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I_2/TBHP-mediated reaction of sulfonylhydrazides with alkynes: synthesis of (*E*)-β-iodovinyl sulfones

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ABSTRACT

An efficient and simple procedure for the syntheses of (*E*)-β-iodovinyl sulfones through TBHP mediated reaction of sulfonylhydrazides and iodine with aryl acetylenes has been developed. This method offers several advantages such as high atom economy, environmentally benign oxidant, less byproduct, and easy operation.

Sulfone-containing molecules have shown interesting biological activities and are primary components of many drugs on market.[1] They are also versatile building blocks in organic synthesis.[2] To construct this type of compounds, addition of sulfonyl radicals to carbon–carbon multiple bonds is a common strategy,[3] of which sulfonyl halides,[4] selenide,[5] cyanide,[6] azide,[7] and sodium sulfinate[8] often serve as the sulfonyl radical precursor. Recently, the Taniguchi group developed a new method to generate sulfonyl radical from sulfonylhydrazide using inexpensive and nontoxic $FeCl_3$ as catalyst and O_2 as oxidant, which allows them to synthesize β-hydroxysulfones from alkenes.[9] Our group also developed a new approach to generate sulfonyl radical from sulfonylhydrazide using TBAI (20 mol %) as catalyst and TBHP (2 equiv) as terminal oxidant (Scheme 1).[10] Addition of thus obtained sulfonyl radical to α-methyl styrene or styrene furnished allylic or vinyl sulfones, respectively (Scheme 1, Eqs. 1 and 2).[10] Encouraged by these results, we continued our research on sulfonylation of alkynes (Scheme 1, Eq. 3).

We initiated our investigation of the sulfonylation of phenylacetylene with standard TBAI–TBHP conditions.[10,11] However, to our surprise, (*E*)-β-iodovinyl sulfone **3aa** was isolated as a single product in 17% yield and, obviously, the catalytic amount TBAI as the sole source of iodine limited the yield of **3aa** (Scheme 1, Eq. 3). The structure of **3aa** was unambiguously confirmed by single crystal X-ray diffraction (Fig. 1).[12]

Typically, (*E*)-β-iodovinyl sulfones are synthesized by the addition of sodium sulfinate to alkynes in the presence of NaI or KI with stoichiometric amount of $Ce(NH_4)_2(NO_3)_6$ or $PhI(OAc)_2$ as oxidant (Scheme 2).[13] In addition to the sensitivity to air and moisture, this approach needs relative expensive oxidants with high molecular weight, which leaves room to further improve the atom economy.

Encouraged by our initial experiment, iodine (0.5 equiv) was used to replace TBAI of the standard conditions (Scheme 2). To our delight, (*E*)-β-iodovinyl sulfone **3aa** was isolated in 94% yield (Table 1, entry 1). Inert atmosphere and dry solvent are not necessary in this process. All iodine atoms are transferred into the product, which is also an improvement compared to using NaI or KI. Therefore, the reactions of various substituted phenylacetylenes with $TsNHNH_2$ were examined under the same reaction conditions. Gratifyingly, good to excellent yields were observed with halogen, trifluoromethyl, methyl, and *n*-pentyl substituted phenylacetylenes (Table 1, entries 2–8). Electron rich *p*-MeO phenylacetylene afforded **3ha** in 62% yield (Table 1, entry 9). Heteroaryl acetylenes, such as pyridyl and thiophenyl acetylenes were also compatible substrates and delivered the corresponding (*E*)-β-iodovinyl sulfones (**3ia** and **3ja**) in 56% and 83% yields, respectively, (Table 1, entries 10–11). However, the yield diminished markedly when aliphatic alkyne was used (Table 1, entry 12).

Phenyl and *p*-bromophenyl substituted sulfonylhydrazides **2b**,**c** were also examined in the reaction with phenylacetylene **1a** (Scheme 3), smoothly led to the corresponding (*E*)-β-iodovinyl sulfones **3ab** and **3ac** in 86% and 88% yields, respectively.

Based on results described above and the previous reports,[10,13] a plausible mechanism is proposed (Scheme 4). Initially,

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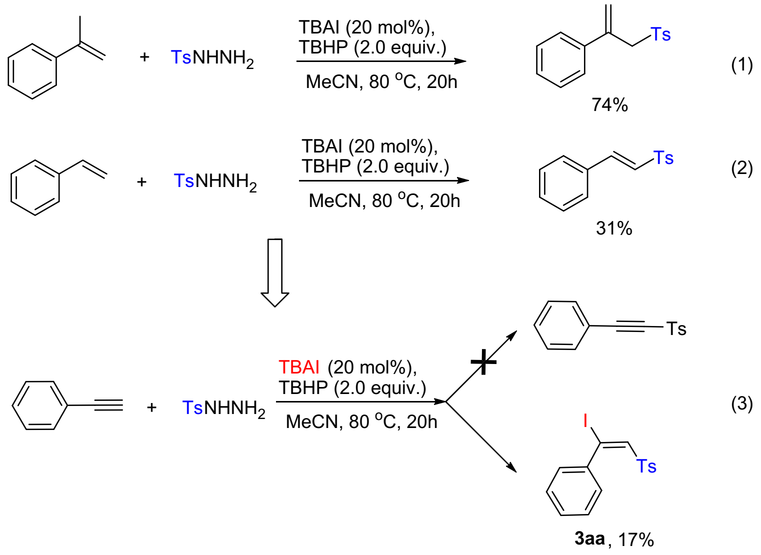
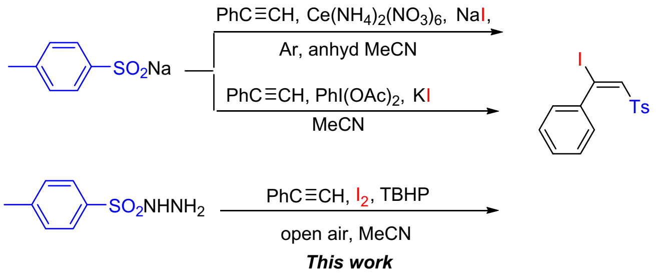
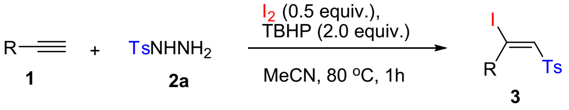


Scheme 1. Reactions of $TsNHNH_2$ with multiple bonds.



Scheme 2. Synthesis of (*E*)-β-iodovinyl sulfones.

Table 1
Scope of the reaction with alkynes[a]



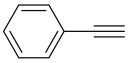
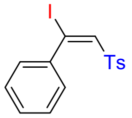
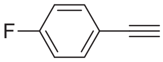
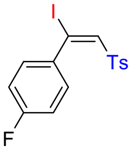
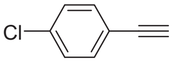
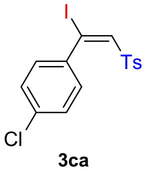
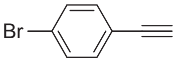
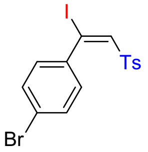
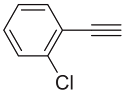
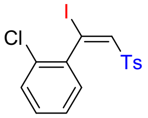
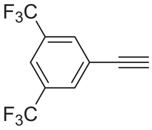
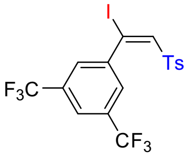
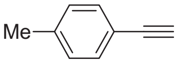
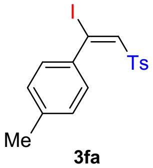
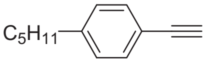
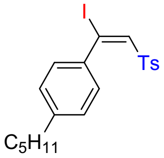
Entry	Substrates	Products	Yield (%)[b]
1	 **1a**	 **3aa**	94
2	 **1b**	 **3ba**	88
3	 **1c**	 **3ca**	93
4	 **1d**	 **3da**	84
5	 **1e**	 **3ea**	93
6	 **1f**	 **3fa**	94
7	 **1g**	 **3fa**	75
8	 **1h**	 **3ga**	84

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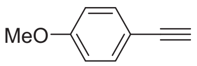
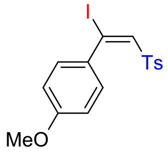
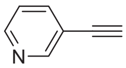
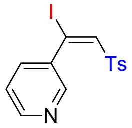
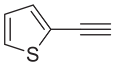
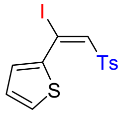
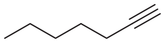
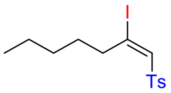
Table 1 (*continued*)

Entry	Substrates	Products	Yield (%)[b]
9	 **1i**	 **3ha**	62
10	 **1j**	 **3ia**	56
11	 **1k**	 **3ja**	83
12	 **1l**	 **3la**	22

[a] Reaction conditions: 0.5 mmol of aryl acetylenes (**1**), 0.6 mmol of $TsNHNH_2$ (**2a**), 0.25 mmol of I_2, 2 equiv of TBHP (70% aqueous solution) in 2.0 mL of MeCN at 80 °C for 1 h.

[b] Isolated yield.

α-*N*-hydrogens of sulfonylhydrazides are abstracted by free radicals generated from the homolysis of TBHP,[14] to generate sulfonyl radicals. Then, the addition of resulting sulfonyl radicals to aryl acetylenes and subsequent trapping of the *C*-centered alkenyl radicals intermediate **I** with I_2 or iodine free radicals afford (*E*)-β-iodovinyl sulfones **3** (Scheme 4, Eq. 1).[13a] It is also possible that **3** is formed via the addition of arenesulphonyl iodides, which was generated from the reaction of sulfonyl radicals with I_2 or iodine free radicals, to aryl acetylenes (Scheme 4, Eq. 2).[13b]

In conclusion, a highly efficient synthetic method for the preparation of (*E*)-β-iodovinyl sulfones has been developed. The reaction is environmentally benign in adoption of inexpensive TBHP and iodine, which are highly atom-economically transferred into products leaving nontoxic *tert*-butanol as the side product. No need of inert atmosphere or dry solvent also allows easy experimental operation. Further investigation of the sulfonylation with sulfonylhydrazides as the sulfonyl radical precursor is underway in our laboratory.

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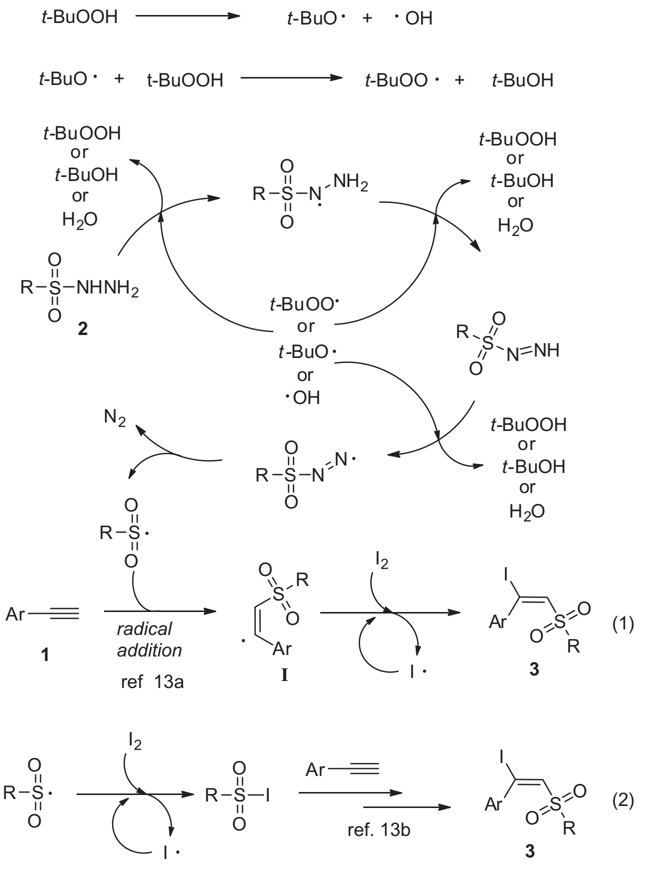


Scheme 4. Possible mechanism.

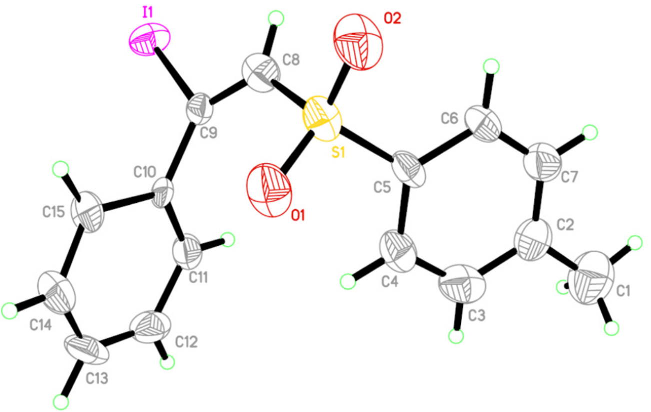
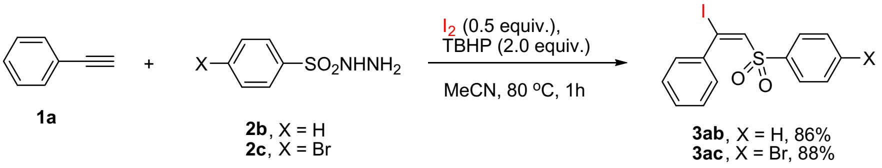


Figure 1. Crystal structure of compound **3aa**.



Scheme 3. Reactions of various sulfonylhydrazides.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.03.117.

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12. CCDC 918095 contains the supplementary crystallographic data for this Letter. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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