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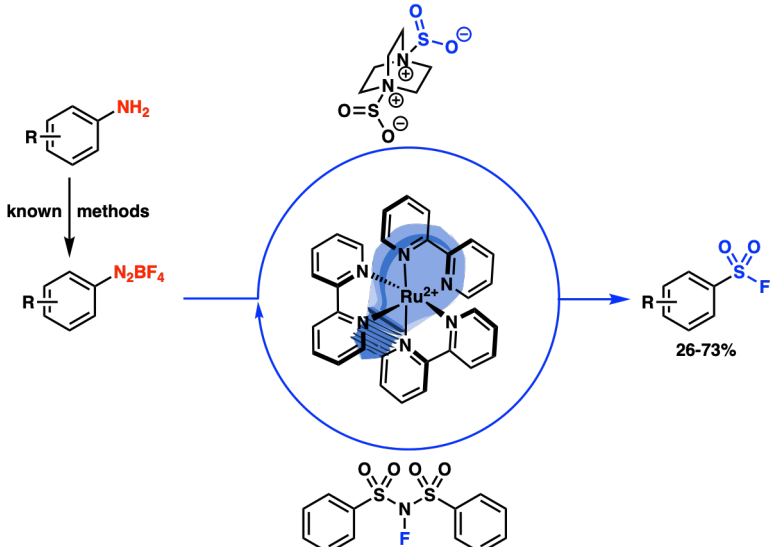
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Photocatalytic Synthesis of Aryl Sulfonyl Fluorides

Cooper A. Vincent,[a] Alexia Ripak,[b] Ludovic Troian-Gautier,[b,*] Uttam K. Tambar[a,*]

[a]*Department of Biochemistry, The University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, Texas 75390-9038, United States*

[b]*Université catholique de Louvain (UCLouvain), Institut de la Matière Condensée et des Nanosciences (IMCN), Molecular Chemistry, Materials and Catalysis (MOST), Place Louis Pasteur 1, bte L4.01.02, 1348 Louvain-la-Neuve, Belgium*



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Photocatalytic Conversion of Aryl Diazonium Salts to Sulfonyl Fluorides

Cooper A. Vincent,[a] Alexia Ripak,[b] Ludovic Troian-Gautier,[b,*] and Uttam K. Tambar[a,*]

[a]*Department of Biochemistry, The University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, Texas 75390-9038, United States*
[b]*Université Catholique de Louvain (UCLouvain), Institut de la Matière Condensée et des Nanosciences (IMCN), Molecular Chemistry, Materials and Catalysis (MOST), Place Louis Pasteur 1, bte L4.01.02, 1348 Louvain-la-Neuve, Belgium*

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ABSTRACT

Sulfonyl fluorides have emerged as powerful tools in chemical biology for the selective labelling of proteins. A photocatalytic method is described for the conversion of aryl diazonium salts to aryl sulfonyl fluorides. The diazonium substrates are easily obtained in one step from functionalized anilines. We present the optimization of this mild method for the synthesis of sulfonyl fluorides, the scope of the transformation with a series of functionalized diazonium salts, and we discuss photophysical measurements that provide detailed information about the mechanism of the photochemical process.

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1. Introduction

In 2014, Sharpless and co-workers introduced the concept of Sulfur(VI) Fluoride Exchange (SuFEx) chemistry of sulfonyl fluorides as a second generation click reaction.[1] This transformation allows for the selective and efficient reactivity of a sulfur(VI) center with a nucleophilic amino side chain under physiological conditions, exchanging the fluoride for a nucleophile.[2] The selective reactivity of sulfonyl fluorides is attributed to the abnormally strong sulfur–fluoride bond and sluggish reactivity at the sulfur(VI) center and it requires activation (H^+, R_3Si^+, etc.) to cleave the sulfur-fluorine bond.[3] Since Sharpless' seminal study, sulfonyl fluorides have emerged as useful chemical warheads for the site-selective modification of proteins in biological systems, with broad applications in drug discovery, biochemistry, and target identification.[4]

As the use of sulfonyl fluorides has increased, so has the demand for novel methods for their synthesis (Figure 1). Aryl sulfonyl fluorides (**1**) can be accessed through the activation and substitution of sulfonyl chlorides, sulfonamides, and sulfonic acids,[5] as well as the transition metal catalyzed activation of aryl halides, triflates, and boronic acids.[6] Recent advances in electrochemistry have enabled the conversion of thiophenols, disulfides, and aryl halides into sulfonyl fluorides.[7]

With an on-going interest in developing mild and general methods to synthesize functionalized sulfonyl fluorides from readily available starting materials, we recently reported a photocatalytic conversion of bench-stable alkyl organoboron substrates into sulfonyl fluorides.[8] Based on this chemistry, we were interested in developing a strategy to access sulfonyl fluorides from aryl diazonium salts (**2**). Herein, we describe the photocatalytic transformation of aryl diazonium salts (**2**) into sulfonyl fluorides (**1**) via a visible light-induced electron transfer pathway.

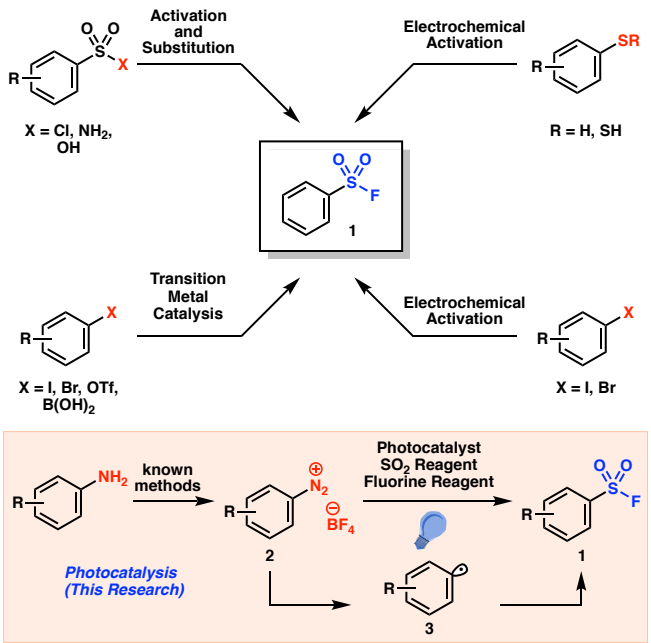


Figure 1. Previous methods for the synthesis of aryl sulfonyl fluorides and our strategy for the conversion from aryl diazonium salts to sulfonyl fluorides.

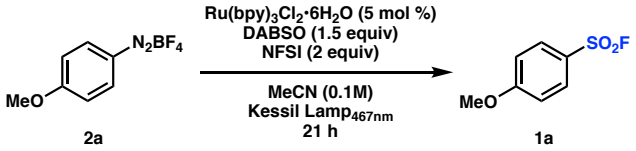
Diazonium salts are versatile substrates that are easily synthesized from anilines in a single step with high conversion.[9,10] When formed with tetrafluoroborate as the counterion, these compounds are easily isolated and recrystallized as stable solids.[11] Diazonium salts have been traditionally used to convert anilines into competent electrophiles for nucleophilic aromatic substitution.[12] They have also become common substrates for transition metal catalyzed cross-couplings.[13] More recently, methods have been developed for the reductive activation of diazonium salts for homolytic cleavage to generate aryl radicals (**3**).[14] Hence, these substrates are of great synthetic utility, as they would enable direct late-stage modifications of aniline-containing drug-like molecules.[15]

Our approach proceeds through a three-component coupling between the transiently formed aryl radical (**3**), a sulfur dioxide reagent, and a fluorine reagent. Recently, Tlili and co-workers reported a similar strategy for the generation of aryl sulfonyl fluorides from diazonium salts.[16] In addition, Chen, Weng, and Von Wangelin have developed transition metal mediated or thermal activations of diazonium salts to achieve similar products.[17] We demonstrate a complementary method that relies on a different photoredox catalyst and a distinct fluorine reagent. We describe detailed photophysical studies that shed light on the mechanism of both methodologies. We demonstrate the compatibility of our method with several aryl diazonium salts, with the goal of utilizing this strategy on medicinally relevant anilines that can be conveniently converted to their corresponding diazonium salts. We anticipate this approach will facilitate the generation of libraries of aryl sulfonyl fluorides from chemically diverse anilines in two steps.

2. Results and Discussion

We began our studies by converting *para*-methoxybenzenediazonium tetrafluoroborate **2a** to sulfonyl fluoride **1a** (Table 1). Under our standard optimized conditions, diazonium salt **2a** was subjected to $Ru(bpy)_3Cl_2{\cdot}6H_2O$, 467 nm LED irradiation, diazabicyclo[2.2.2]octane bis(sulfur dioxide) adduct (DABSO) as a source of sulfur dioxide,[18] and *N*-fluorobenzenesulfonimide (NFSI) as a fluorinating reagent in acetonitrile. The desired sulfonyl fluoride product **1a** was formed in 93% NMR yield, 73% isolated yield (entry 1). When the photocatalyst was replaced with Eosin Y (entry 2) or $[Ir(ppy)_2(dtbbpy)]PF_6$ (entry 3), the NMR yield of desired product diminished to 85% and 71%, respectively. With a different sulfur dioxide source (aqueous sulfurous acid, entry 4) or fluorine source (Selectfluor™, entry 5), the yields dropped significantly to 6% and 39%, respectively. In the presence of a different light source at a higher energy wavelength, the yield dropped slightly to 83% (entry 6). In 1,2-dichloroethane, the yield diminished slightly to 80% (entry 7) and when toluene was used, the yield of product decreased significantly to less than 5% (entry 8). Control experiments revealed that both the photocatalyst and light source are required for reactivity, as in the absence of both there was no product formation (entries 9 and 10).

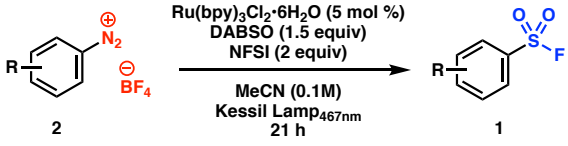
With optimal reaction conditions, we synthesized a small library of aryl sulfonyl fluorides to display the robustness of the method (Table 2). The reaction was productive on a wide range of substrates. Good isolated yields of products were observed. with electron donating substituents such as methoxy (entry 1), as well as electron withdrawing groups such as nitro (entry 2) and trifluoromethyl (entry 3). Overall, the transformation was tolerant of carbonyl groups, including a ketone (entry 4) and ester (entry 5). We were also pleased to see product formation with sterically hindered diazonium salts with an *ortho*-methoxy substituent (entry 6), *meta*-methoxy substituent (entry 7), *meta*-nitro substituent (entry 8), and multi-substituted aromatic rings (entries 9-10).



Entry	Variation from Standard Conditions	Yield (%)[a]
1	None	93 (73)
2	Eosin Y as photocatalyst	85
3	$[Ir(ppy)_2(dtbbpy)]PF_6$ as photocatalyst	71
4	SO_2H as SO_2 Source	6
5	Selectfluor as Fluorine Source	39
6	427 nm light source	83
7	DCE as Solvent	80
8	PhMe as solvent	< 5
9	No photocatalyst	< 5
10	No light source	< 5

Table 2. Development of sulfonyl fluorination of aryl diazonium salts.

Reaction conditions: Diazonium salt **2a** (0.23 mmol), photocatalyst (5 mol%), SO_2 source (1.5 equiv), fluorine source (1.5 equiv), Kessil lamp, solvent (0.1 M), 23 °C, 21 h. (a) NMR yield based on dimethoxybenzene (DMB) as internal standard. Isolated yield in parenthesis



Entry	Substrate		Product	Yield (%)[a]
1	N_2BF_4	R = OMe	SO_2F	73
2		R = NO_2		48
3	R	R = CF_3	R	26
4		R = COMe		43
5		R = CO_2Et		38
6	N_2BF_4 OMe		SO_2F OMe	49
7	N_2BF_4	R = OMe	SO_2F	36
8	R	R = NO_2	R	45
9	N_2BF_4 Cl Cl		SO_2F Cl Cl	33
10	Me N_2BF_4 Me Me		Me SO_2F Me Me	34

Table 3. Development of sulfonyl fluorination of aryl diazonium salts.

Reaction conditions: Diazonium salt **2** (0.23 mmol), $Ru(bpy)_3Cl_2•6H_2O$ (5 mol%), DABSO (1.5 equiv), NFSI (12 equiv), 467 nm Kessil lamp, MeCN (0.1 M), 23 °C, 21 h. (a) Isolated yield.

3. Mechanistic Experiments

Tables 1 and 2 inform that the choice of diazonium salt, solvent, fluorine reagent, and source of sulfur dioxide all play a role in the overall yields. To gain mechanistic information, we first turned to excited-state quenching experiments using the Stern-Volmer approach (Figure 2A-C). The experiments were carried out in argon-purged acetonitrile containing 0.1 M $TBABF_4$ to maintain a constant ionic strength throughout the experiment and avoid salt effects that could originate when the concentration of diazonium tetrafluoroborate salts is increased.[19] When *para*-methoxybenzenediazonium tetrafluoroborate **2a** was used, intense excited-state quenching was observed (Figure 2A). Stern-Volmer analysis yielded a linear relationship, and from the slope a quenching rate constant, k_q, of 1.5 x10^9 $M^{-1}s^{-1}$ was determined (Figure 2C). A much larger quenching rate constant (k_q = 10.2 x10^9 $M^{-1}s^{-1}$) was obtained when *para*-nitrobenzenediazonium tetrafluoroborate **2b** was used (Figure 2B-C). Low excited-state quenching that quickly reached a plateau was observed when NFSI was used as the quencher (Figure S3). DABSO led to excited-state quenching that also appeared to decrease/plateau when the concentration reached 5 mM (Figure S3). Furthermore, when DABSO was used as quencher, the formation of an unidentified white precipitate occurred over time, which hindered rigorous excited-state quenching experiments. That observation, coupled to the lack of photoproducts by photolysis (*vide infra*) point towards an artifact in excited-state quenching measurements with DABSO or an excited-state electron transfer coupled to very fast back-electron transfer with extremely small cage-escape yields.[20] Although electron transfer cannot be certified via these steady-state photoluminescence quenching experiments, the increase in quenching rate constant observed between MeO- and NO_2-substituted benzenediazonium salts was consistent with an increased driving force for electron transfer from the excited photosensitizer to the *para*-nitrobenzenediazonium tetrafluoroborate **2b**. Excited-state quenching was also observed with Selectfluor™ (Figure S3), which represents a competitive quenching pathway that could explain the decreased product yields observed when this reagent was used as the fluorine source (Table 1, entry 5).

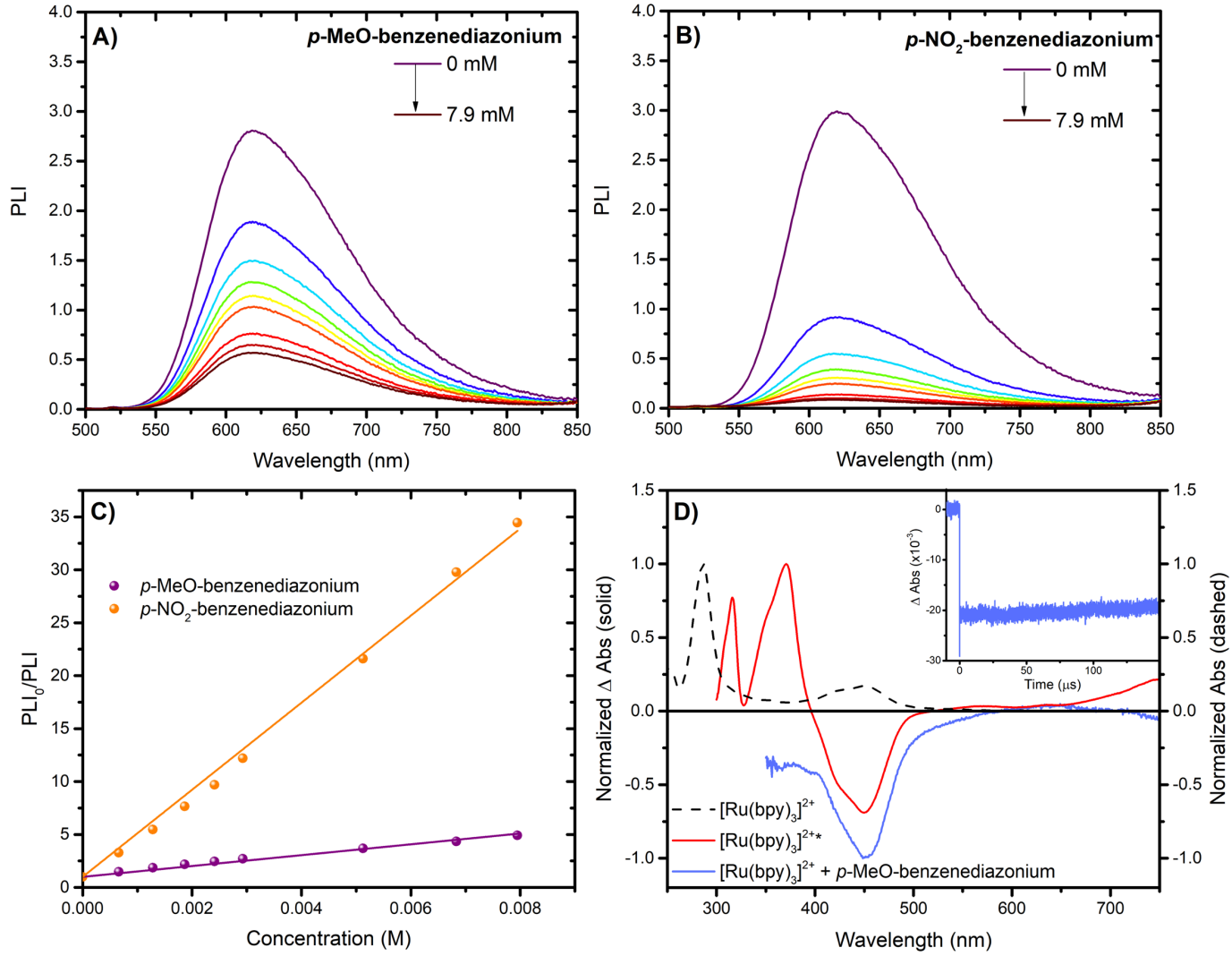


Figure 2. Steady-state photoluminescence quenching of $[Ru(bpy)_3]^{2+}$ recorded in argon purged CH_3CN containing 0.1 M $TBABF_4$ electrolyte with increasing amounts of *para*-methoxybenzenediazonium **2a** (A) and *para*-nitrobenzenediazonium **2b** (B), and the corresponding Stern-Volmer plots (C). Panel D shows the ground-state (dashed), excited-state (red) and transient absorption with 30 mM *para*-methoxybenzenediazonium (blue) spectra recorded in argon-purged

acetonitrile. Both excited-state and transient absorption spectra are recorded 50 ns after pulsed 420 nm light excitation. The inset shows the single wavelength absorption changes recorded at 450 nm after pulsed 420 nm light excitation.

The excited-state quenching experiments were also corroborated by steady-state photolysis experiments (Figure S1-S2) and nanosecond transient absorption spectroscopy (Figure 2D). Photolysis of $[Ru(bpy)_3]^{2+}$ in argon-purged acetonitrile in the presence of 15 mM of *para*-methoxybenzenediazonium tetrafluoroborate **2a** led to the gradual decrease of the metal-to-ligand charge transfer (MLCT) transition at 450 nm, indicative of oxidation of Ru(II) to Ru(III).[21] Similar results were obtained in 1,2-dichloroethane, although the oxidation proceeded slower than in acetonitrile, presumably due to the lower solubility of *para*-methoxybenzenediazonium **2a** (Figures S1-S2). Photolysis experiments could not be carried out in toluene due to the extremely low solubility of $[Ru(bpy)_3]^{2+}$, explaining the low sulfonyl fluorination yields. When similar experiments were carried out with DABSO, the overall absorbance increased drastically, indicative of scattering (Figure S4). This observation was corroborated by the appearance of an unidentified white solid, as noted during the excited-state quenching experiments. The authentic spectra of $[Ru(bpy)_3]^{2+}$ was recovered when the solution was syringe-filtered, indicating the absence of excited-electron transfer from $[Ru(bpy)_3]^{2+}$ to DABSO (Figure S4).

Nanosecond transient absorption was then carried out to provide unequivocal evidence that oxidative excited-state electron transfer was indeed occurring (Figure 2D). First, the excited-state absorption spectra of $[Ru(bpy)_3]^{2+}$ was recorded in argon-purged acetonitrile. Spectral data exhibited the prototypical changes associated with MLCT transitions, which include a ground-state bleach around 450 nm corresponding to the depopulation of Ru(II) states to form the corresponding Ru(III) and the 2,2'-bipyridine radical, as evidenced by the positive absorption features below 410 nm and above 690 nm (Figure 2D, red trace).[22] When similar experiments were carried out in the presence of 30 mM of *para*-methoxybenzenediazonium tetrafluoroborate **2a**, bleached signals were observed in almost the entire spectral window (Figure 2D, blue trace). The absence of positive absorption features coupled with the greater than 150 µs lifetime of the transient species (Figure 2D, inset) are clear indicators of excited-state electron transfer and formation of the corresponding Ru(III) center.[20]

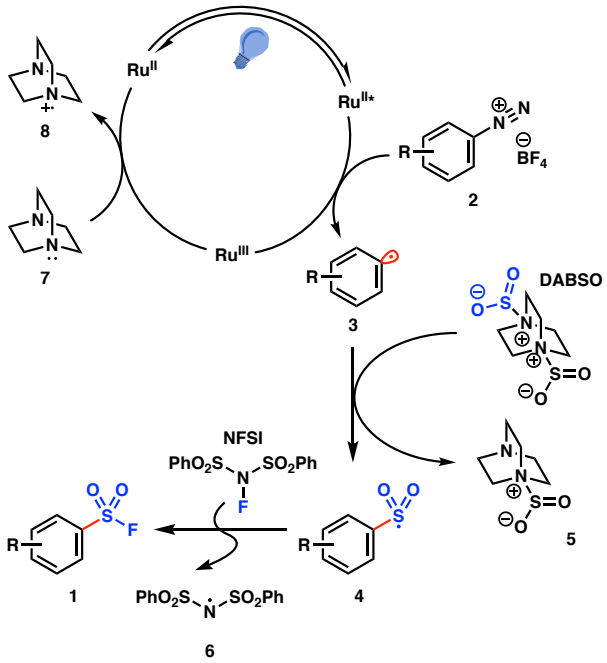


Figure 3. Proposed mechanism based on photolysis and experimental results.

Our proposed mechanism is depicted in Figure 3. Steady-state and time-resolved experiments are in line with light-induced population of a $[Ru(bpy)_3]^{2+}$* excited-state that is able to efficiently transfer an electron to aryl-diazonium derivatives **2**, with quenching rate constants in the 10^9-10^{10} $M^{-1}s^{-1}$ range. This electron transfer generates the corresponding aryl radical **3**, N_2, and the corresponding oxidized $[Ru(bpy)_3]^{3+}$. Subsequent coupling of aryl radical **3** with DABSO results in the formation of sulfonyl radical **4**, which reacts with NFSI to form sulfonyl fluoride product **1**.[18] Attempts to determine the regeneration pathway of $[Ru(bpy)_3]^{2+}$ were performed through photolysis experiments using DABSO or NFSI. Experiments were frustrated once again by the appearance of a white precipitate when DABSO was used, but the recovery of Ru(II) was somewhat more efficient when DABSO was used instead of NFSI (Figures S5-S6). Therefore, we propose that the reaction of oxidized Ru(III) with diazabicyclo[2.2.2]octane mono(sulfur dioxide) adduct **5** or DABCO **7** regenerates Ru(II).

4. Conclusion

We have reported a mild photocatalytic procedure that allows to convert readily available aryl diazonium tetrafluoroborate substrates **2** into the corresponding sulfonyl fluoride products **1**. $[Ru(bpy)_3]^{2+}$ outperformed the two other photosensitizers investigated herein and exhibited good photostability in acetonitrile and 1,2-dichloroethane (Figures S7-S8). Excited-state quenching experiments and nanosecond transient absorption spectroscopy confirmed efficient excited-state electron transfer from the photosensitizer to the aryl diazonium derivatives with quenching rate constants in the 10^9-10^{10} $M^{-1}s^{-1}$ range. Overall, the method will enable the mild and safe installation of sulfonyl fluorides into functionalized aryl-diazonium tetrafluoroborate substrates.

5. Experimental Section

5.1 General Procedure

Aryl diazonium tetrafluoroborate salt **2** (0.23 mmol), DABSO (0.345 mmol, 1.5 equiv, 81 mg), NFSI (0.345 mmol, 1.5 equiv, 107 mg), and $Ru(bpy)_3Cl_2•6H_2O$ (0.0115 mmol, 5 mol%, 8 mg) were added to a flame-dried cylindrical septum-sealed reaction vial under argon. The vial was degassed and purged three times with argon, and anhydrous acetonitrile (0.1 M, 2.3 mL) was added under argon. The solution was stirred while irradiated with a 467 nm Kessil lamp (100% intensity, ~3 cm from the vial) for 21 hours. The vial was kept at room temperature with a cooling fan. Upon completion of the reaction, the mixture was quenched with a solution of saturated aqueous ammonium chloride (30 mL), and extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried with anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The resulting aryl sulfonyl fluoride **1** was purified by silica gel flash column chromatography with hexanes/EtOAc as the eluent.

5.2 Characterization Data

4-methoxybenzenesulfonyl fluoride (1a): Prepared according to the general procedure and purified by silica gel column chromatography using hexanes/EtOAc (10:1) as eluent (73% yield): **^{1}H NMR** (600 MHz, $CDCl_3$): 7.94 (d, J = 8.8Hz, 2H) 7.06 (d, J = 9.11Hz, 2H), 3.92 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$):165.12, 130.78, 124.04, 114.79, 55.84 **^{19}F NMR** (564.5 MHz, $CDCl_3$): 67.31. **ESI-MS** calculated for $[C_7H_8FO_3S, M+H]^+$:191.0178, Found 191.0178.

4-nitrobenzenesulfonyl fluoride (1b): Prepared according to the general procedure and purified by silica gel column chromatography using hexanes/EtOAc (10:1) as eluent (48% yield): **^{1}H NMR** (600 MHz, $CDCl_3$): 8.50 (d, J = 9.0Hz, 2H), 8.25 (d, J = 9.0Hz, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$): 151.72, 138.37, 129.95, 124.82. **^{19}F NMR** (564.5 MHz, $CDCl_3$): 66.27 **ESI-MS** calculated for $[C_6H_4FNO_4S, M]$: 204.9845, Found 204.9861.

4-(trifluoromethyl)benzenesulfonyl fluoride (1c): Prepared according to the general procedure and purified by silica gel column chromatography using hexanes/EtOAc (10:1) as eluent (26% yield): **^{1}H NMR** (600 MHz, $CDCl_3$): 8.18 (d, J = 8.4Hz, 2H), 7.93 (d, J = 8.4Hz, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$): 137.45, 136.74, 127.80 (t, J = 3.3 Hz, 1C), 123.77, 121.96. **^{19}F NMR** (564.5 MHz, $CDCl_3$): 65.96, -63.49 **ESI-MS** calculated for $[C_7H_3F_4O_2S, M-H]^-$: 226.9795, Found 226.9804.

4-acetylbenzenesulfonyl fluoride (1d): Prepared according to the general procedure and purified by silica gel column chromatography using hexanes/EtOAc (10:1) as eluent (43% yield): **^{1}H NMR** (600 MHz, $CDCl_3$):8.17(d, J = 8.4Hz, 2H), 8.12 (d, J = 8.6 Hz, 2H), 2.69 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$): 196.29, 142.31, 136.01, 129.40, 129.01, 27.10. **^{19}F NMR** (564.5 MHz, $CDCl_3$): 65.87. **ESI-MS** calculated for $[C_8H_8FO_3S, M+H]^+$: 203.0178, Found 203.0178.

Ethyl 4-(fluorosulfonyl)benzoate (1e): Prepared according to the general procedure and purified by silica gel column chromatography using hexanes/EtOAc (10:1) as eluent (38% yield): **^{1}H NMR** (600 MHz, $CDCl_3$): 8.22 (d, J = 8.6Hz, 2H), 8.02 (d, J = 8.7Hz, 2H), 4.38 (q, J = 7.3Hz, 2H), 1.36 (t, J = 7.3Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$): 164.58, 136.99, 130.81, 128.62, 127.16, 62.30, 14.35. **^{19}F NMR** (564.5 MHz, $CDCl_3$): 65.84 **ESI-MS** calculated for $[C_9H_{10}FO_4S, M+H]^+$: 233.0284 Found 233.0302.

2-methoxybenzenesulfonyl fluoride (1f): Prepared according to the general procedure and purified by silica gel column chromatography using hexanes/EtOAc (10:1) as eluent (49% yield): **^{1}H NMR** (600 MHz, $CDCl_3$):7.93, (d, J = 7.7Hz, 1H), 7.70 (t, J = 7.8Hz, 1H), 7.11 (s, 1H) 7.10 (s, 1H), 4.01 (s, 3H) **^{13}C NMR** (150 MHz, $CDCl_3$): 158.19, 137.48, 131.36, 121.43, 120.60, 112.84, 56.66. **^{19}F NMR** (376.6 MHz, $CDCl_3$): 58.57 **ESI-MS** calculated for $[C_7H_7FO_3S, M]$: 190.0100, Found 190.0106.

3-methoxybenzenesulfonyl fluoride (1g): Prepared according to the general procedure and purified by silica gel column chromatography using hexanes/EtOAc (10:1) as eluent (36% yield): **^{1}H NMR** (400 MHz, $CDCl_3$):7.60 (d, J = 8.2Hz, 1H), 7.53 (t, J = 8.2Hz, 1H), 7.47 (m, 1H), 7.28 (d, J = 8.5Hz, 1H), 3.89 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$): 160.29, 130.84, 129.81, 122.37, 120.72, 112.76, 56.00. **^{19}F NMR** (376.6 MHz, $CDCl_3$): 65.63 **ESI-MS** calculated for $[C_7H_8FO_3S, M+H]^+$:191.0178, Found 191.0181.

3-nitrobenzenesulfonyl fluoride (1h): Prepared according to the general procedure and purified by silica gel column chromatography using hexanes/EtOAc (10:1) as eluent (45% yield): **^{1}H NMR** (400 MHz, $CDCl_3$):8.88 (m, 1H), 8.65 (d, J = 7.7Hz, 1H),8.37 (d, J = 7.7Hz, 1H), 7.91 (t, J = 7.7Hz, 1H) **^{13}C NMR** (150 MHz, $CDCl_3$): 148.58, 135.18, 133.91, 131.49, 130.14, 124.05. **^{19}F NMR** (376.6 MHz, $CDCl_3$):66.43 **ESI-MS** calculated for $[C_6H_4FNO_4S, M]$:204.9845, Found 204.9822.

3,5-dichlorobenzenesulfonyl fluoride (1i): Prepared according to the general procedure and purified by silica gel column chromatography using hexanes/EtOAc (10:1) as eluent (33% yield): **^{1}H NMR** (600 MHz, $CDCl_3$): 7.90 (s, 2H), 7.76 (s, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$): 136.88, 135.70, 129.54, 126.77 **^{19}F NMR** (564.5 MHz, $CDCl_3$): 66.43. **ESI-MS** calculated for $[C_6H_4Cl_2FO_2S, M+H]^+$: 228.9293, Found 228.9291.

2,4,6-trimethylbenzenesulfonyl fluoride (1j): Prepared according to the general procedure and purified by silica gel column chromatography using hexanes/EtOAc (10:1) as eluent (34% yield): **^{1}H NMR** (600 MHz, $CDCl_3$): 7.03 (s, 2H), 2.64 (s, 6H), 2.35 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$): 145.18, 140.21, 131.96, 129.26, 22.51, 21.34. **^{19}F NMR** (564.5 MHz, $CDCl_3$): 68.19. **ESI-MS** calculated for $[C_9H_{12}FO_2S, M+H]^+$: 203.0542, Found 203.05430.

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Supplementary Material

PDFs of NMR (^{1}H, ^{13}C, ^{19}F) and IR data for all new compounds are available online at DOI:

References and Notes

[1] Dong, J.; Krasnova, L.; Finn, M. G.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2014,** *53*, 9430-9448.

[2] (a) Chen, W.; Dong, J.; Plate, L.; Mortenson, D. E.; Brighty, G. J.; Li, S.; Liu, Y.; Galmozzi, A.; Lee, P. S.; Hulce, J. J.; Cravatt, B. F.; Saez, E.; Powers, E. T.; Wilson, I. A.; Sharpless, K. B.; Kelly, J. W. *J. Am. Chem. Soc.* **2016,** *138*, 7353-7364. (b) Liu, Z.; Li, J.; Li, S.; Li, G.; Sharpless, K. B.; Wu, P. *J. Am. Chem. Soc.* **2018,** *140*, 2919-2925. (c) Kitamura, S.; Zheng, Q.; Woehl, J. L.; Solania, A.; Chen, E.; Dillon, N.; Hull, M. V.; Kotaniguchi, M.; Cappiello, J. R.; Kitamura, S.; Nizet, V.; Sharpless, K. B.; Wolan, D. W. *J. Am. Chem. Soc.* **2020,** *142*, 10899-10904.

[3] Davies, W.; Dick, J. H. *J. Chem. Soc.* **1932**, 2042-2046.

[4] (a) Narayanan, A.; Jones, L. H. *Chem. Sci.* **2015,** *6*, 2650-2659. (b) Chinthakindi, P. K.; Arvidsson, P. I. *Eur. J. Org. Chem.* **2018,** 3648-3666. (c) Jones, L. H. *ACS Med. Chem. Lett.* **2018,** *9*, 584-586. (d) Barrow, A. S.; Smedley, C. J.; Zheng, Q.; Li, S.; Dong, J.; Moses, J. E. *Chem. Soc. Rev.* **2019,** *48*, 4731-4758.

[5] (a) Davies, W.; Dick, J. H. *J. Chem. Soc.* **1931**, 2104-2109. (b) Boiko, V. N.; Filatov, A. A.; Yagupolskii, Y. L.; Tyrra, W.; Naumann, D.; Pantenburg, I. Fischer, H. T. M.; Shulz, F. *J. Fluor. Chem*. **2011**, *132*, 1219-1226. (b) Davies, W.; Dick, J. H. *J. Chem. Soc.* **1932**, 483-486. (c) Bianchi, T. A.; Cate, L. A. *J. Org. Chem.* **1977**, *42*, 2031-2032. (d) Kang, S. O.; Powell, D. V. W.; Bowman-James, K. *Angew. Chem. Int. Ed.* **2006**, *45*, 1921-1925. (e) Beaman, A. G.; Robins, R. K. *J. Am. Chem. Soc.* **1961**, *83*, 4038-4044. (f) Brown, D. J.; Hoskins, J. A. *J. Chem. Soc. Perkin Trans.* **1972**, *1*, 522-527. (g) Narayan, S.; Muldoon, J.; Finn, M. G.; Fokin, V. V.; Kolb, H. C.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2005**, *44*, 3275-3279. (h) Caddick, S., Wilden, J. D.; Bush, H. D.; Wadman, S. N.; Judd, D. B. *Org. Lett.* **2002**, *4*, 2549-2551. (i) Caddick, S.; Wilden, J. D.; Judd, D. B. *Chem. Comm*. **2005**, *21*, 2727-2728. (j) Vedovato, V.; Talbot, E. P. A.; Willis, M. C. *Org. Lett.* **2018**, *20*, 5493-5496. (k) Kim, J.-G.; Jang, D. O. *Synlett* **2010**, 3049-3052. (l) Jiang, Y.; Alharbi, N. S.; Sun, B.; Qin, H.-L. *RSC Adv.* **2019**, *9*, 13863-13867. (m) Gómez-Palomino, A.; Cornella, J. *Angew. Chem. Int. Ed.* **2019**, *58*, 18235-18239. (n) Pérez-Palau, M.; Cornella, J. *Eur. J. Org. Chem.* **2020**, 2497-2500. (o) Segall, Y.; Quistad, G. B.; Casida, J. E. *Synth. Comm.* **2003**, 33, 2151-2159. (p) Brouwer, A. J.; Ceylan, T.; Linden, T. V. D.; Liskamp, R. M. J. *Tet. Lett.* **2009**, *50*, 3391-3393.

[6] (a) Tribby, A. L.; Rodriguez, I.; Shariffudin, S.; Ball, N. D. *J. Org. Chem.* **2017**, *82*, 2294-2299. (b) Nguyen, B.; Emmett, E. J.; Willis, M. C. *J. Am. Chem. Soc.* **2010**, *132*, 16372-16373. (c) Richards-Taylor, C. S.; Blakemore, D. C.; Willis, M. C. *Chem. Sci.* **2014**, *5*, 222–228. (d) Emmett, E. J.; Hayter, B. R.; Willis, M. C. *Angew. Chem. Int. Ed*. **2014**, *53*, 10204-10208. (e) Deeming, A. S.; Russell, C. J.; Willis, M. C. *Angew. Chem. Int. Ed*. **2016**, *55*, 747-750. (f) Johnson, M. W.; Bagley, S. W.; Mankad, N. P.; Bergman, R. G.; Mascitti, V.; Toste, F. D. *Angew. Chem. Int. Ed*. **2014**, *53*, 4404-4407. (g) Chen, Y.; Willis, M. C. *Chem. Sci*. **2017**, *8*, 3249-3253. (h) Lo, P. K. T.; Chen, Y.; Willis, M. C. *ACS Catal.* **2019**, *9*, 10668-10673. (i) Lou, T. S.-B.; Bagley, S. W.; Willis, M. C. *Angew. Chem. Int. Ed*. **2019**, *58*, 18859-18863.

[7] (a) Lou,T. S.-B.; Kawamata, Y.; Ewing, T.; Correa-Otero, G. A.; Collins, M. R.; Baran, P. S. *Angew. Chem. Int. Ed.* **2022**, *61*, e202208080. (b) Laudadio, G.; Bartolomeu, A.; Verwijlen, L. M. H. M.; Cao, Y.; de Oliveira, K. T.; Noël, T. *J. Am. Chem. Soc.* **2019**, *141*, 11832-11836.

[8] Vincent, C. A.; Chiriac, M. I.; Troian-Gautier, L.; Tambar, U. K. *ACS Catalysis* **2023***, 13,* 3668-3675.

[9] (a) O'Leary, P. *Sci. Synth.* **2007,** *31b*, 1361-1400. (b) Kubik, S. *Sci. Synth.* **2010,** *41*, 507-541.

[10] (a) Mo, F.; Dong, G.; Zhang, Y.; Wang, J. *Org. Biomol. Chem.* **2013,** *11*, 1582-1593. (b) Mo, F.; Qiu, D.; Zhang, L.; Wang, J. *Chem. Rev.* **2021,** *121*, 5741-5829.

[11] (a) Zollinger, H. *Accounts Chem. Res.* **1973,** *6*, 335-341.

[12] (a) Bravo-Diaz, C. *Mini-Rev. Org. Chem.* **2009,** *6*, 105-113. (b) Micheletti, G.; Boga, C. *Synthesis* **2017,** *49*, 3347-3356. (c) Crampton, M. R. *Org. React. Mech.* **2019**, 251-333. (d) Rohrbach, S.; Smith, A. J.; Pang, J. H.; Poole, D. L.; Tuttle, T.; Chiba, S.; Murphy, J. A. *Angew. Chem. Int. Ed.* **2019,** *58* (46), 16368-16388.

[13] (a) Roglans, A.; Pla-Quintana, A.; Moreno-Manas, M. *Chem. Rev.* **2006,** *106*, 4622-4643. (b) Bonin, H.; Fouquet, E.; Felpin, F.-X. *Adv. Synth. Catal.* **2011,** *353*, 3063-3084. (c) Oger, N.; d'Halluin, M.; Le Grognec, E.; Felpin, F.-X. *Org. Process Res. Dev.* **2014,** *18*, 1786-1801. (d) Koziakov, D.; Wu, G.; Jacobi von Wangelin, A. *Org. Biomol. Chem.* **2018,** *16* (27), 4942-4953.

[14] (a) Galli, C. *Chem. Rev.* **1988,** *88*, 765-792. (b) Heinrich, M. R. *Chem. - Eur. J.* **2009,** *15*, 820-833. (c) Hari, D. P.; Koenig, B. *Angew. Chem. Int. Ed.* **2013,** *52*, 4734-4743. (d) Ghosh, I.; Marzo, L.; Das, A.; Shaikh, R.; Koenig, B. *Acc. Chem. Res Zhang, X.; Mei, Y.; Li, Y.; Hu, J.; Huang, D.; Bi, Y. Asian J. Org. Chem. **2021,** 10, 453-463.* **2016,** *49*, 1566-1577. (e) Hofmann, J.; Heinrich, M. R. *Tetrahedron Lett.* **2016,** *57*, 4334-4340. (f) Babu, S. S.; Muthuraja, P.; Yadav, P.; Gopinath, P. *Adv. Synth. Catal.* **2021,** *363*, 1782-1809. (g) Kvasovs, N.; Gevorgyan, V. *Chem. Soc. Rev.* **2021,** *50*, 2244-2259. (h)

[15] Cernak, T.; Dykstra, K. D.; Tyagarajan, S.; Vachal, P.; Krska, S. W. *Chem. Soc. Rev.* **2016**, *45*, 546-576.

[16] Louvel, D.; Chelagha, A.; Rouillon, J.; Payard, P.-a.; Khrouz, L.; Monnereau, C.; Tlili, A. *Chem. Eur. J.* **2021**, *27*, 8704-8708.

[17] (a) Liu, Y.; Yu, D.; Guo, Y.; Xiao, J-C.; Chen, Q-Y.; Liu, C. *Org. Lett.* **2020**, *22*, 2281-2286. (b) Zhong, T.; Pang, M-K.; Chen, Z-D.; Zhang, B.; Weng, J.; Lu, G. *Org. Lett.* **2020**, *22*, 3072-3078. (c) Májek, M.; Neumeier, M.; von Wangelin, A. J. *Chem. Sus. Chem.* **2016**, *10*, 151-155.

[18] (a) Qiu, G.; Zhou, K.; Gao, L.; Wu, J. *Org. Chem. Front.* **2018,** *5*, 691-705. (b) Andrews, J. A.; Willis, M. C. *Synthesis* **2022,** *54*, 1695-1707. (c) Seyed Hashtroudi, M.; Fathi Vavsari, V.; Balalaie, S. *Org. Biomol. Chem.* **2022,** *20*, 2149-2163.

[19] Ripak, A.; De Kreijger, S.; Sampaio, R. N.; Vincent, C. A.; Cauët, É.; Jabin, I.; Tambar, U. K.; Elias, B.; Troian-Gautier, L. *Chem Catal.* **2023**, *3*, 100490.

[20] (a) Stern, O.; Volmer, M. *Phyzik. Z.* **1919,** 20, 183-188. (b) Lakowicz, J. R., *Principles of Fluorescence Spectroscopy*. ed.; Springer US, New York: 2006. (c) Rosemann, N. W.; Chábera, P.; Prakash, O.; Kaufhold, S.; Wärnmark, K.; Yartsev, A.; Persson, P. *J. Am. Chem. Soc.* **2020**, *142*, 8565-8569. (d) Troian-Gautier, L.; Turlington, M. D.; Wehlin, S. A. M.; Maurer, A. B.; Brady, M. D.; Swords, W. B.; Meyer, G. J. *Chem. Rev.* **2019**, *119*, 4628-4683.

[21] Thompson, D. W.; Ito, A.; Meyer, T. J. *Pure Appl. Chem.* **2013**, *85*, 1257-1305.