xphos)[12] gave 71% yield of **2j** with smaller amounts of **3j** and **5j** (entries 2 and 3). The use of the electron-deficient ligand would have led to facile one-electron reduction of [alkenylPd(Xphos)]OTf and suppressed the formation of the byproducts. In contrast to the aryl triflates, addition of TBAB did not improve the yield of **2j** (entry 4). It should be noted that the carboxylation proceeded very rapidly and was completed within only 15 min (entry 5).

Then we expanded the scope of alkenyl triflates (Scheme 3). Irradiation for 2 h was found to be sufficiently long for the full conversion of all the alkenyl triflates. Cyclohexenyl triflates **1k**−**o** gave the desired methyl esters **4k**−**o** in moderate to good yields, including acetal **4n** and tetrasubstituted olefin **4o**.

Scheme 3. Substrate Scope of Alkenyl Triflates
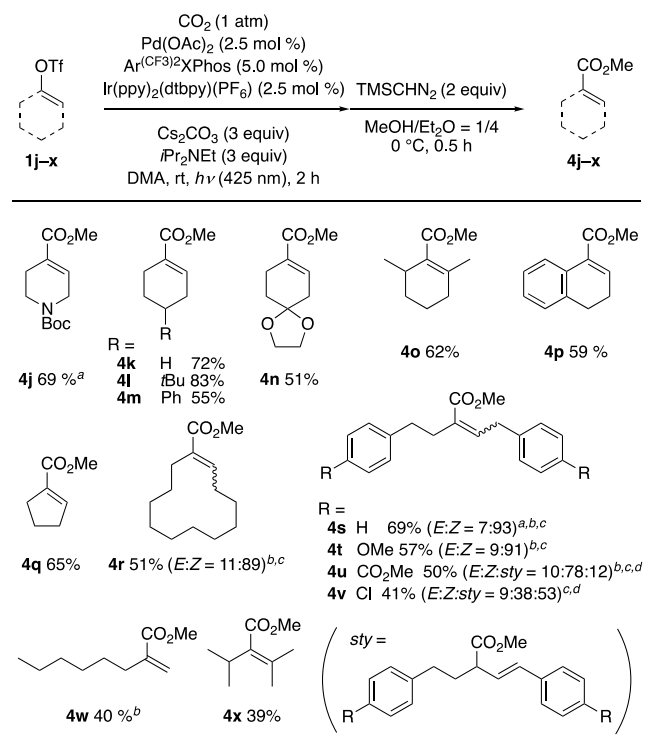
^{a}0.5 h. ^{b}MeCN was used as a solvent. ^{c}**1r** ($E/Z = 7:93$) and **1s**–**v** ($E/Z \sim 1:3$) were used. ^{d}Styrene-type products were obtained due to isomerization.

Tetralone-derived cyclic triflate **1p** was also successfully converted into **4p**. Besides the 6-memberd ring triflates, cycloheptenyl triflate **1q** and cyclododecenyl triflate **1r** provided the desired products **4q** and **4r**, respectively. Importantly, this carboxylation procedure was effective for acyclic alkenyl triflates with slight modification. When the acyclic olefin **1s** was subjected to the optimized conditions, elimination of the triflate predominated and an alkyne was obtained as the main byproduct (Table S7). Though the formation of the alkyne was also observed only with Cs_2CO_3 in the absence of the Pd and Ir catalysts, addition of the Pd catalyst increased the amount of the alkyne, suggesting the involvement of [alkenylPd(Xphos)]OTf for the formation of the alkyne. We found that the use of MeCN as a solvent greatly suppressed the alkyne formation and increased the yield of **4s** up to 69% probably due to the stabilization of the cationic Pd species. Other acyclic triflates **1t**–**x** including methyl ether **1t**, methyl ester **1u**, and chloride **1v** were also applicable without losing the functional groups, although isomerization of the C=C double bonds occurred for electron-deficient products **4u** and **4v**. Aliphatic acyclic alkenyl triflates **1w** and **1x** gave the desired methyl esters in moderate yields. It should be noted that the alkenyl triflate **1w** was not suitable for the carboxylation reaction developed by Tsuji et al.,[7] and this is the first example of carboxylation of acyclic alkenyl triflates.

The proposed mechanism of this carboxylation for aryl and alkenyl triflates in the absence of TBAB is shown in Scheme 4.[13] Electron-deficient cationic [RPd(Xphos)]OTf **B**, which would be readily generated by oxidative addition of R–OTf to Pd(0)(Xphos) **A**, would undergo one-electron reduction to give nucleophilic RPd(I)(Xphos) **C**. This Pd(I) species would react with CO_2 to give the corresponding (RCOO)Pd(I)-

Scheme 4. Proposed Catalytic Cycle
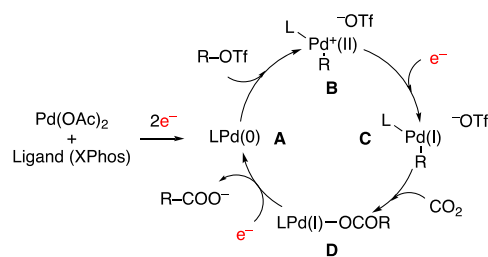
(Xphos) **D**, which would be further reduced to Pd(0)(Xphos) **A** with release of RCOO⁻.[14]

In conclusion, we have developed a facile and convenient method for carboxylation of aryl and alkenyl triflates under photocatalytic conditions. This carboxylation proceeds faster than the previous carboxylations and is compatible with a variety of functional groups because of the mild conditions. Acyclic alkenyl triflates can also be utilized as substrates with suppression of the alkyne formation for the first time. Further investigation into the reaction mechanism is now ongoing in our laboratory.

■ ASSOCIATED CONTENT

ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b01340.

Detailed experimental procedures, spectral data, and analytical data (PDF)

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Notes

The authors declare no competing financial interest.

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(11) The carboxylation of **1g** with PhXphos in the absence of light gave only a trace amount of the phenol (4% NMR yield), which indicates **1g** was not hydrolyzed under the reaction conditions. It has been reported that aryl triflates can be reduced to the corresponding phenols by a single-electron donor. See: Jolly, P. I.; Fleary-Roberts, N.; O'Sullivan, S.; Doni, E.; Zhou, S.; Murphy, J. A. *Org. Biomol. Chem.* **2012**, *10*, 5807.

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(13) We suppose the mechanism of the carboxylation of the aryl triflates in the presence of TBAB is similar to that of our carboxylation of aryl halides.[2a]

(14) For the formation of hydrogenated byproducts **3**, we suppose that the hydrogen source is a proton released by iPr$_2$NEt because amines generally work as electron and proton donors in photoredox reactions. The reduced Pd intermediate **C** shown in Scheme 4 would be protonated to give hydrogenated products **3**, although the detailed reaction mechanism is still unclear. To support this hypothesis, we conducted the carboxylation of **1j** in the absence of Cs_2CO_3. The yield of the hydrogenated product **3j** was 21% (NMR), which is higher than the yield in the presence of Cs_2CO_3 (12% in Table 2, entry 3). This result suggests Cs_2CO_3 works as a base to trap the protons generated from iPr$_2$NEt, as mentioned in our previous paper on the photoredox carboxylation of aryl halides.[2a]