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The Different Faces of $[Ru(bpy)_3Cl_2]$ and *fac*$[Ir(ppy)_3]$ Photocatalysts: Redox Potential Controlled Synthesis of Sulfonylated Fluorenes and Pyrroloindoles from Unactivated Olefins and Sulfonyl Chlorides

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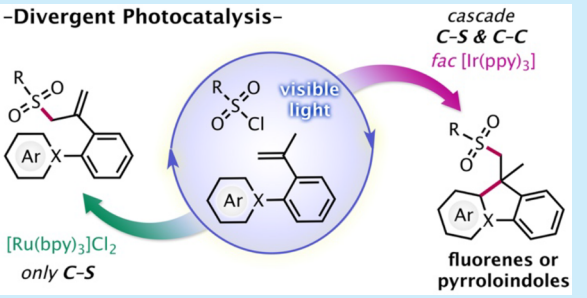
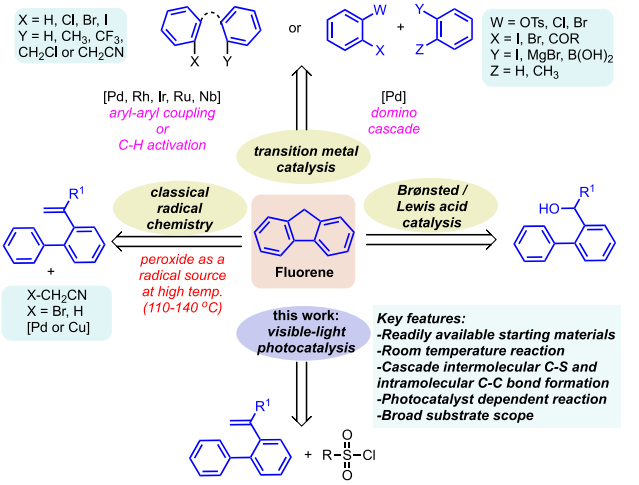
ABSTRACT: A cascade alkene sulfonylation that simultaneously forges C−S and C−C bonds is a highly efficient and powerful approach for directly accessing structurally diverse sulfonylated compounds in a single operation. The reaction was enabled by visible-light-mediated regioselective radical addition of sulfonyl chlorides to 2-arylstyrenes using *fac*$[Ir(ppy)_3]$ as a photocatalyst, demonstrating its unique role in a photocascade process to execute atom transfer radical addition (ATRA) followed by photocyclization. A new class of sulfonyl-substituted fluorenes and pyrroloindoles, which are useful in the field of photoelectronic materials and medicinal chemistry, was produced in excellent yields by this photocascade reaction. In contrast, the cyclization was interrupted when using the $[Ru(bpy)_3Cl_2]$ catalyst having lower reduction potential, leading only to the formation of a C−S bond and the production of acyclic sulfonylated 2-arylstyrenes under identical reaction conditions. The synthetic utility of the present room-temperature photocatalysis is enhanced by the broad availability of bench-stable sulfonyl chlorides and unactivated olefins, thereby providing a cost-effective and broad-scope protocol.



Over the past few decades, fluorenes and pyrroloindoles were identified as important building blocks for synthetic, medicinal, and materials chemistry because of their unique physical, chemical, and biological properties.[1] Fluorene, in particular, is a promising skeletal structure[2] that is widely used for manufacturing advanced materials,[3] biologically and pharmaceutically important compounds,[4] ligands, as well as unique protecting groups.[5] To date, a number of research groups exploring various synthetic strategies to access such fused tricyclic systems have revealed transition-metal-catalyzed/mediated reactions[6] or Friedel−Crafts alkylations promoted by Brønsted/Lewis acids.[7] Despite the various advantages of these conventional synthetic methods,[8] recent advances in this field identified the utility of radical reactions with olefins as a more attractive tool[9] that allows for the direct use of unactivated and less engineered starting materials (Scheme 1).[10] Classical approaches,[11] however, generally require peroxides as a radical initiator and elevated temperatures,[12] which severely limits their practical applications.[13] We reasoned that the recently emerging visible-light photocatalysis could be strategically exploited for this purpose to promote radical processes under sustainable and mild conditions.[14] To the best of our knowledge, radical-mediated synthesis of fluorenes has rarely been explored.[10a] We anticipated that photoredox sulfonylation using sulfonyl chlorides would be suitable for integration into unactivated olefins,[15] where a sulfur-centered radical[16] would play a pivotal role in

Scheme 1. State-of-the-Art: Representative Routes to Fluorenes



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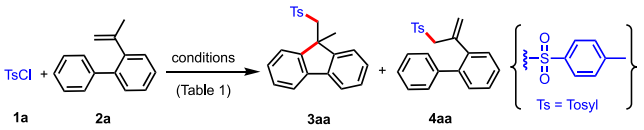
constructing the requisite tricyclic systems with a resulting pendant sulfone functionality. Arylsulfonyl chlorides are inexpensive, bench-stable solids with many derivatives readily available. The biological activity and/or physical properties of the resulting organic compounds can be significantly enhanced by the introduction of a sulfur group.[17] Sulfonyl-containing polycyclic compounds, in particular, have extensive applications in synthesis, agrochemical industries, and pharmaceuticals.[18] Thus, sulfonylative construction of fluorenes warrants further development. Herein, we report an efficient photocascade protocol[19] toward the synthesis of sulfonylated fluorenes and pyrroloindoles, which is operationally simple and works under mild and neutral conditions.

Given the wide availability of industrially produced *p*-toluenesulfonyl chloride **1a** (TsCl), we initiated our studies by investigating the reaction using **1a** in combination with readily prepared 2-phenyl-α-methylstyrene **2a**. We first attempted to perform the reaction with Na_2CO_3 in anhydrous CH_3CN at room temperature under an oxidative quenching cycle with the $[Ru(bpy)_3Cl_2]$[20] ($E_{1/2(III/II*)}$ = −0.81 V vs SCE, bpy = 2,2′-bipyridine) photocatalyst (PC) and blue-light irradiation (LED_{455}) (Table 1, entry 1). Unexpectedly, acyclic sulfonylated compound **4aa** (79%) was produced, and the desired sulfonylated fluorene **3aa** was not observed. We switched the PC to *fac*$[Ir(ppy)_3]$,[21] which has stronger reduction potential ($E_{1/2(IV/III*)}$ −1.73 V vs SCE, ppy = 2-phenylpyridine).[22] Intriguingly, photocatalysis with the latter Ir-based PC significantly altered the product profile; the desired **3aa** was obtained in 76% yield with less than 10% of undesired acyclic **4aa** (Table 1, entry 3). The Na_2CO_3 base improved the yield and ratio of **3aa**/**4aa** (Table 1, entries 3 vs 4), while other inorganic bases, such as K_2HPO_4, were less effective in both Ru- and Ir-based photocatalysis (Table 1, entries 5 and 6). The results of control experiments indicated that achieving the desired sulfonylation required the combination of light irradiation and a PC (Table 1, entries 7 and 8).

The reductive quenching cycle is thermodynamically unfavorable due to the large excited-state oxidation potential difference between the photocatalysts (Ru_{M*/M^-} = +0.77 V; Ir_{M*/M^-} = +0.31 V)[23] and the olefins used (+1.0 to +1.75 V).[22]

Table 1. Optimization of the Reaction Parameters[a]



		redox potentials of PC			yield[b] (%)	
entry	PC	$E_{M^+/M*}$ (V)	E_{M*/M^-} (V)	base	**3aa**	**4aa**
1	[Ru]	−0.81	+0.77	Na_2CO_3	0	79
2	[Ru]	−0.81	+0.77		0	61
3	[Ir]	−1.73	+0.31	Na_2CO_3	76	10
4	[Ir]	−1.73	+0.31		61	14
5	[Ru]	−0.81	+0.77	K_2HPO_4	0	45
6	[Ir]	−1.73	+0.31	K_2HPO_4	65	13
7[c]	[Ir]	−1.73	+0.31	Na_2CO_3	0	0
8[d]				Na_2CO_3	0	0

[a]TsCl **1a** (0.5 mmol, 1 equiv), **2a** (0.75 mmol, 1.5 equiv), PC (1 mol %), base (0.75 mmol, 1.5 equiv), dry CH_3CN (2 mL), LED_{455}, rt, 36 h. [b]Isolated yields. [c]Without a light source. [d]Without PC. [Ru] = $[Ru(bpy)_3Cl_2]$ and [Ir] = *fac*$[Ir(ppy)_3]$.

According to previous reports,[24] the sulfonylation reaction is expected to proceed via an atom-transfer radical addition (ATRA)[25] to form key intermediate **I** (Figure 1).[24a] Under the

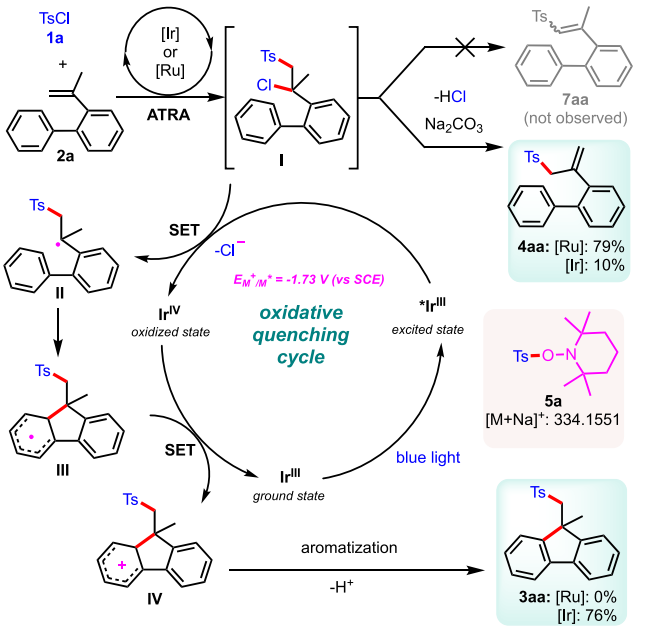


Figure 1. Plausible reaction mechanism.

Ru-PC photocatalytic conditions, intermediate **I** undergoes rapid dehydrochlorination to form acyclic **4aa**. In contrast, in the case of Ir-PC, the subsequent single electron transfer from photoexcited *fac*$[Ir(ppy)_3]$* to **I** occurs to form a corresponding stable benzylic radical **II** concurrent with the oxidation of *fac*$[Ir(ppy)_3]$* to *fac*$[Ir(ppy)_3]^+$ (Figure 1).[26] The obvious disparity in the photocatalytic reaction outcome is attributed to the large difference in the excited-state reduction potentials between the $[Ru(bpy)_3Cl_2]$ and *fac*$[Ir(ppy)_3]$ PCs to reduce the benzylic chloride unit of intermediate **I**.[22,25e] The excited-state reduction potential of $[Ru(bpy)_3Cl_2]$ is significantly lower (−0.81 V vs SCE) than that of *fac*$[Ir(ppy)_3]$ (−1.73 V vs SCE),[22] which likely determines the fate of benzyl chloride intermediate **I**. The formation of a tosyl radical was confirmed by trapping it with TEMPO to give **5a** (HRMS $[M + Na]^+$ = 334.1551), whereas any attempt to trap benzylic radical **II** to obtain **6aa** failed (Scheme 2a), implying that intramolecular cyclization of **II** rapidly proceeds to give radical **III**. **III** is likely more prone to oxidation by *fac*$[Ir(ppy)_3]^+$, affording carbocation **IV** with concurrent closing of the photocatalytic cycle. The resulting **IV** rapidly aromatizes to deliver the desired fluorene derivative **3aa**.

As shown in Figure 1, the Ru-catalyzed reaction exclusively gave exo-olefin product **4aa** over vinyl sulfone **7aa**, suggesting that the steric factor overrides the inherent pK_a of the protons in this deprotonation process. When the flanking Me group was replaced with phenyl (**2b**) to disrupt the terminal deprotonation process, intramolecular cation cyclization predominantly proceeded to afford cyclized product **3ab**, indicating the reluctance of the α-protons of the sulfone to participate in the deprotonation (<10% of **7ab** (*E*/*Z* mixture)) (Scheme 2b).[27] In contrast, a truncated substituent (**2c**) resulted in the exclusive formation of vinyl sulfone **7ac** (*E*/*Z* mixture), suggesting that the Thorpe−Ingold effect contrib-

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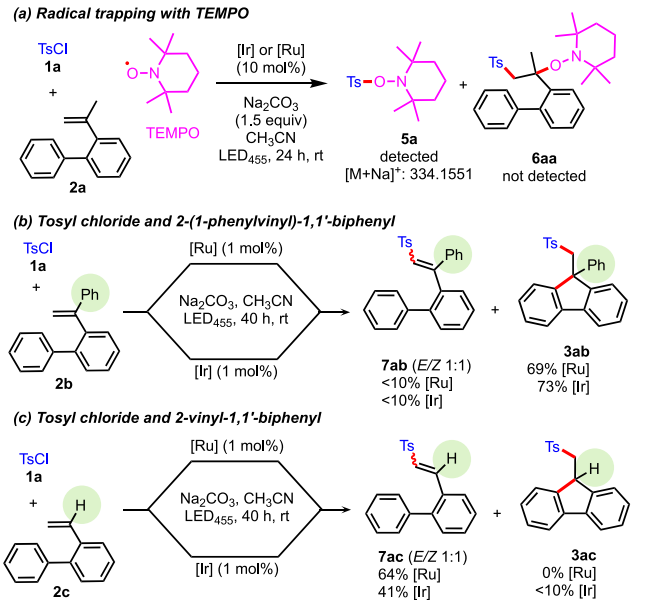
Scheme 2. Control Experiments



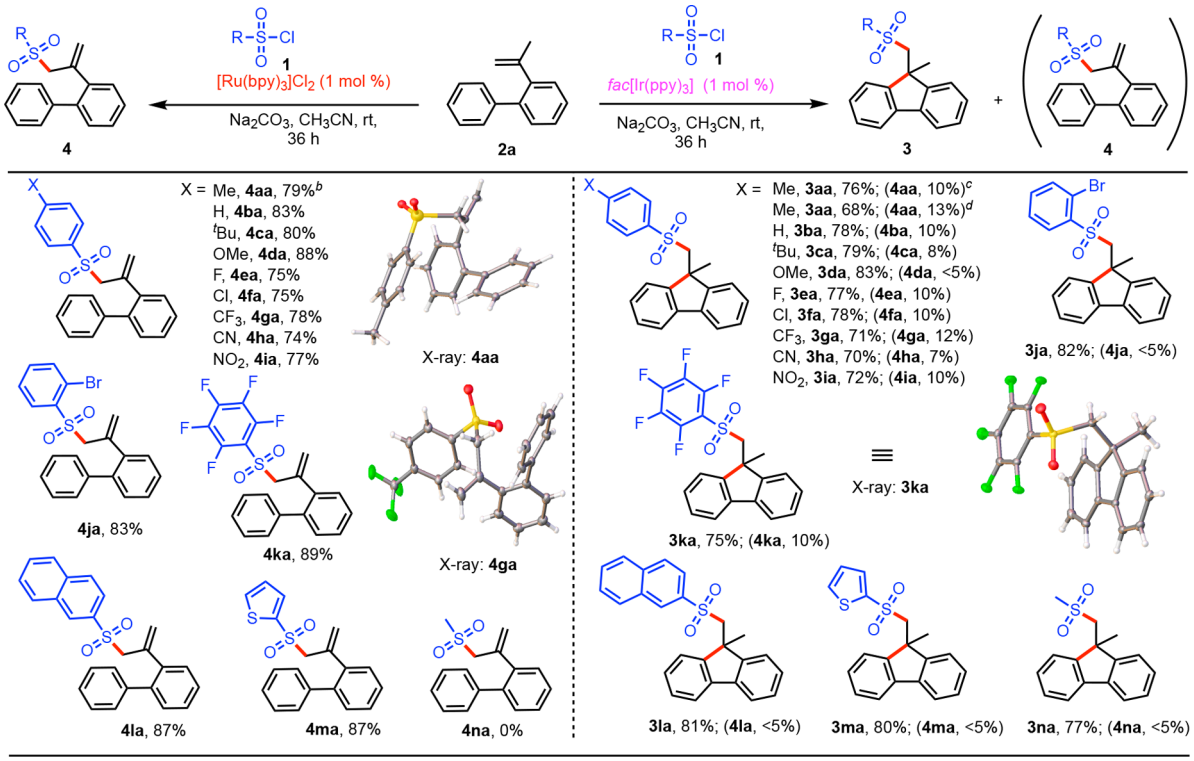
uted to the override of the formation of cyclized product **3ab** in the case of **2b** (Scheme 2b,c).[28]

Having developed the divergent sulfonylation protocols for cyclic (fluorene derivatives) and acyclic products, we next investigated the substrate generality. We initially tested a range of commercially available arylsulfonyl chlorides **1** with 2-phenyl-α-methylstyrene **2a** using either Ru- or Ir-based PCs (Table 2). In the case of *para*-monosubstituted arylsulfonyl chlorides **1**, irrespective of electron-donating (Me, ^{t}Bu, MeO) or electron-withdrawing (F, Cl, CF_3, CN, NO_2) substituents, the Ir-catalyzed reaction predominantly gave cyclized fluorene derivatives **3aa**−**3ia** with a marginal amount of the corresponding acyclic products **4** (Table 2, right). *Ortho*-substitution was also accommodated, as exemplified by the successful production of *o*-bromophenyl (**3ja**) and pentafluorophenyl (**3ka**) derivatives, and the fluorenyl skeleton of the latter was unambiguously confirmed by X-ray crystallography. Other aromatics, e.g., 2-naphthyl (**3la**) and 2-thienyl (**3ma**), as well as methyl (**3na**) substitution were compatible to give corresponding sulfonylated fluorenes in high yield and with high selectivity. By switching the PC from *fac*[Ir(ppy)$_3$] to [Ru(bpy)$_3$Cl$_2$] under otherwise identical conditions, the same substrate sets exclusively provided acyclic sulfonylated compounds **4** (Table 2, left).

Although a wide range of electronically diverse arylsulfonyl chlorides were tolerated, the reaction employing MsCl failed to produce mesylated styrene derivative **4na** (Table 2, left). This is presumably due to its higher reduction potential (−1.39 vs SCE)[24d] than that of [Ru(bpy)$_3$Cl$_2$] (−0.81 V vs SCE), which was not sufficient to generate the sulfonyl radical via the single-electron-transfer process in this particular case.[22,23]

Encouraged by the Ir-catalyzed sulfonylative cascade cyclization, we next investigated the scope of various olefins **2** with TsCl **1a** as a standard sulfonylation reagent (Table 3). Various *para*-substituted substrates afforded the corresponding fluorene derivatives **3ad**−**3ag**, irrespective of their electronic nature (e.g., Me, MeO, MeS, F). *o*-Tolyl and *m*-xylyl substrates

Table 2. Scope of Sulfonyl Chlorides[a]



[a]Reaction conditions: arylsulfonyl chloride **1** (0.5 mmol, 1 equiv), **2a** (0.75 mmol, 1.5 equiv), *fac*[Ir(ppy)$_3$] or [Ru(bpy)$_3$Cl$_2$] (1 mol %), Na_2CO_3 (0.75 mmol, 1.5 equiv), dry CH_3CN (2 mL), LED_{455}, rt, 36 h. [b]Isolated yields. [c]The yields of the acyclic products **4** are reported in parentheses. [d]2 mmol scale reaction.

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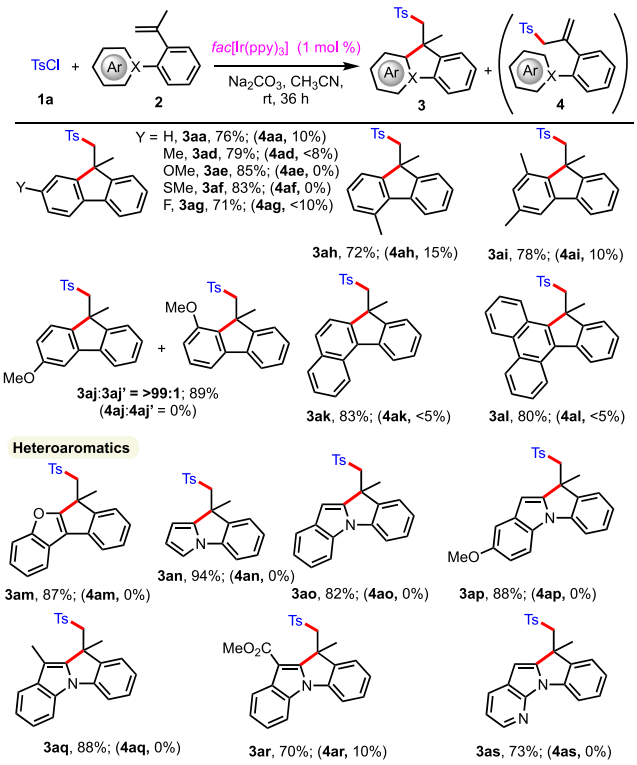
Table 3. Scope of alkenes 3[a]



[a]Reaction conditions: TsCl **1a** (0.5 mmol, 1 equiv), **2** (0.75 mmol, 1.5 equiv), *fac*[Ir(ppy)$_3$] (1 mol %), Na_2CO_3 (0.75 mmol, 1.5 equiv), dry CH_3CN (2 mL), LED_{455}, room temperature, 36 h. Yields of acyclic products **4** are reported in parentheses.

were compatible (**3ah** and **3ai**), and intriguingly, mono *m*-MeO-substituted substrates gave **3aj** almost exclusively over regioisomeric **3aj′**, likely due to steric effects. The naphthalene and phenanthrene units could be employed to undergo radical cyclization, delivering fluorene derivatives **3ak** and **3al** fused with the π-system. Heteroaromatic substrates were successfully implemented to expand the synthetic utility of the present photocatalysis. A substrate containing an oxygen-functionalized benzofuran as well as various nitrogen-functionalized heterocycles were amenable to provide a range of polycyclic systems without appreciable contamination of undesired acyclic products **4**. Integration with pyrrole and indole units allowed for rapid access to a polycyclic pyrroloindole system (**3an**–**3as**) in good to excellent yields (Table 3). Notably, these structurally more complex pyrroloindole derivatives are found in a myriad of biologically active molecules.[1b,29] Introducing a sulfonyl handle into the privileged skeleton produced a unique class of fused pyrroloindoles. The marginal formation of undesired acyclic product **4ar** may be due to the presence of an electron-withdrawing methoxycarbonyl group, which potentially retards radical cyclization en route to the desired **3ar**.

In conclusion, we exploited differences in the redox potentials of photocatalysts to control the synthesis of structurally different products from the same set of substrates. Sulfonylated fluorenes and pyrroloindoles were rapidly assembled using readily accessible olefins and commercially available sulfonyl chlorides under operationally simple room-temperature protocols utilizing the clean visible-light photochemical conditions. This photocascade method provides a new avenue for designing various sulfonyl-containing condensed polycyclic systems as a promising scaffold for biologically active compounds and π-rich organic photoelectronic materials.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c02760.

Experimental procedures and characterization of new compounds (PDF)

Accession Codes

CCDC 2022778–2022780 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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