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Metal-free catalyzed synthesis of the (E)-vinyl sulfones via aromatic olefins with arylsulfonyl hydrazides

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Synthesis of vinyl sulfones from aromatic olefins and arylsulfonyl hydrazides *via* I_2-TBHP catalyzed system under the N_2 atmosphere is described. Owing to no use of metal, only producing N_2 and water as the byproducts and directly available reactants, this reaction could validly avoid many disadvantages of the transition metal catalysts. In addition, the desired product can be collected with moderate to excellent yields under the suitable conditions.

Introduction

With the decrease of fossil energy and pollution of the environment, finding alternative sustainable processes, which are used to build new structures through functionalization of inactive C—H bonds, is a requirement for organic chemists.[1] In recent years, cross-coupling reactions have attracted a mass of current interests due to their potential advantages.[2] Especially, transition-metal-catalyzed C—C and C—heteroatom (N, O, P) bond formations have been researched by more and more chemists in recent decades.[3] Above their supports, we found that transition-metal-catalyzed cross-coupling reactions require very long reaction time. At the same time, transition-metal-catalyzed coupling reactions have many other drawbacks, such as expensive price for transition-metal catalysts, ligands, toxic catalysts or co-catalysts and so on.[4] But in many transition-metal-catalyzed cross-coupling reactions, there are a few of the efficient constructions of C—S bonds with high selectivity relatively, probably owing to the deactivation of the catalyst for the sulfur species.[5] So metal-free catalyst probably is a wonderful possibility for the construction of C—S bonds, avoiding of many disadvantages of transition-metal-catalyzed coupling reactions.[6]

Vinyl sulfone is an important function group in a great deal of biologically active molecules and pharmaceuticals.[7] For example, vinyl sulfones are widely used in sortase,[8] cysteine proteases,[9] protein tyrosine phosphatases[10] and so on. Based on the significance of these compounds in different areas, various approaches to produce vinyl sulfones have been discovered, like addition-elimination sequences, the Pd- and Cu-catalyzed cross-coupling reactions of sulfinate salts with vinyl halides[11] and so on. However, these methods inevitably suffered from certain shortcomings, for instance, producing a mixture of isomers.[12] In recent years, sulfonyl hydrazides have received considerable attention (Scheme 1). In 2014, Jiang and co-workers obtained vinyl sulfone with high yield by a copper-catalyzed transformation of styrene with $TsNHNH_2$ in dimethyl sulfoxide at 100 °C (Scheme 1a),[13] obviously, there are some metal catalyst. Subsequently, Lei and co-workers achieved parallel reactions with different catalyst (Scheme 1b).[14] Last several years, Singh and co-workers synthesized (*E*)-vinyl sulfones by cross-coupling, while cinnamic acids and arylsulfonyl hydrazides were performed under DBU as base condition (Scheme 1c).[15] In 2015, Yuan and co-works obtained (*E*)-vinyl sulfones via I_2-mediated decarboxylative cross-coupling reactions of sodium sulfinates with cinnamic acids(Scheme 1d).[16]

Sulfonyl hydrazine, an available synthesis intermediate in organic compounds, can be used to synthesis hydrazones, heterocycles directly,[17] as aryl sources by means of C—S bond cleavage,[18] as sulfone and reductants by means of *N*—S cleavage. Furthermore, there are also some chemical synthesis by cleavage of the O—S of sulfonyl hydrazides.[19] In comparison to other sulfenylation/sulfonation agents, sulfonyl hydrazides are stable in the air and readily accessible. More importantly, N_2 and water are the only byproducts in this reaction.[20] Given conventional synthetic strategies and reactants, herein, we reported the method for synthesis of

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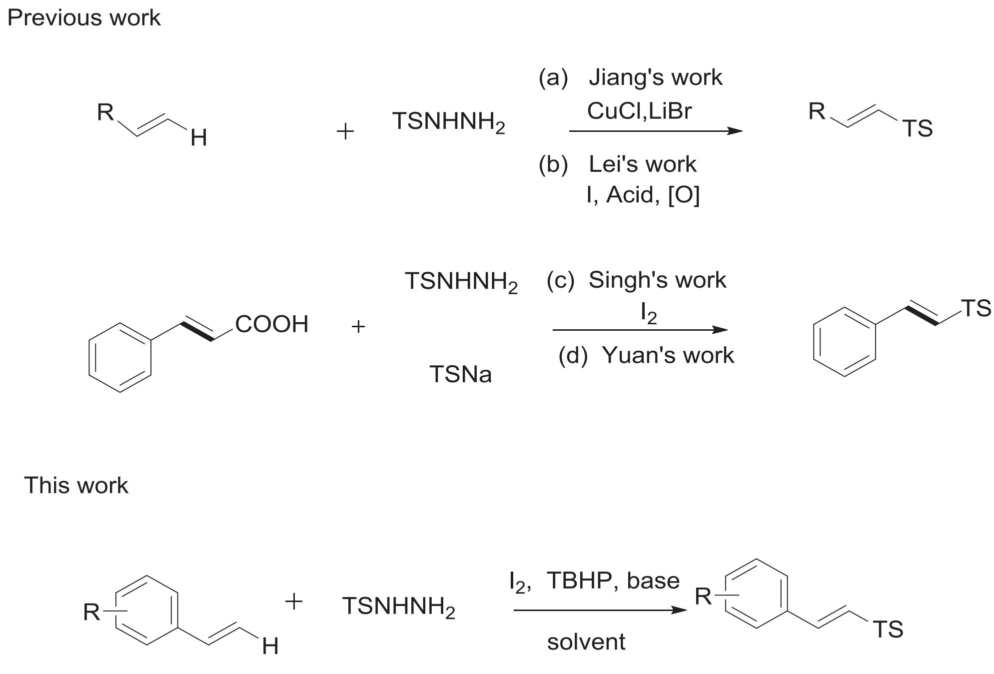


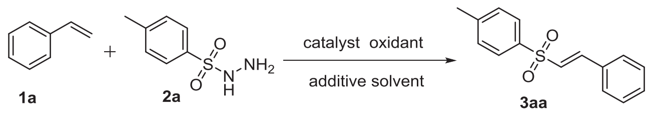
Scheme 1. C—S functionalization by aromatic olefins and arylsulfonyl hydrazides.

vinyl sulfones via I_2—TBHP-catalyzed oxidative cross-coupling between styrenes and sulfonyl hydrazine.

Organisation of the template

Firstly, p-toluenesulfonyl hydrazide **(1a)** and styrene **(2a)** were used as model substrates to examine various reaction conditions, the reaction of **1a** with **2a** was performed with 1.0 equiv. of I_2 as catalyst, 4.0 equiv. of TBHP as oxidant, and 1, 4-dioxane as the solvent in an open atmosphere at 90 °C for 3 h, the desired product **3aa** was isolated in 38% yield as shown in Table 1 (entry 1). At the same time, we performed the reaction in different solvent, to our delight, the corresponding product **3aa** was collected in 45% yield in toluene (entry 2). In order to find the best additives, we

Table 1
Optimization of reaction conditions[a].



Entry	Catalyst	Solvent	Additive	Oxidant	Yield (%)[b]
1	I_2	1,4-Dioxane	no	TBHP	38
2	I_2	Toluene	no	TBHP	45
3	I_2	DMA	no	TBHP	38
4	I_2	Toluene	Na_2CO_3	TBHP	70
5	I_2	Toluene	NaOH	TBHP	53
6	I_2	Toluene	$KHCO_3$	TBHP	60
7	I_2	Toluene	DBU	TBHP	53
8	I_2	Toluene	TEA	TBHP	65
9	I_2	Toluene	Na_2CO_3	No	Trace
10	I_2	Toluene	Na_2CO_3	H_2O_2	53
[c]11	I_2	Toluene	Na_2CO_3	TBHP	76
[d]12	I_2	Toluene	Na_2CO_3	TBHP	79
[d,e]13	I_2	Toluene	Na_2CO_3	TBHP	74
[d,f]14	I_2	Toluene	Na_2CO_3	TBHP	70
[d,g]15	I_2	Toluene	Na_2CO_3	TBHP	63
[d,h]16	I_2	Toluene	Na_2CO_3	TBHP	88
[d,i]17	I_2	Toluene	Na_2CO_3	TBHP	65
[d,h]18	TABI	Toluene	Na_2CO_3	TBHP	64
[d,h]19	I_2	Toluene	Na_2CO_3	DTBP	35

[a] Reaction conditions: 1a (0.2 mmol), 2a (0.24 mmol), catalyst (1.0 equiv.), oxidant (4 equiv.), solvent (2 mL), time (3h), temp (90 °C).base (1.0 equiv.) under air atmosphere.

[b] Isolated yield.

[c] Base (2.0 equiv.).

[d] (base (2.0 equiv.) oxidant (2.0 equiv.)).

[e] Catalyst (0.5 equiv.).

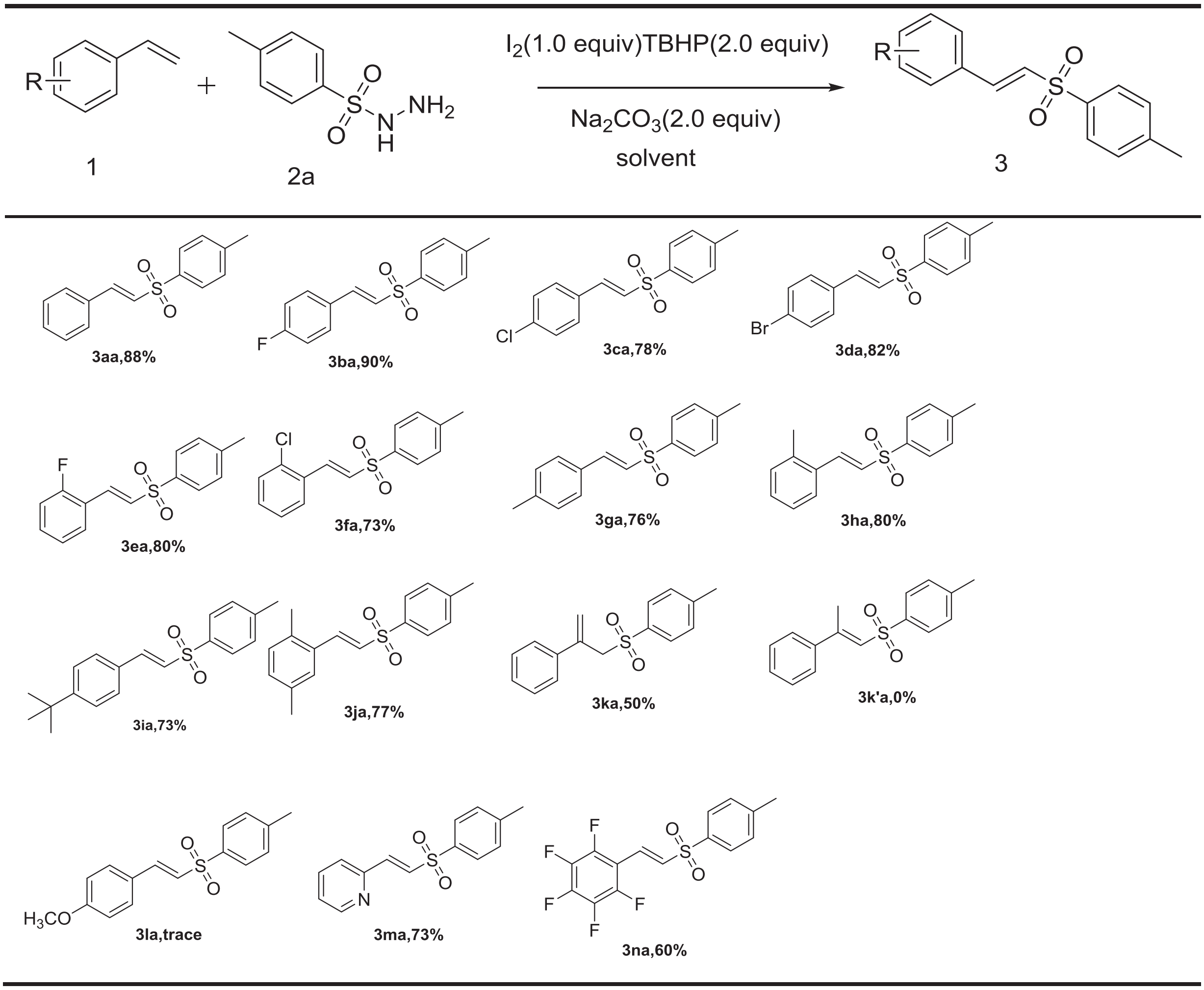
[f] At 70 °C. [g]At 110 °C. [h]under N_2 atmosphere. [i]under O_2 atmosphere. TBHP: *tert*-butyl hydroperoxide, DMA: N, *N*-dimethylacetamide, DBU: 1, 5-diazabicycloundec-5-ene, TEA: triethylamine.

chose Na_2CO_3, NaOH, $KHCO_3$, DBU and TEA as base, the results showed that $Na_2CO_3$was more favorable than other bases, the yield of (*E*)-1-methyl-4-(styrylsulfonyl) benzene **(3aa)** could be increased to 70% (entry 4–8). In addition, we found the yield of **3aa** did not enhance in absence of oxidant or other oxidants instead of TBHP (entry 9–10). Next, we optimized the dosages of the base, oxidant, and catalyst (entry 11–13). We found when the reaction was performed in an increase in the equiv. of Na_2CO_3 to 2.0, 2.0 equiv. of TBHP and 1.0 equiv. of catalyst the yield of **3aa** was achieved to 79% (entry12). Other temperatures (70 °C and 110 °C) were further tested, however, the yield of **3aa** was not improved (entry 14–15). At last, reaction was respectively performed under the O_2 atmosphere and N_2 atmosphere (entry 16–17). To our surprised, the yield of **3aa** was improved to 88% when reaction was carried out under the N_2 atmosphere (entry 16). We use TABI to replace iodine and get the corresponding product in yield (entry 18). And the same time, we use DTBP to replace TBHP in optimal condition and get the desired product in 38% yield (entry 19). After all, the use of I_2, TBHP, and Na_2CO_3 were crucial for this reaction, by using the optimized reaction conditions [1.0 equiv. of I_2, and 2.0 equiv. of TBHP, 2.0 equiv. of Na_2CO_3 in toluene, under the N_2 atmosphere] (entry 16), the generality of the method was subsequently explored (See Table 2).

In the optimal reaction conditions, various styrenes having various substitution groups underwent a smooth sulfono functionalization and the desired products were obtained in excellent yields. Some styrenes which have electron-withdrawing substituents on the phenyl ring could be performed smoothly to afford the corresponding products in available yields **(3ba-3fa),** obviously, the yield of product was declined when o-styrenes (2-F, 2-Cl) with p-toluenesulfonyl hydrazide was performed relative to p-styrenes (4-F, 4-Cl, 4-Br), perhaps primary reason is steric hindrance. In addition, we did other styrenes with electron-donating group on the phenyl ring (4-Me, 2-Me, 4-*t*-Bu, 2, 5-2Me), and the yields of the corresponding products ranged from 73% to 80% **(3ga-3ja)**. When α-Methyl-styrene was reacted, we did not get desired product ((*E*)-1-methyl-4-((2-phenylprop-1-en-1-yl) sulfonyl) benzene (**3k'a**), however, we collected another product (1-methyl-4-((2-phenylallyl) sulfonyl) benzene) (**3ka**). What is more, when styrene with electron-donating group on the phenyl ring (4-OCH_3) was performed, only trace desired product was detected **(3la)**. In addition, we also did some heterocyclic compound and other substituted groups, 2-vinypyridine, 2, 3, 4, 5, 6-pentafluorostyrene, the corresponding yields ranged from 50 to 73% (**3ma-3na**) (See Table 3).

At the same time, sulfonyl hydrazides with electron-withdrawing group or electron-donating group on the phenyl ring (3-F, 3-Br,

Table 2
Scope of the reaction with styrene.



Using 1 (0.24 mmol), 2a (0.2 mmol), I_2 (100 mol%), Na_2CO_3 (2.0 equiv.), TBHP (2.0 equiv.) in toluene under N_2 atmosphere at 90 °C for 3 h.

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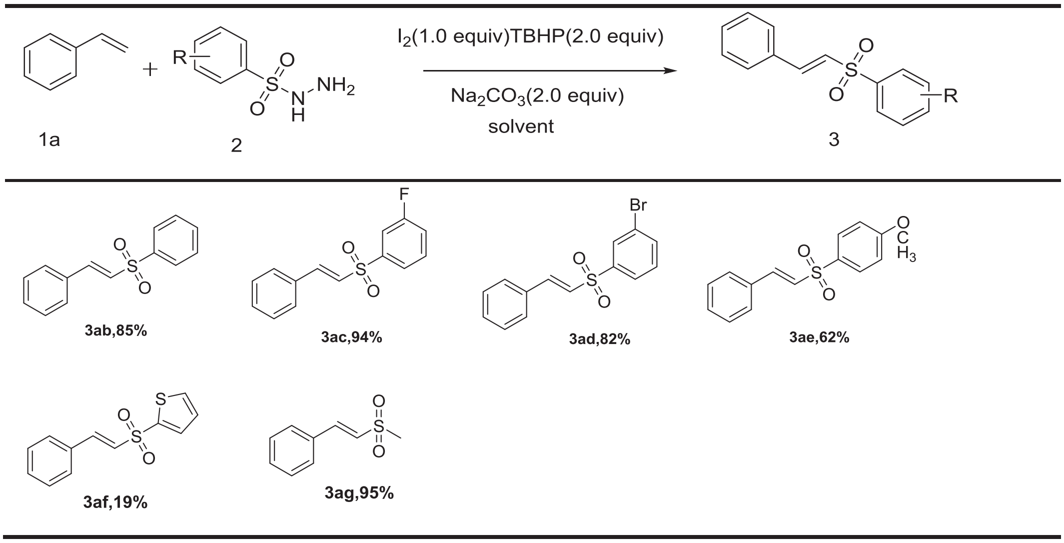
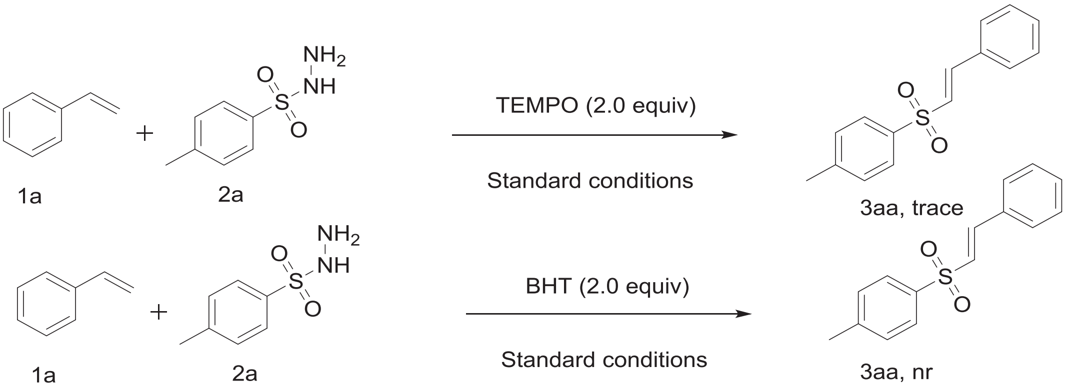
Table 3
Scope of the reaction with sulfonyl hydrazides.



Using 1a (0.24 mmol), 2 (0.2 mmol), I_2 (100 mol%), Na_2CO_3 (2.0 equiv), TBHP (2.0 equiv) in toluene under N_2 atmosphere at 90 °C for 3 h.



Scheme 2. Some controlling experiment.

4-OCH_3, 4-H) also could be performed, and yields of corresponding products range from 62% to 94% **(3ab-3af)**. And then we chose thiophene-2-sulfonohydrazide as the substrate, but the yield of product was 19%. We performed the methanesulfonyl hydrazide and styrene in the optimal condition, the corresponding product **3 ag** was collected in 95% yield. That showed the reaction was suitable for alkyl sulfonyl hydrazides.

In order to further explore possible reaction mechanism, we did some controlling experiments (Scheme 2). The reaction of styrenes with p-toluenesulfonyl hydrazide were performed under the standard conditions in the presence of radical inhibitors 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or 2,6-di-*tert*-butyl-4-methylphenol (BHT) respectively, the reaction was suppressed obviously, which indicated a radical reaction pathway be involved possible.

Based on the results of control experiments, a possible reaction mechanism was proposed in Scheme 3. Initially, *tert*-butyl hydroperoxide is decomposed into tertiary butyl free radicals, subsequently, *tert*-butoxyl radical abstracts hydrogen atom from sulfonyl hydrazide **1a,** which leads to the generation of sulfonyl radicals **(I-1)**, water, and the release of molecular nitrogen.[15,21] Afterwards, the radical addition reaction of **I-1** and olefin **2** generates carbon radical **I-2**.[22] The most important step for alkenylation is that radical **I-2** reacts with in situ generated iodine to generate iodosulfone **I-3** and then HI elimination from **I to 3** affords the final alkenylation product under the base.[23] At last, iodide is oxidized by TBHP under basic conditions to generate iodine and *tert*-butoxyl radical.[24]

Conclusions

In conclusion, the pathway to synthesize (*E*)-vinyl sulfone from available aromatic olefin and arylsulfonyl hydrazides was developed. The reaction was carried through an I_2 –TBHP catalyzed radical addition result, and an abundance of groups was well tolerated. This transformation provides a general method to the functionalization of styrenes, and the same time, N2 and water as byproduct, so this reaction shows its unexceptionable application prospect in organic synthesis area. What is more, the reaction provides good chemoselectivity and stereoselectivity.

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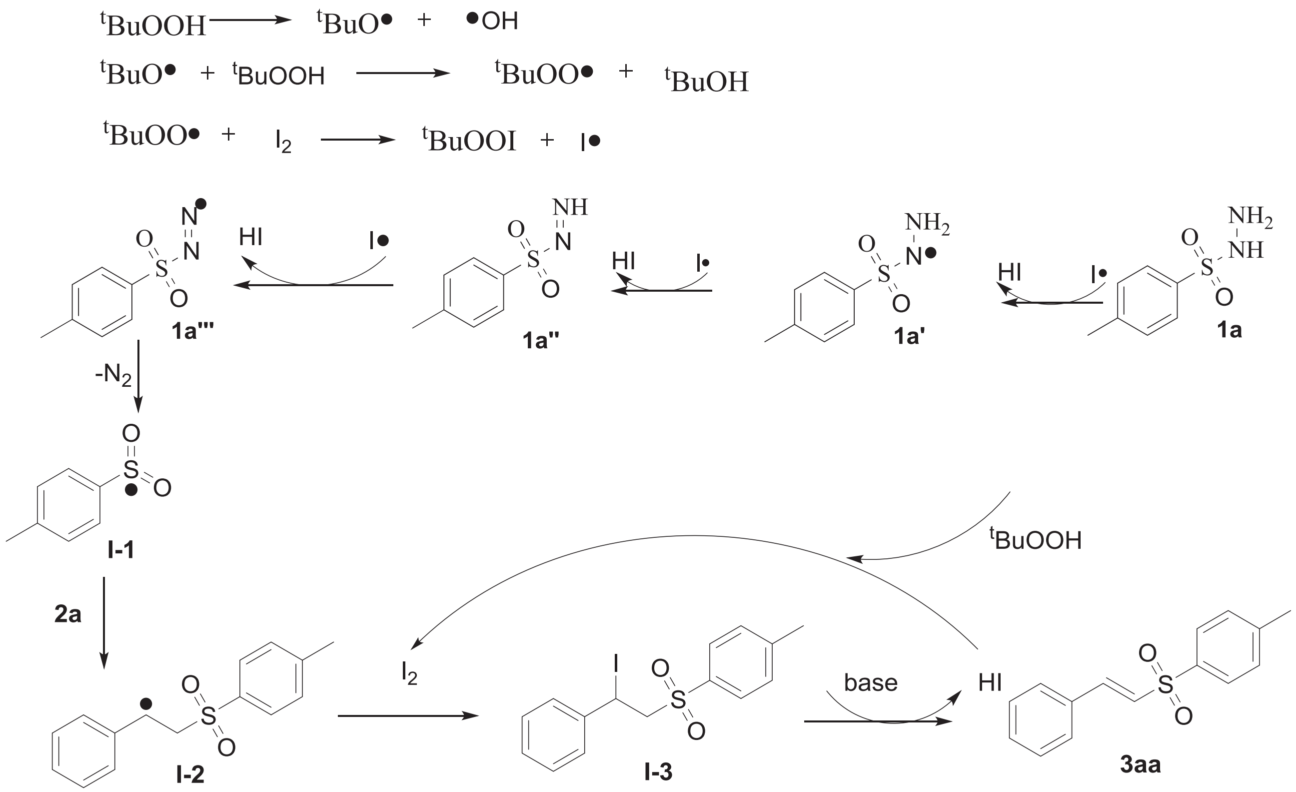

Scheme 3. Possible reaction mechanism.

A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.tetlet.2018.02.078.

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