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Tetrabutylammonium iodide catalyzed allylic sulfonylation of α -methyl styrene derivatives with sulfonylhydrazides[†]

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Sulfonyl radicals generated from sulfonylhydrazides by the Bu₄NI– *tert*-butyl hydroperoxide (TBHP) catalysis system underwent addition to a variety of α -methyl styrene derivatives to give the corresponding allylic sulfones. This selective allylic sulfonylation is metal-free, operationally simple, and environmentally friendly.

The construction of highly valuable functionalized allylic compounds represents a highly desirable goal and long-term challenge. The well-known Tsuji–Trost reaction,¹ a palladium-catalysed allylic substitution reaction, is one versatile and reliable methodology which has been widely applied in the synthesis of natural products and biologically active compounds.² A drawback of this reaction is the necessity to use prefunctionalized allylic compounds, such as allyl acetates and allyl bromides, thus adding steps towards the formation of desired products. Hence, the direct introduction of a new functionality *via* direct allylic C–H bond activation has drawn much attention in recent years.³ Although several transition metal catalysts have proven to be highly effective in such direct functionalization processes,^{4,5} the development of new, cost-effective, and environmentally benign metal-free catalysis processes remains a significant challenge.⁶

Tetrabutylammonium-iodide (TBAI) has recently emerged as a promising alternative as a catalyst for functionalization of C–H bonds due to its low cost, low toxicity, and the mild reaction conditions.⁷ The postulated *tert*-butoxyl and *tert*-butylperoxy radical intermediates generated from TBAI catalyzed TBHP (*tert*-butyl hydroperoxide) decomposition^{7b–e} enabled numerous important organic transformations such as C–O^{7c,d} and C–N^{7b,e} bond formation. In particular, Wan *et al.* elegantly utilized the TBAI–TBHP system for the synthesis of allylic esters *via* allylic radicals.⁸

Allylic sulfones are exceptionally versatile building blocks in organic synthesis.⁹ Generally, they are synthesized by Tsuji–Trost reaction of a sulfinate anion with allyl acetates and allyl bromides.¹⁰ The addition of sulfonyl radicals produced by the

 Table 1 Optimization of reaction conditions^a

	↓ +	TsNHNH ₂ —			
	1a	2a			3aa
Entry	1a/2a	TBHP (eq.)	Solvent	Temp (°C)	Yield ^b (%)
1	1:1.5	3	MeCN	80	74
2	1:1.5	3	EtOAc	75	51
3	1:1.5	3	MeCN	70	57
4	1:1.2	2	MeCN	80	74

^{*a*} Reaction conditions: 0.5 mmol of α -methylstyrene (1a), TsNHNH₂ (2a), 20 mol% TBAI, TBHP (70% aqueous solution) in 2.0 mL of solvent for 20 h. ^{*b*} Isolated yield.

thermolysis or photolysis of sulfonyl chlorides and iodides in the presence or absence of copper catalysts to alkenes followed by dehydrohalogenation was also reported.¹¹ Recently, Taniguchi *et al.* have developed an environmentally friendly method for the formation of radicals from hydrazine compounds with iron catalysts and air.¹² The only byproduct in this process is molecular nitrogen. Herein, we wish to report a new metal-free allylic sulfonylation based on radical addition employing TBAI and TBHP.

We initiated this work with the anticipation that the generation of sulfonyl radicals from sulfonylhydrazides can also be achieved with the TBAI-TBHP oxidative system. For our initial experiments, 1.5 equivalents of p-toluenesulfonylhydrazide (TsNHNH₂) 2a were chosen as a radical precursor and treated with one equivalent of α -methyl styrene 1a using 20 mol% of TBAI as a catalyst and 3 equivalents of TBHP (70 wt% in water) as an external oxidant in MeCN at 80 °C. Gratifyingly, the desired allylic sulfone 3aa was obtained in 74% yield (Table 1, entry 1). In contrast, only 51% of the desired product is achieved in EtOAc (Table 1, entry 2). A lower reaction temperature led to a significantly lower yield of 3aa (Table 1, entry 3), whereas no effect on yield was observed with lower amounts of TsNHNH2 and TBHP (Table 1, entry 4). No formation of other oxidation side-products was observed under the standard reaction conditions.

The allylic sulfonylations of a variety of substituted α -methyl styrenes with TsNHNH₂ were then examined under the standard reaction conditions, and representative results are summarized in Table 2. The results indicated that a wide range

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Table 2	Scope of	the	reaction	with	α-methyl	styrene
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			TBAI (20 mol%) TBHP (2.0 eq.)	, L ,Ts	
$Ar \rightarrow + IsinHinH_2$			MeCN, 80 °C, 20 h	Ar 🔨	
	1	2a		3	
Ent	ry Ar		Product 3	$\operatorname{Yield}^{b}(\%)$	
1	C ₆ H ₅	, 1 a	3aa	74	
2	<i>p</i> -Me	C_6H_4 , 1b	3ba	62	
3	o-Me	C_6H_4 , 1c	3ca	50	
4	<i>p</i> -Me	OC_6H_4 , 1d	3da	60	
5	m-Me	eOC ₆ H ₄ , 1e	3ea	70	
6	p-FC	₆ H ₄ , 1f	3fa	75	
7	p-ClC	C ₆ H ₄ , 1g	3ga	64	
8	p-BrC	C_6H_4 , 1h	3ha	68	
9	m-Br	C_6H_4 , 1i	3ia	57	
10	p-CF	$_{3}C_{6}H_{4}$, 1j	3ja	21	
11	3,4-D	MeOC ₆ H	, 1k 3ka	73	
12	1-Na	phthyl, 1	3la	70	
13	2-Thi	ophenyl, 11	n 3ma	61	

^{*a*} Reaction conditions: 0.5 mmol of α-methylstyrene (**1a**), 0.6 mmol of TsNHNH₂ (**2a**), 20 mol% TBAI, 2 equiv. of TBHP (70% aqueous solution) in 2.0 mL of MeCN at 80 °C for 20 h. ^{*b*} Isolated yield.

of substituted groups, such as methyl, methoxyl, fluoro, chloro, bromo, trifluoromethyl and naphthyl, were well tolerated and the desired sulfones were produced in moderate to good yields (Table 2, entries 1–12). Heteroaryl species such as thiophenyl also underwent the desired reaction to give the corresponding product in 61% yield (Table 2, entry 13).

Next, the reaction was examined with phenyl and *p*-bromophenyl substituted sulfonylhydrazides **2b–c**, which were treated with α -methylstyrene **1a** under the standard reaction conditions (Scheme 1). The sulfonylation worked smoothly, leading to the formation of the corresponding sulfones **3ab** and **3ac** in 61% and 60% yields, respectively.

Finally, a series of other terminal alkenes were investigated. Both exocyclic and noncyclic styrene derivatives underwent the allylic sulfonylation, leading to the formation of sulfones in moderate to excellent yields (Table 3). Notably, the reaction shows high regioselectivity. In all cases, the sulfonylations took place at the terminal carbon of double bonds with the migration of the double bonds. Thus, α -ethyl styrene resulted in the formation of two isomeric double bonds of sulfone 3pa in 71% yield (Z : E = 3/1) (Table 3, entry 3). α -Benzyl styrene 1q was also a compatible substrate for this transformation and gave rise to a single Z isomer of stilbene 3qa in 37% yield (Table 3, entry 4), perhaps as a result of steric hindrance. But internal alkenes such as cyclohexene failed in the reaction to give the desired allylic sulfone due to the steric effect.^{12b} Surprisingly, attempts to carry out the corresponding allylic sulfonylation of vinylcyclohexane and allylbenzene were also unsuccessful. It is worth mentioning that in allylic amination employing a hypervalent iodine(III) reagent reported by Muñiz et al.⁶ and allylic esterification employing the TBAI-TBHP



Scheme 1 Reactions of various sulfonylhydrazides.

 Table 3
 Scope of the reaction with styrene derivatives⁴



^{*a*} Reaction conditions: 0.5 mmol of alkenes (1), 0.6 mmol of TsNHNH₂ (2a), 20 mol% TBAI, 2 equiv. of TBHP (70% aqueous solution) in 2.0 mL of MeCN at 80 °C for 20 h. ^{*b*} Isolated yield. ^{*c*} The ratio of isomers was determined by ¹H NMR spectroscopy of the isolated product.

system reported by Wan *et al.*,⁸ the migration of the carbon– carbon double bond also happened. However, different mechanisms were proposed for these selective allylic C–H bond functionalization processes. An iodo(III)cyclopropane mechanism was involved in the former reaction, while the radical coupling pathway was postulated in the latter one.

Several control experiments were conducted to elucidate the mechanism. Firstly, TEMPO, a radical-trapping reagent, was introduced into the reaction mixture and the formation of the desired sulfone was completely suppressed (Scheme 2, eqn (1)), indicating that the reaction presumably underwent a radical pathway. Then, α -methyl styrene alone was treated with TEMPO under the standard conditions, and no adduct of TEMPO and the allylic radical was isolated (Scheme 2, eqn (2)). This result implied that the reaction pathway may be not followed in catalysis involving allylic radicals.¹³ Thus, selective coupling of sulfonyl and allylic radicals should be excluded. At last, the coupling of styrene with TsNHNH₂





Scheme 2 Investigation into the reaction mechanism.



Scheme 3 Proposed preliminary mechanisms.

could also take place to form sulfone **4**, albeit in lower yield (Scheme 2, eqn (3)). Hence, the radical addition pathway is most likely involved.¹¹

On the basis of results described above and in previous reports,^{8,12} a plausible mechanism is proposed (Scheme 3). Initially, TBHP decomposes to generate the *tert*-butoxyl and *tert*-butylperoxy radicals with the assistance of the iodide anion. These radicals subsequently abstract hydrogen atoms from sulfonylhydrazides to generate sulfonyl radicals with the release of molecular nitrogen. The addition of resultant sulfonyl radicals to alkenes and subsequent abstraction of the resultant radical intermediate by *tert*-butoxyl or *tert*-butylperoxy radicals affords sulfones **3**. One should note that the highly selective H-abstraction of the radical intermediate in this reaction is unexpected as it was reported that the C-centered radicals generated by radical addition can be trapped with *tert*-butylperoxyl radicals.¹⁴

In summary, we have developed a new metal-free direct allylic sulfonylation reaction, in which the generation of sulfonyl radicals from sulfonylhydrazides with the TBAI–TBHP system was involved. The use of cheap and nontoxic TBAI as a catalyst and the elimination of molecular nitrogen as a byproduct during the sulfonyl radicals generation make this selective allylic sulfonylation environmentally friendly. Investigation of a detailed mechanism and radical reactions based on the TBAI–TBHP system catalyzed radical species generation from other hydrazine compounds is underway in our laboratory.

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