EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201500038

Radical Decarboxylative Fluorination of Aryloxyacetic Acids Using *N*-Fluorobenzenesulfonimide and a Photosensitizer

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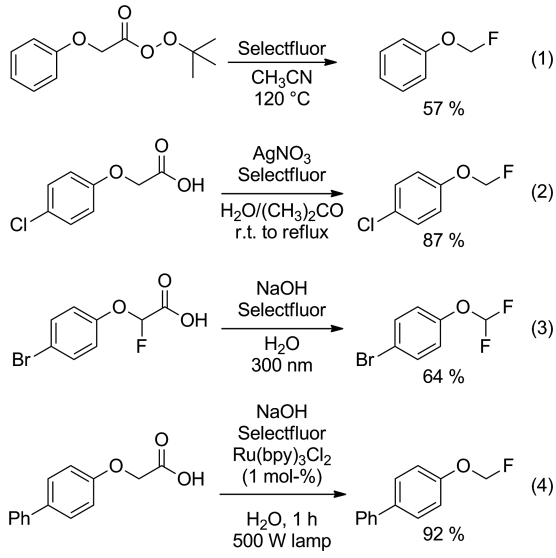
Keywords: Radicals / Photochemistry / Photosensitizer / Fluorine

Fluorinated methoxy arenes are emerging as important motifs in both agrochemicals and pharmaceuticals. A novel technique for the synthesis of monofluoromethoxy arenes through the direct fluorodecarboxylation of carboxylic acids was developed that uses photosensitizers and *N*-fluorobenzenesulfonimide (NFSI). Utilization of the oxidatively mild fluorine transfer agent NFSI enabled the synthesis of fluoromethyl ethers that were previously inaccessible with decarboxylative fluorinations performed with Selectfluor. Mechanistic studies are consistent with the photosensitizer effecting oxidation of the aryloxyacetic acid.

Introduction

Fluorinated methoxy arenes are increasingly pervasive in both the agrochemical and the pharmaceutical industries.[1] The growing importance of these motifs in biologically active molecules has led to a concomitant increase in the development of new synthetic methodologies focused on the preparation of fluoro ethers.[1–4] Mono-, di-, and trifluoromethoxy-substituted arenes have traditionally been prepared from either ionic[3] or carbene[4] reactive intermediates. Free-radical-based synthetic methods are attractive alternatives, but there are only a few reports of their use in the preparation of fluoromethoxy arenes.[5–9] A viable and widely applicable radical-based approach to fluorinated ethers would provide a complementary solution to this important chemical challenge.

The earliest reported example of a radical-based method utilized xenon difluoride for the preparation of monofluoromethoxy arenes.[5] Xenon difluoride is a versatile synthetic reagent,[10] but its expense and high reduction potential[11] limit its utility. In 2012, we demonstrated that the electrophilic fluorine sources Selectfluor[12] and *N*-fluorobenzenesulfonimide (NFSI)[13] are viable radical fluorine transfer reagents that could be utilized in the thermal fluorination of α-phenoxy *tert*-butyl peresters [Scheme 1, Equation (1)].[6] Subsequently, the Li group demonstrated that Selectfluor, in combination with a silver catalyst, could also be employed for the synthesis of both alkyl fluorides as well as an example of a monofluoromethoxy arene [Scheme 1, Equation (2)].[7]



Scheme 1. Synthesis of fluoromethoxy ethers by using radical decarboxylative fluorination; bpy = 2,2′-bipyridine.

We recently reported two different photochemical decarboxylative fluorination methods for the preparation of fluoromethoxy arenes.[8,9] The first method[8] utilizes UV light and Selectfluor as both the oxidant and fluorine transfer agent to afford either monofluoromethoxy arenes or difluoromethoxy arenes [Scheme 1, Equation (3)]. The second method[9] utilizes visible light with a photoredox catalyst to effect the oxidation and decarboxylation [Scheme 1, Equation (4)]. Both of these reactions can be successfully employed if the arene is electron neutral or electron deficient. However, several substrate classes, such as naphthyl and electron-rich arenes, afford low yields of the desired fluorination product and instead provide products corresponding to ionic ring fluorination.

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201500038.

The most significant factor contributing to limited generality and scope for radical-based fluorination methodologies is the ability of Selectfluor to directly fluorinate electron-rich aryl rings.[14] It has been postulated that the electrophilic reactivity of the fluorinating agents correlates with their efficiency as an oxidant (i.e., higher reduction potentials).[15] The challenge is that most of the known sources of atomic fluorine, such as molecular fluorine and xenon difluoride, have significantly higher reduction potentials [E = 2.87 V and 2.64 V (SHE), respectively][1a,11] than Selectfluor [E = 0.57 V (SHE)][16] (Figure 1), and thus they will likely have similar, or even more significant, substrate limitations.

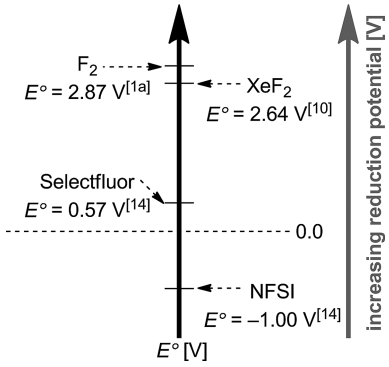
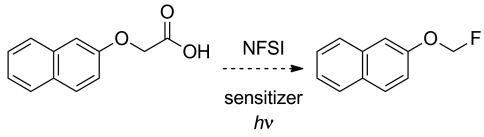


Figure 1. Comparison of fluorodecarboxylation reagents by increasing reduction potential in reference to the standard hydrogen electrode (SHE).

As a possible solution, we turned our attention to NFSI. NFSI has been demonstrated to be a weaker electrophilic source of atomic fluorine in aryl fluorination reactions than Selectfluor and has been measured to be a weaker oxidant [E = –1.00 V (SHE)][16] than any other known source of atomic fluorine.[17] Unfortunately, NFSI was significantly inferior to Selectfluor in our previously developed photochemical decarboxylative fluorination methodologies.[8,9] A new photodecarboxylative fluorination that can utilize a mild oxidant, such as NFSI, has the potential to access a wider substrate scope than any previous methodology that uses either thermal conditions or Selectfluor. Herein, we report a new approach to these photodecarboxylative fluorination reactions by using a combination of NFSI and a photosensitizer (Scheme 2).



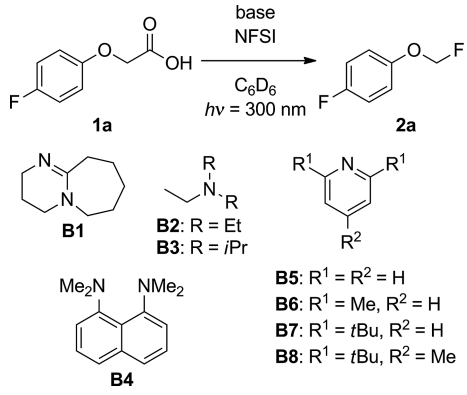
Scheme 2. This work: radical decarboxylative fluorination with NFSI.

Results and Discussion

Reaction Development

Investigations into the development of a general photodecarboxylative fluorination began with *para*-fluoroaryloxy acid **1a** (Table 1), a substrate that is known to undergo photofluorodecarboxylation by using our previously developed Selectfluor-based methodologies.[8,9] All initial experiments were run in deuterated benzene to facilitate analysis by ^{1}H NMR spectroscopy. As expected from previous studies that indicated a base facilitates the reaction,[8] the control experiment with just NFSI and 300 nm light (Table 1, entry 1) led to fluorinated product **2a** in only 7% yield, as determined by NMR spectroscopy.

Table 1. Effect of organic bases on the photodecarboxylative fluorination of **1a**.[a]



Entry	Base (equiv.)	Yield[b] [%]
1	no base (0)	7
2	**B1** (1.0)	61[c]
3	**B2** (1.0)	46[c]
4	**B3** (1.0)	43[c]
5	**B4** (1.0)	0[d]
6	**B5** (1.0)	55
7	**B6** (1.0)	80
8	**B7** (1.0)	75[e]
9	**B8** (1.0)	81[e]
10	**B8** (0.5)	81[e]
11	**B8** (0.25)	65[f]

[a] Reaction conditions: base (as indicated), NFSI (4.0 equiv.), **1a** (1.0 equiv., 0.05 mmol) at 0.1 M in deuteriobenzene, irradiated at 300 nm for 2 h. [b] Determined by ^{1}H NMR spectroscopy by using ethyl trifluoroacetate as an internal standard. [c] NFSI reacts with base to form an ammonium fluoride. [d] Electrophilic aromatic fluorination of the base was observed. [e] Average value of three trials. [f] Average value of two trials.

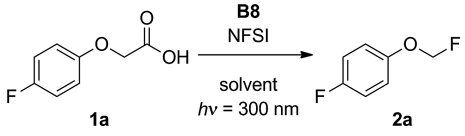
Our optimization began by investigations into non-pyridine amine bases **B1**–**B4** that have solubility profiles similar to that of NSFI (Table 1, entries 2–5). DBU (**B1**) and trialkylamine bases **B2** and **B3** afforded fluoro ether **2a** in moderate yields, whereas **B4** was incompatible with NFSI and simply underwent electrophilic aromatic fluorination. The moderate yields in entries 2–4 (Table 1) may be the result of the direct fluorination of bases **B1**–**B3** with NFSI.[15a] Indeed, analysis of a mixture of NFSI and triethylamine (Table 1, entry 3) by ^{19}F NMR spectroscopy showed the formation of a fluorotrialkylammonium species ($\delta \approx$ 63 ppm), which confirmed that fluorine transfer between the amines had occurred. An experiment performed with the use of an excess amount of triethylamine (**B2**) was performed to test if the newly formed fluorotrialkylammonium

was a viable source of atomic fluorine. Analysis by ^{19}F NMR spectroscopy showed complete conversion of **B2** into fluorotriethylammonium, and fluorination product **2a** was not observed after irradiation at 300 nm for 2 h. Thus, the fluorotrialkylammonium species is not a viable source of atomic fluorine and fluoro ether product **2a** is formed exclusively from NFSI.

We next focused on less nucleophilic bases that were less likely to react with NFSI (i.e., **B5**–**B8**). Gratifyingly, hindered pyridine bases (Table 1, entries 7–9) afforded fluorination product **2a** in good yields, and 2,6-lutidine (**B6**) performed comparably to sterically hindered *tert*-butyl analogues **B7** and **B8**. However, in solvents such as acetone, the **B6**–**1a** salt precipitated from solution. Thus, **B8** was chosen as the base for further optimization. The amount of base could be decreased to 0.5 equiv. without impacting the reaction (Table 1, entry 10), likely because the fluorine transfer product from NFSI, bis(phenylsulfonyl)amide, can also serve as a base in the reaction. A further decrease in the amount of base provided inconsistent results with yields ranging from 51 to 78%.

Photodecarboxylative fluorination with **B8** and NFSI shows broad solvent tolerance with high yields of fluorination in nonpolar solvents (Table 2, entries 1–4). With polar solvents, solubility problems were encountered; aqueous acetone or acetonitrile mixed-solvent systems as well as neat methanol (Table 2, entry 8) did not solubilize NFSI. Fluorination failed to occur in neat DMSO, likely because the solvent begins to absorb UV light at 330 nm. However, trace amounts of DMSO could be added into acetone or acetonitrile to improve substrate solubility if necessary. A suitable balance of effective fluorination and reagent solubility were found for acetone and acetonitrile (Table 2, entries 6 and 7), both of which provided fluoro ether **2a** in high yields.

Table 2. Effect of solvent on the photodecarboxylative fluorination of **1a**.[a]



Entry	Solvent	Yield[b] [%]
1	benzene	81
2	toluene	69
3	CH_2Cl_2	85
4	$CHCl_3$	81
5	DMSO	0[c]
6	acetone	80[d]
7	MeCN	82[d]
8	MeOH	0[e]

[a] Reaction conditions: **B8** (0.5 equiv.), NFSI (4.0 equiv.), **1a** (1.0 equiv., 0.05 mmol) at 0.1 M in deuterated solvent, irradiated at 300 nm for 2 h. [b] Determined by ^1H NMR spectroscopy by using ethyl trifluoroacetate as an internal standard. [c] No photofluorodecarboxylation observed; **1a** was recovered completely. [d] Average value of four trials. [e] NFSI displayed poor solubility.

Unlike acetonitrile, acetone is a known triplet sensitizer[18] and has been shown to catalyze the photodecarboxylation of alkyl carboxylates in the presence of single-electron-transfer (SET) acceptors, such as phthalimides.[19] To determine if acetone was directly involved in the reaction, we investigated the decarboxylative fluorination by using 350 nm light. The emission range of the 350 nm light source is sufficiently narrow such that substrate **1a**, NFSI,[20] and acetonitrile will not absorb, and thus, no reaction should occur. However, the emission range is well within the acetone absorption profile.[21] As hypothesized, no reaction was observed upon running the decarboxylative fluorination in acetonitrile, but the reaction in acetone provided **2a** in 85% yield. Visible-light sources failed to promote decarboxylative fluorination, and no reaction was observed under thermal conditions, regardless of the solvent.

Reaction time was the last reaction parameter we optimized. As shown in Figure 2, photodecarboxylative fluorination with NFSI was significantly faster in acetone than in acetonitrile. Within 10 min, the reaction in acetone was >90% complete with full conversion of aryloxyacetic acid **1a** after 1 h. For the reaction in acetonitrile to be >90% complete, 1 h of irradiation was necessary. Complete conversion of aryloxyacetic acid **1a** required 2 to 3 h.

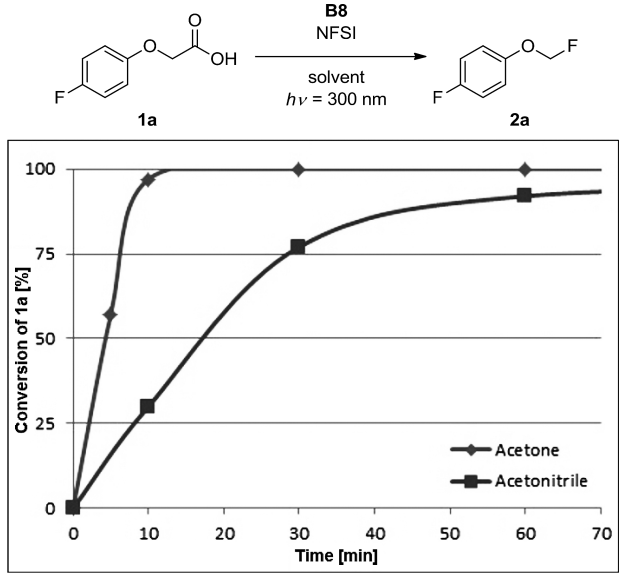


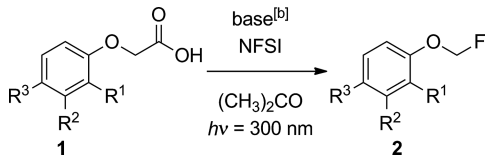
Figure 2. Effect of irradiation time on the photodecarboxylative fluorination. Reaction conditions: **B8** (0.5 equiv.), NFSI (4.0 equiv.), **1a** (1.0 equiv., 0.05 mmol) at 0.1 M in deuterated solvent (as indicated), irradiated at 300 nm for time as indicated. Conversions were determined by ^1H NMR spectroscopy by using ethyl trifluoroacetate as an internal standard.

Substrate Scope

The first substrates investigated (i.e., **1a**–**f**) were chosen because they are all viable in the previously developed Selectfluor-mediated methodologies[8,9] and, thus, provide a benchmark for comparison (Table 3). Decarboxylative

fluorination of **1a** provided **2a** in an average yield of 80%, which was slightly lower than the related photodecarboxylative fluorination with Selectfluor (Table 3, entry 1). By using the new NFSI conditions, decarboxylative fluorination of **1b**, **1c**, **1d**, and **1f** provided **2b**, **2c**, **2d**, and **2f** in yields that were nearly identical to those obtained from the related decarboxylative fluorination by using our previous methodologies (Table 3, entries 2–4, 6).[8,9] Further electronic deactivation of the aryloxy ring with two chlorine substituents reduced the effectiveness of fluorination with NFSI (Table 3, entry 5).

Table 3. Comparison of photodecarboxylative fluorination with NFSI to fluorination with Selectfluor.[a]

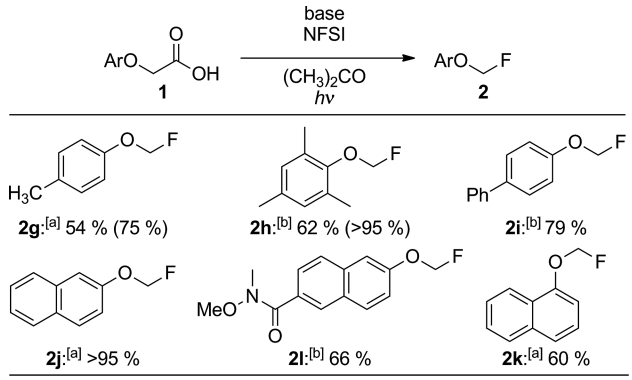


Entry	R^1	R^2	R^3	Compound	Yield [%] NFSI[c]	Selectfluor[d]
1	H	H	F	**1a**	(80)[e,f]	(94)
2	H	H	H	**1b**	(82)[e,g]	(84)
3	H	H	Br	**1c**	68[h]	60
4	H	Br	H	**1d**	73[h]	57 (72)
5	Cl	H	Cl	**1e**	54[h] (70)	86
6	H	*t*Bu	H	**1f**	84	83

[a] Reaction conditions: NFSI (4.0 equiv.), **1** (1.0 equiv., 0.4 mmol) at 0.15 M in argon-sparged acetone irradiated at 300 nm for 3 h. [b] **B8** (0.5 equiv.) was employed as the base unless otherwise indicated. [c] Yield of isolated product, yields in parentheses represent yields determined by ^{1}H NMR spectroscopy by using ethyl trifluoroacetate as an internal standard. NMR-scale reactions were performed on 0.05 mmol scale in deuterioacetone and were irradiated at 300 nm for 2 h. [d] Values taken from the literature are reproduced for ease of comparison. Yield of isolated product, yields in parentheses represent yields determined by ^{1}H NMR spectroscopy. [e] Owing to the volatility of **2**, isolation-scale reaction was not performed. [f] Average value of four trials. [g] Average value of three trials. [h] **B7** (0.5 equiv.) was employed as the base.

With new, viable photodecarboxylative fluorination methodology in hand, we tested the principal hypothesis of the study: whether the lower reduction potential of NFSI would allow the decarboxylative fluorination of more electron-rich aryloxy acetic acids. All of the substrates shown in Table 4[22] either provided low yields or failed completely under our former conditions with UV light and Selectfluor.[23] Whereas decarboxylative fluorination of substrate **1g** provided **2g** in only 34% yield (as determined by NMR spectroscopy) with Selectfluor and UV light,[8] our new NFSI conditions afforded **2g** in 75% yield (as determined by NMR spectroscopy), and ring fluorination was not observed. The decrease in the yield of the NMR product was due to substrate volatility. Decarboxylative fluorination of substrate **1h** proved to be unsuccessful with the use of UV light and Selectfluor. With NFSI, this substrate proceeded with high conversion and in good yield. Whereas 4-phenyl acid **1i** required the addition of a small amount of DMSO for solubility, the decarboxylative fluorination afforded **2i** in 79% yield.

Table 4. Substrate scope of the new photodecarboxylative fluorination.[a–c]

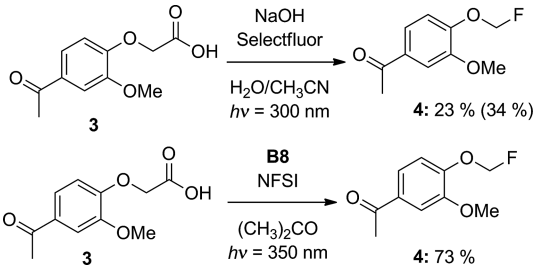


[a] Reaction conditions: NFSI (4.0 equiv.), **B7** (0.5 equiv.), **1** (1.0 equiv., 0.4 mmol) at 0.15 M in argon-sparged acetone irradiated at 300 nm for 3 h. [b] Reaction conditions: NFSI (3.0 equiv.), **B8** (0.5 equiv.), **1** (1.0 equiv., 0.4 mmol) at 0.15 M in argon-sparged acetone irradiated at 350 nm for 3 h. [c] Yield of isolated product, yields in parentheses represent yields determined by ^{1}H NMR spectroscopy by using ethyl trifluoroacetate as an internal standard on 0.05 mmol scale in deuterioacetone and irradiated at 300 nm for 2 h.

Encouraged by the successful use of phenyloxyacetic acid substrates, fluorodecarboxylation was investigated with naphthyloxyacetic acids, a substrate class that is incompatible with both the original UV light/Selectfluor conditions[8] and our photocatalytic conditions (Table 4).[9] For each of these substrates (i.e., **1j–l**), nonselective aryl fluorination and oxidation of the naphthyloxy ring outcompeted the desired decarboxylative fluorination reaction. By using our newly developed methodology, **2j** was isolated in near quantitative yield. Naphthyloxy substrates with an altered substitution pattern (see compound **1k**) or with an added electron-withdrawing group (see compound **1l**) were also viable in the newly developed reaction and provided good yields of the isolated products. Increasing the electron density of the aryloxy moiety further with a methoxy substituent (4-methoxyphenyloxyacetic acid) was still a limitation, and nonspecific aryl fluorination outcompeted the desired decarboxylative fluorination.

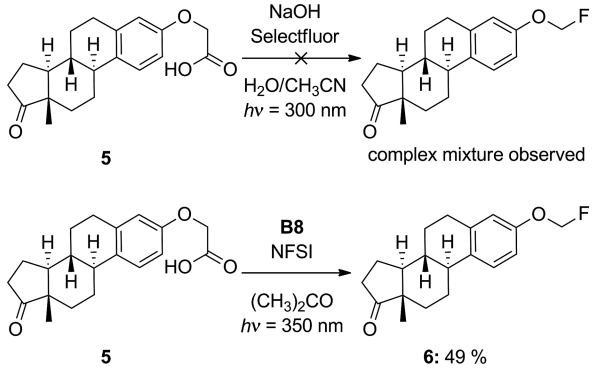
We next investigated the decarboxylative fluorination by using a natural product analogue, apocynin derivative **3** (Scheme 3). The counterbalance of the electron-donating and electron-withdrawing substituents on the aryl ring provided an intriguing test for our newly developed photodecarboxylative fluorination methodology. Additionally, apocynin derivative **3** was not a good substrate for our aqueous Selectfluor conditions, as it only provided **4** in 23% yield (34% by NMR spectroscopy). However, the photosensitized reaction with NFSI in acetone was very successful, and **4** was isolated in 73% yield. Substrates without the

counterbalanced electron-withdrawing acyl group, such as *para*-methoxyarylacetic acid, afforded ring-fluorinated products.



Scheme 3. Photodecarboxylative fluorination of apocynin derivative **3**.

To further test our methodology, we examined estrone derivative **5** (Scheme 4). Photodecarboxylative fluorination of this steroid derivative presents a formidable challenge to the Selectfluor-mediated system, as the tertiary benzylic position can be readily oxidized. Indeed, under conditions that employed UV light and Selectfluor,[8] no fluorination product was detected. However, photosensitized decarboxylative fluorination by employing NFSI successfully provided fluoromethoxy steroid **6** in 49% yield.[24]



Scheme 4. Photodecarboxylative fluorination of estrone derivative **5**.

Mechanistic Investigations

Future reaction developments for the photodecarboxylative fluorination with NFSI required a detailed understanding of the reaction mechanism, particularly as the solvent selection appeared to influence the rate of reaction. Photodecarboxylative fluorination with NFSI in acetonitrile closely matched the overall reaction profile of the decarboxylative fluorination with Selectfluor. If the new conditions with NFSI were used in acetone, the reaction rates significantly increased and the viable wavelengths needed to promote the reaction broadened. To probe the specifics of the reaction mechanism more deeply, we began with a study of the nonsensitized photoreaction in acetonitrile.

Nonsensitized Photodecarboxylative Fluorinations

The proposed acetonitrile nonsensitized photoreaction mechanism, presented in Figure 3, is analogous to the mechanism for the previously developed decarboxylative fluorination with Selectfluor. Excitation of the B-band transition ($\pi \rightarrow \pi^*$) of the phenoxy nucleus of **1** creates excited state **7**, which undergoes reversible single-electron transfer[25] with NFSI. Following base-mediated deprotonation and decarboxylation, radical **10** is fluorinated by the NFSI radical anion through either direct radical abstraction of fluorine or back electron transfer from the radical anion to **10**, followed by ionic fluorination. Another possible mechanism involves internal electron transfer (from the carboxylate to the benzenoid core) followed by radical decarboxylation of the resulting carboxy radical.

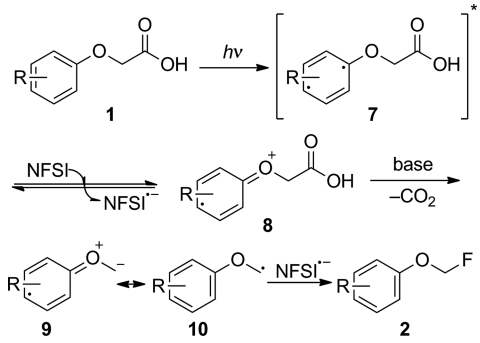
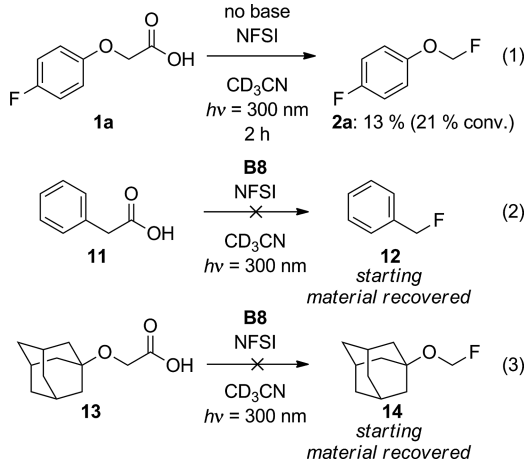


Figure 3. Proposed reaction mechanism for nonsensitized photodecarboxylative fluorination.

All of the photodecarboxylative fluorination optimization experiments with NFSI support the mechanism indicated in Figure 3. As established by the experiments listed in Table 1 and Scheme 5 [Equation (1)], efficient decarboxylative fluorination requires a base in the nonsensitized reaction. The deprotonation step appears to facilitate irreversible decarboxylation of **8**, which supports the necessity of a carboxylate for either the Strecker-type decarboxylation[26] mechanism or the internal single-electron-transfer mechanism. Furthermore, no reaction is observed under



Scheme 5. Mechanistic investigations on the nonsensitized photodecarboxylative fluorination reaction in acetonitrile.

thermal conditions, which suggests that the reaction does not proceed through a Hunsdiecker-type reaction[27] with acyl hypofluorite intermediates.

We next investigated the decarboxylative fluorination of phenyl acetic acid (**11**), as it contains both aryl and carboxylate chromophores. Using our standard reaction conditions with NFSI in acetonitrile, no reactivity was observed [Scheme 5, Equation (2)]. This further supports the assertion that hypofluorites are not involved in the reaction mechanism and that, additionally, the direct oxidation of the carboxylate by NFSI does not occur.

Finally, to investigate the necessity of the aryloxy ring, we irradiated α-alkoxy acid **13** [Scheme 5, Equation (3)] with 300 nm light. As expected, the starting material did not react under the standard conditions with NFSI. This suggests that the α-oxygen atom is not critical but that the aryl chromophore is required for reactivity.

Sensitized Photodecarboxylative Fluorinations

A photosensitizer, such as acetone, can alter the reaction mechanism in two possible ways:[28] acetone can serve as a mediator for energy transfer or it can act as a single-electron oxidant. If acetone serves as a mediator for energy transfer, then the overall reaction mechanism would be similar to that presented in Figure 3, with the exception that acetone could facilitate the excitation of substrate **1** to excited species **7**. Alternatively, photoexcited acetone can serve as a single-electron oxidant (Figure 4). Photoexcited ketone **15** can oxidize **1** in a reversible single-electron transfer to lead to radical cation **8**. Deprotonation by radical anion **16**, or from another base in solution,[29] leads to rapid and irreversible decarboxylation to aryloxymethyl **9** and **10**, which can be fluorinated by NFSI to yield **2**. The ketone sensitizer can be regenerated by back electron transfer from the bis(phenylsulfonyl)amidyl radical.

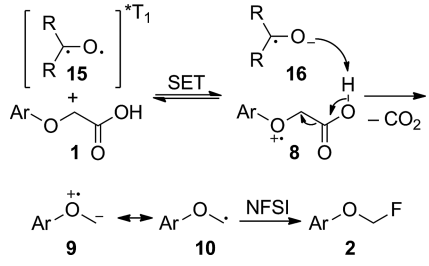
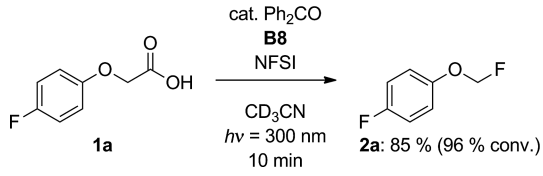


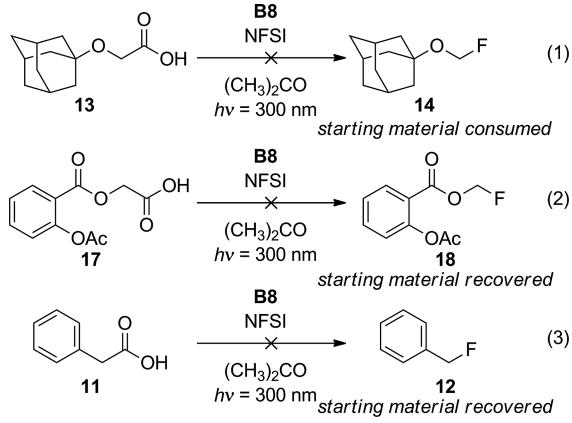
Figure 4. Proposed reaction mechanism for photosensitized photodecarboxylative fluorination through reversible electron transfer.

To differentiate between these two mechanistic possibilities, we explored adding a catalytic amount of the commonly employed photooxidant benzophenone[30] to the nonsensitized reaction in acetonitrile. Addition of benzophenone to the photodecarboxylative fluorination of substrate **1a** in acetonitrile (Scheme 6) led to a similar acceleration in the reaction rate; after only 10 min, the benzophenone-sensitized reaction in acetonitrile provided results analogous to those obtained for the reaction performed in acetone in terms of both conversion and yield. The similarity of this result suggests that acetone acts as a single-electron oxidant in the reaction.



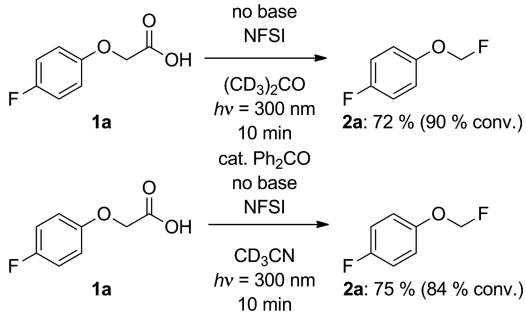
Scheme 6. Photodecarboxylative fluorination of **1a** by using a catalytic amount of benzophenone.

If acetone acts as an oxidant, there are two functional groups that may assist the oxidation: the aryl ring and the oxygen atom of the ether. To determine which functionalities were required, we examined the photodecarboxylative fluorination of acetic acid derivatives **13**, **17**, and **11** (Scheme 7).[31] Photodecarboxylative fluorination of **13** provided complete decarboxylation, and several fluorinated products were detected [Scheme 7, Equation (1)].[32] This proved that aryl substitution on the substrate is not necessary for the decarboxylation to occur. We next studied the reactivity of **17** and phenylacetic acid (**11**) [Scheme 7, Equations (2) and (3)]. Substrate **17** possesses a carboxylic acid with electronic properties similar to those of aryloxy acid **1**, but the ether oxygen atom is more difficult to oxidize. Phenylacetic acid has the carboxylic acid moiety but lacks the ether oxygen atom. Both of these substrates were not viable in the photodecarboxylative fluorination in acetone, which suggests the ether oxygen atom is crucial for reactivity.



Scheme 7. Mechanistic investigations on the sensitized photodecarboxylative fluorination in acetone.

On the basis of the mechanism depicted in Figure 4, radical anion **16** could act as the base and facilitate decarboxylation. Sensitized photodecarboxylative fluorinations, in both acetone and acetonitrile (with catalytic amounts of benzophenone), proceeded smoothly to give high conversions of **1a** after only 10 min (Scheme 8), which thus supports the mechanism in which the photosensitizer promotes the photodecarboxylation as both an oxidant and a base.[33]



Scheme 8. Base-free photosensitized decarboxylative fluorination.

Conclusions

We successfully developed a new photosensitized decarboxylative fluorination reaction of aryloxyacetic acids by employing *N*-fluorobenzenesulfonimide (NFSI) that significantly increases the substrate scope relative to that of previously reported photodecarboxylative fluorinations. Detailed mechanistic investigations into this new photodecarboxylative fluorination reaction uncovered a novel fluorination mechanism that involves photoexcitation of a sensitizer molecule, which facilitates single-electron transfer from the benzenoid core of the aryloxyacetic acids, which is followed by base-mediated decarboxylation and radical fluorination.

Utilization of an oxidatively mild radical fluorine source, NFSI, enabled the synthesis of fluoromethyl ethers that contain more electron-rich aromatic components including natural product derivatives. Most notably, photodecarboxylative fluorination with NFSI enabled the class of naphthyl fluoromethyl ethers to be synthesized, a class of compounds that was previously inaccessible by using any of the photochemical methods performed with Selectfluor. This constitutes a significant advance in the synthetic utility of photodecarboxylative fluorination.

Experimental Section

Photodecarboxylative Fluorination Optimization Studies: Solutions containing aryloxyacetic acid **1** (1 equiv.), base (0.5–1.0 equiv.), NFSI (1–4 equiv.), and ethyl trifluoroacetate (1.0 equiv.) in deuterated solvent (0.1 M in **1**) were partitioned to borosilicate NMR tubes. One sample was set aside as the $t = 0$ sample, and the remaining sample(s) was(were) placed on a rotating carousel inside a photochemical reactor (containing 16× 8 W lamps) and exposed to 300 nm light for 2 h. Analysis by NMR spectroscopy was performed directly on the crude reaction mixtures.

Isolation-Scale Photodecarboxylative Fluorination: The corresponding aryloxyacetic acid **1** (1 equiv.), **B8** or **B7** (0.5 equiv.), and NFSI (3–4 equiv.) were added to an argon-sparged solution of acetone (0.15 M in **1**) in an argon-filled borosilicate glass culture tube. The reaction vessel was then placed on a rotating carousel inside a photochemical reactor (containing 16× 8 W lamps) and exposed to 300 or 350 nm light for 3 h. Purification by flash column chromatography (petroleum ether/diethyl ether) afforded fluoromethyl ether **2**, **4**, or **6**.

Acknowledgments

The authors thank Dr. P. Kennepohl for guidance during computational work. This work was supported by the University of British Columbia (UBC) and a doctoral fellowship from the Natural Sciences and Engineering Research Council of Canada (NSERC) to J. C. T. L. We would also like to thank M. Rueda-Becerril and C. Chatalova-Sazepin for assistance with preparing the manuscript.

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[22] With the exception of substrate **1g**, which was originally reported in a previous Selectfluor reactivity study (ref.[8]), all compounds are new. See the Supporting Information for experimental details.
[23] Substrates **2g**, **2h**, and **2i** could be synthesized by using our photoredox catalysis method (ref.[9]) owing to the lower energy light that was utilized.
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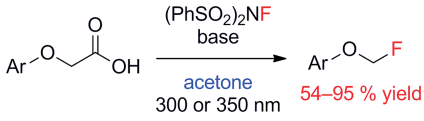
[32] As product **14** is relatively unstable, we primarily focused on the decarboxylation rather than the appearance of specific radical products.
[33] Whereas **B7** and **B8** are not mechanistically necessary as bases, in: sensitized photofluorodecarboxylations, the addition of these pyridine bases leads to the formation of fewer fluorinated byproducts with select substrates. See the Supporting Information for additional details.

Received: January 12, 2015
Published Online: ■

EurJOC European Journal of Organic Chemistry

Photodecarboxylative fluorination methodology involving the use of photosensitizers and *N*-fluorobenzenesulfonimide (NFSI) provides facile access to monofluoromethoxy-substituted arenes through the direct fluorodecarboxylation of carboxylic acids. Utilization of NFSI enables the synthesis of fluoromethyl ethers that were previously inaccessible with decarboxylative fluorinations performed with Selectfluor.



Radical Decarboxylative Fluorination

Keywords: Radicals / Photochemistry / Photosensitizer / Fluorine

