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Copper-Catalyzed Arylsulfonylation and Cyclizative Carbonation of *N*-(Arylsulfonyl)acrylamides Involving Desulfonative Arrangement toward Sulfonated Oxindoles

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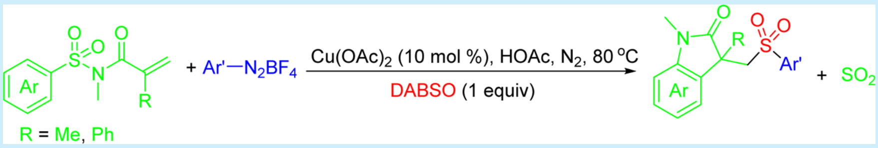
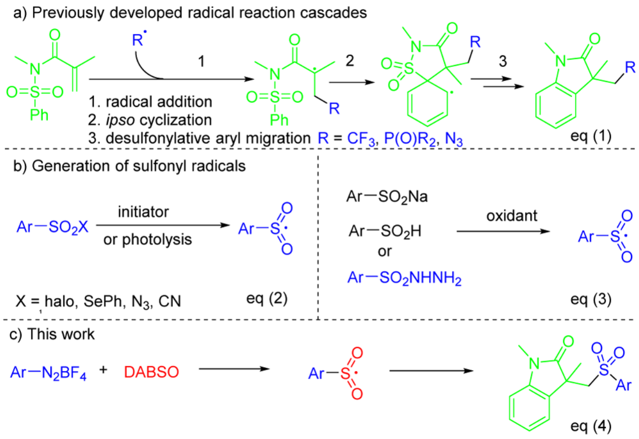
Supporting Information



ABSTRACT: Sulfonated oxindoles are accessed by a Cu(OAc)$_2$-catalyzed three-component reaction of *N*-(arylsulfonyl)-acrylamides, DABSO, and aryldiazonium tetrafluoroborates. This transformation is triggered by the formation of arylsulfonyl radicals in situ from the reaction of aryldiazonium tetrafluoroborates and DABSO. Afterward, the sequential radical addition, radical cyclization, and desulfonylative 1,4-aryl migration take place to provide the final product by the formation of four new bonds in one pot. This procedure shows good functional group tolerance.

Oxindoles and their derivatives represent a class of important *N*-heterocycles possessing advanced pharmaceutical and biologic activities.[1] Recently, the difunctionalization of *N*-(arylsulfonyl)acrylamide has been widely developed in the synthesis of functionalized oxindoles, whereby the carbonation and other functionalization of vinyl proceeds with sequential addition of radical to alkenyl, radical 1,4-aryl migrations by *ipso* cyclization, and desulfonylation (Scheme 1a, eq 1).[2] For instance, trifluoromethyl,[3a−d] phosphonyl,[3e] and azidinyl[3f] oxindoles were efficiently accessed, which were applied in anticholinergic drugs, insecticides, herbicides, and versatile intermediates.[4] With this strategy, triggered by the addition of sulfonyl radicals to vinyl, the arylsulfonylation and cyclizative carbonation of *N*-(arylsulfonyl)acrylamide may provide a facile pathway toward sulfonated oxindoles. Notably, sulfones are ubiquitous in pharmaceuticals, agrochemicals, and materials.[5] Sulfonyl radicals were derived from corresponding sulfonyl halides, sulfonyl selenides, sulfonyl azides, sulfonyl cyanides (Scheme 1b, eq 2),[6] sulfinates,[7] sulfinic acids,[8] and sulfonyl hydrazides[9] (Scheme 1, eq 3). From the synthesis point of view, the formation of sulfonyl radicals derived from two components would be beneficial to the diversity of these species. Wu pioneered the application of sulfonyl radicals derived from DABSO and aryldiazonium in organic synthesis.[10] Herein, we wish to report a copper(II) acetate-catalyzed three-component reaction of *N*-(arylsulfonyl)acrylamides, DABSO, and aryldiazonium tetrafluoroborates, leading to sulfonated oxindoles.

Scheme 1. Radical Reactions of *N*-(Arylsulfonyl)acrylamide and Generation of Sulfonyl Radicals



We began our investigation with the reaction of *N*-methyl-*N*-tosylmethacrylamide **1a**, phenyldiazonium tetrafluoroborate **2a**, and DABSO in HOAc at 60 °C. After 12 h, the 1,3,6-trimethyl-3-((phenylsulfonyl)methyl)indolin-2-one **3a** was isolated in 48% yield (Table 1, entry 1). The yield dramatically increased to 62% (60 °C) and 72% (80 °C) in the presence of copper(II) acetate (10 mol %, Table 1, entry 2). Other solvents, such as ethanol (52%), DCM (50%), DCE (48%), 1,4-dioxane (43%), toluene (trace), MeCN (trace), and DMF (trace) were inferior to HOAc (Table 1, entries 3−10). Replacing Cu(OAc)$_2$ with Cu(OTf)$_2$ decreased the reaction efficiency (51%, Table 1, entry 11). Among the catalysts tested, such as CuCl$_2$ (42%), CuBr$_2$ (53%), Cu$_2$O (61%), CuS (50%), and CuBr (42%), an Cu(OAC)$_2$ were the best (Table 1, entries 12−16). The

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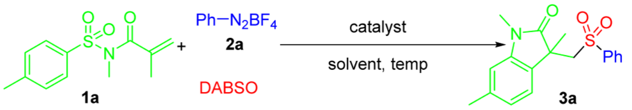
Table 1. Selected Results for Screening the Optimized Reaction Conditions[a]



entry	cat.	sol.	temp	yield (%)
1		HOAc	60	48
2	$Cu(OAc)_2$	HOAc	60	62
3	$Cu(OAc)_2$	EtOH	60	52
4	$Cu(OAc)_2$	DCM	60	50
5	$Cu(OAc)_2$	DCE	60	48
6	$Cu(OAc)_2$	dioxane	60	43
7	$Cu(OAc)_2$	toluene	60	trace
8	$Cu(OAc)_2$	MeCN	60	trace
9	$Cu(OAc)_2$	DMF	60	trace
10	$Cu(OAc)_2$	HOAc	80	72/62[b]/37[c]/0[d]
11	$Cu(OTf)_2$	HOAc	80	51
12	$CuCl_2$	HOAc	80	42
13	$CuBr_2$	HOAc	80	53
14	Cu_2O	HOAc	80	61
15	CuS	HOAc	80	50
16	CuBr	HOAc	80	42

[a] Reaction conditions: **1a** (0.1 mol), **2a** (0.15 mmol), DABSO (0.1 mmol), $Cu(OAc)_2$ (10 mol %), solvent (1.0 mL), under N_2 for 12 h, isolated yields. [b] Under air. [c] DABSO (0.05 mmol). [d] DABSO (5 mol %): DABCO = 1,4-diazabicyclo[2.2.2]octane-1,4-diium-1,4-disulfinate.

reaction became retarded under air (62%, Table 1, entry 10). Changing the loading of DABSO (0.05 mmol) decreased the yields, while it did not work in the catalytic amount of DABSO (5 mol %, Table 1, entry 10). The practicality of this procedure was increased since this reaction was applicable in a 1 mmol scale to provide **3a** in an acceptable 64% isolated yield.

With the optimized catalytic system in hand, the scope of aryldiazonium in this three-component reaction was studied, as shown in Figure 1. As expected, the reaction efficiency was not sensitive to the electronic property of the phenyl ring of aryldiazonium tetrafluoroborates as substrates bearing both electron-donating (**3b**−**f**, 53−78%) and electron-withdrawing groups (**3g**−**j**, 66−77%) all ran smoothly under the standard procedure. The halo groups survived well after the reaction (**3g**−**i**). Unfortunately, the attempt to access 1,3,6-trimethyl-3-((pyridin-3-ylsulfonyl)methyl)indolin-2-one failed.

Next, the scope of *N*-(arylsulfonyl)acrylamide was studied, as shown in Figure 2. Once again, the reaction efficiency was not sensitive to the electronic property of the groups on the phenyl ring of *N*-(arylsulfonyl)acrylamide as substrates bearing both electron-donating groups (**3p**, 69%) and electron-withdrawing groups (**3m**−**o**, 56−67%; **3q**, 55%; **3r**, 54%) worked well with moderate to good yields. Pleasingly, the functional groups, such as fluoro (**3m**, 67%), chloro (**3n**, 56%), and bromo (**3o**, 61%) tolerated well under the standard conditions, providing facile handles for potentially further functionalizations. Interestingly, the substrate with a phenyl adjacent to the carbonyl of the acrylamide moiety (phenyl, **3t**, 58%) showed reactivity under the procedure. However, the ethyl analogue resulted in complex mixtures. Notably, the naphthalene groups and *N*-heteroaryl analogues worked well with moderate yields, such that **3l** and **3s** were isolated in 59% and 42% yields.

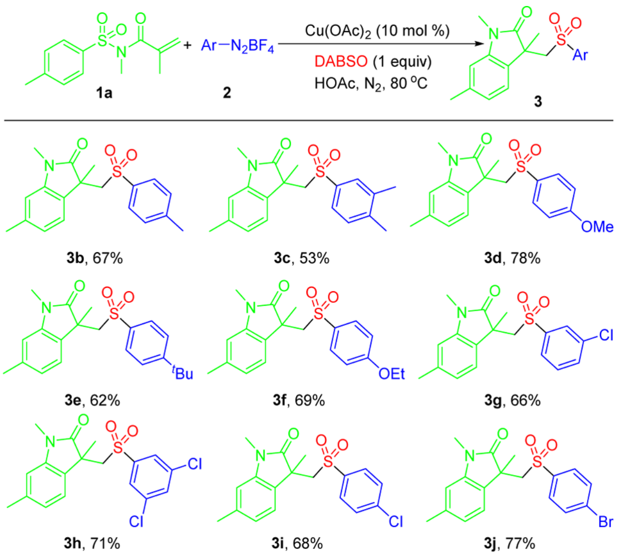


Figure 1. Substrates scope of aryldiazonium tetrafluoroborate. Reaction conditions: *N*-Ts acrylamide **1a** (0.1 mmol), aryldiazonium tetrafluoroborate **2** (0.15 mmol), DABSO (0.1 mmol), $Cu(OAc)_2$ (10 mol %), HOAc (1.0 mL), at 80 °C under N_2 for 12 h, in a sealed Schlenk tube.

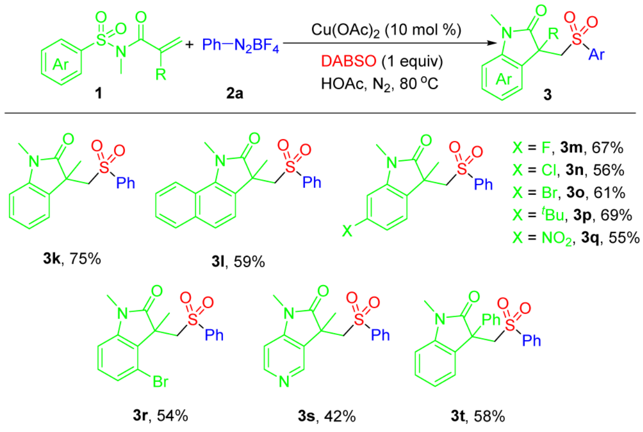
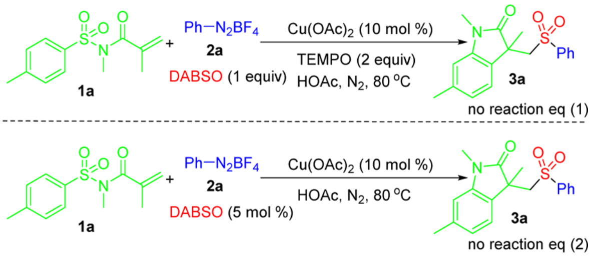


Figure 2. Substrates scope of *N*-(arylsulfonyl)acrylamide. Reaction conditions: *N*-(arylsulfonyl)acrylamide **1** (0.1 mmol), phenyldiazonium tetrafluoroborate **2a** (0.15 mmol), DABSO (0.1 mmol), $Cu(OAc)_2$ (10 mol %), HOAc (1.0 mL), at 80 °C under N_2 for 12 h, in a sealed Schlenk tube.

More experiments were conducted to get some insights into this transformation. This transformation was terminated when 2.0 equiv of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) were added to the standard reaction, indicating the involvement of a radical pathway (Scheme 2, eq 1). Moreover, in a control experiment by employing DABSO (5 mol %) in the reaction of *N*-methyl-*N*-tosylmethacrylamide **1a** with phenyldiazonium

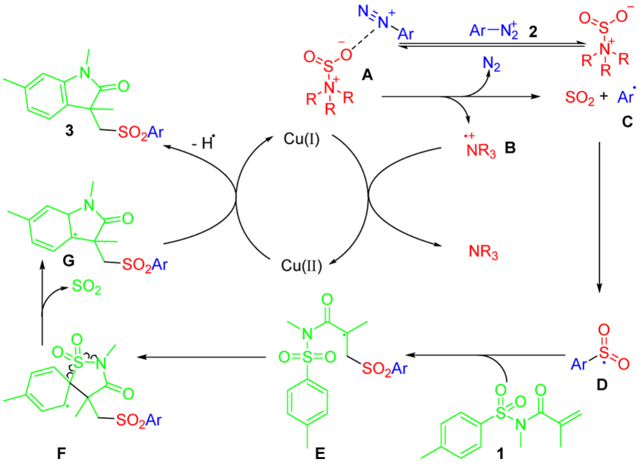
Scheme 2. Preliminary Mechanism Study



tetrafluoroborate **2a** under the conditions (Scheme 2 eq 2), no free sulfur dioxide (SO_2) gas was detected (see the Supporting Information for details), which indicated the important role of the tertiary amine in DABCO.

Based on the aforementioned experimental observations and previous reports,[10,11] a plausible mechanism was proposed (Scheme 3). The arydiazonium cation **2** would combine with DABSO to generate the complex **A** through electrostatic interaction. Then the complex **A** produced cation intermediate **B**, aryl radical **C**, and free SO_2 by the homolytic cleavage of the N−S bond[12] and a single-electron transfer. After the reaction of aryl radical **C** and free SO_2, the produced arylsulfonyl radical **D** attacked the C═C bond of **1** to afford the intermediate **E**.[13] Afterward, it underwent *ipso* cyclization toward cyclized intermediate **F**.[14] Then the desulfonylative migration took place to provide intermediate **G**. Finally, the intermediate **G** was oxidized by the Cu(II) to afford product **3** proceeding with single-electron transfer. Meanwhile, Cu(I) was oxidized into copper(II) by radical cation **B** to fulfill the catalytic cycle.

Scheme 3. Proposed Mechanism



In conclusion, we have developed an efficient three-component reaction of *N*-(arylsulfonyl)acrylamides, DABSO, and aryldiazonium tetrafluoroborates catalyzed by copper(II) to access sulfonated oxindole in moderate to good yields. The in situ generated arylsulfonyl radical via addition of an aryl radical to sulfur dioxide and the subsequent single electron transfer served to be the key steps for the reaction.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.7b02827.

Experimental procedures and spectra (PDF)

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Notes

The authors declare no competing financial interest.

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