Stereoselective Synthesis of (*E***)-Alkenyl Sulfones from Alkenes or Alkynes via Copper-Catalyzed Oxidation of Sodium Sulfinates**

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Abstract: Alkenyl sulfones can be stereoselectively synthesized from alkenes or alkynes using sodium sulfinates. The reaction can be performed by a copper-catalyzed oxidation of sodium sulfinates in air. The reaction of alkenes gives (*E*)-alkenyl sulfones via *anti* addition of sulfonyl cation and elimination process. Furthermore, the employment of alkynes produces (*E*)- β -haloalkenyl sulfones in the presence of potassium halides.

Key words: alkenyl sulfone, copper catalyst, sodium sulfinate, alkene, alkyne

Transition-metal-catalyzed carbon–sulfur bond formations are important methodologies for preparations of various organosulfur derivatives.¹ The compounds obtained herein have been widely utilized in organic synthesis.² In particular, alkenyl sulfones are employed as convenient synthetic intermediates or reagents.³

To prepare sulfones, numerous procedures have been developed so far.^{1,4} For instance, methods by Horner– Emmons reaction, aldol condensation, and oxidation of vinyl sulfides are well-known.

On the contrary, utilizations of sulfinic acid salts as sulfonylation reagents⁵ are restricted to Michael addition⁶ or a transition-metal-catalyzed coupling with alkenyl halides.⁷

Furthermore, catalytic syntheses of alkenyl sulfones from nonactivated alkenes or alkynes have not been reported to date.



Scheme 1 Strategy of the catalytic alkenyl sulfone synthesis using sulfinic acid salts

In order to carry out sulfonylations of normal alkenes using sulfinic acid salts, a generation of sulfonyl radical or cation by oxidation is required at first step (Scheme 1).

In usual method, stoichiometric oxidants such as CAN are well utilized.⁸ Regrettably, the catalytic reaction could not be currently achieved. Although, the use of commercially available sulfonyl chlorides can produce alkenyl sulfones from alkenes,⁹ it is not the convenient and the effective

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 Table 1
 Investigation of Suitable Conditions for the Synthesis of Alkenyl Sulfones in Air^a



Entry	CuX	Additive	Condition	Ratio of 3ab/4/5 ^b	3ab (%) ^c
1	CuI	none	DMF ^d	_	0
2	CuI	none	DMSO ^d	_	0
3	CuI	none	$AcOH^d$	67:33:0	14
4	CuI	none	AcOH, DMSO ^e	50:8:42	35
5	CuI	KI	AcOH, DMSO ^e	86:7:7	82
6	CuI	<i>n</i> -Bu ₄ NI	AcOH, DMSO ^e	74:15:11	30
7	CuI	KBr	AcOH, DMSO ^e	80:12:8	55
8	None	none	AcOH, DMSO ^e	0:67:33	0
9	CuCl	KI	AcOH, DMSO ^e	77:23:0	31
10	CuBr	KI	AcOH, DMSO ^e	80:16:4	37
11	CuCl ₂	KI	AcOH, DMSO ^e	83:17:0	29
12	CuBr ₂	KI	AcOH, DMSO ^e	84: 8:8	80
13	Cu(OAc) ₂	KI	AcOH, DMSO ^e	84:16:0	81
14 ^f	CuI	KI	AcOH, DMSO ^e	59:35:6	39
15 ^g	CuI	KI	AcOH, DMSO ^e	71:29:0	48
16 ^h	CuI	none	AcOH, DMSO ^e	53:26:21	5

^a The mixture of 1a (0.3 mmol), 4-MeC₆H₄SO₂Na (**2b**, 0.33 mmol), additive (0.15 mmol) and CuI–bpy (1:1, 0.024 mmol) was treated in DMSO or/and AcOH.

^b The ratio was determined by ¹H NMR.

^c Isolated yields after silica gel chromatography.

^d 0.3 mL of solvent was used.

^e AcOH (0.15 mL) and DMSO (0.15 mL) were used.

^f TMEDA was used instead of bpy.

^g 2,2'-Bis(2-oxazoline) was used instead of bpy.

^h No bpy was employed.

method. The reaction is necessary for two steps including addition and elimination process, and only limited substrates are available.

As an approach to explore one-step reaction in one pot, a copper-catalyzed reaction in air was investigated,¹⁰ and it was found that (*E*)-alkenyl sulfones can be stereoselectively synthesized from sodium sulfinates with alkenes or alkynes.

The methodology is described in this paper.

Initially, a reaction of alkenes with sodium sulfinates was investigated. When a mixture of styrene **1a** (0.3 mmol) and 4-MeC₆H₄SO₂Na (**2b**, 0.3 mmol) in DMF or DMSO was treated by CuI–bpy (1:1, 8 mol%) catalyst, the expected alkenyl sulfone **3ab** was not detected at all (Table 1, entries 1 and 2). However, the reaction using acetic acid as a solvent afforded **3ab** in 14% yield (Table 1, entry 3). When a mixture of acetic acid and DMSO used as the solvent, the production of **3ab** increased to 35% yield (Table 1, entry 4).

Fortunately, the addition of KI (0.15 mmol) facilitated the reaction, and **3ab** was obtained in 82% yield with a trace of hydroxysulfone **4** and a trace of β -ketosulfone **5** as byproducts (Table 1, entry 5). The stereochemistry of **3ab** was *E*.^{7c} The addition of *n*-Bu₄NI or KBr reduced the production to 30% or 55% yield, respectively (Table 1, en-

tries 6 and 7). The reaction in the absence of a copper catalyst and KI could not produce **3ab** (Table 1, entry 8). Then, the employment of CuBr_2 and $\text{Cu}(\text{OAc})_2$ were also available, and the reactions afforded satisfied results (Table 1, entries 12 and 13). On the contrary, other copper salts (CuCl, CuBr, and CuCl₂) could not promote the reaction (Table 1, entries 9–11). The reactions using other ligands [TMEDA and 2,2'-Bis(2-oxazoline)] were also lower yields (Table 1, entries 14 and 15).

On the basis of the developed procedure, numerous alkenyl sulfoxides were prepared (Table 2).^{11,12} The reaction of terminal alkenes **1** with sodium sulfinates afforded the corresponding alkenyl sulfones **3** in 60–94% yields (Table 2, entries 1–11). Similarly, the use of allyl trimethylsilane produced allyl sulfone **3gb** in 43% yield (Table 2, entry 11).

Not only terminal alkenes but also internal alkenes were available in this procedure (Table 2, entries 12–15). Reactions of (*E*)- or (*Z*)- β -methylstyrenes afforded same (*E*)-alkenyl sulfone **3hb** without formations of other stereo-isomers (Table 2, entries 12 and 13).

Unfortunately, the reaction of stilbene or cyclohexene barely proceeded (Table 2, entries 16 and 17).

$R^1 \xrightarrow{R^2} 1$	R ³ SO ₂ Na (2), Cul-bpy (8 mol%), KI (50 mol%) AcOH, DMSO, air, 100 °C	R ¹ SO ₂ R ³ R ² 3		
Entry	1	3	Time (h)	Yield of $3 (\%)^{\mathrm{b}}$
1	Ph	Ph SO ₂ Ph	18	94
2		Ph SO ₂ C ₆ H ₄ Me-4 3ab	18	82
3		Ph SO ₂ C ₆ H ₄ OMe-4	18	80
4		Ph $SO_2C_6H_4Cl-4$ 3ad	18	80
5		Ph SO ₂ Me 3ad	18	74
6	4-MeC ₆ H ₄	4-MeC ₆ H ₄ SO ₂ C ₆ H ₄ Me-4	18	71
7	4-CIC ₆ H ₄	$4-\text{CIC}_6\text{H}_4 \xrightarrow{\text{SO}_2\text{C}_6\text{H}_4\text{Me-4}}$	18	85
8		SO ₂ C ₆ H ₄ Me-4 3db	18	66

 Table 2
 Copper-Catalyzed Synthesis of Alkenyl Sulfones from Alkenes^a (continued)



^a Conditions: The mixture of alkene 1 (0.3 mmol), R³SO₂Na 2 (0.33 mmol), KI (0.15 mmol), and CuI-bpy (1:1, 0.024 mmol) in DMSO (0.15 mL) and AcOH (0.15 mL) was stirred at 100 °C.

^b Isolated yields after silica gel chromatograpy.

^c Acetate was also obtained in 5% yield.

Attention was then focused on the sulfonylation of alkynes. As shown in Table 3, the reaction was performed by CuI-bpy (1:1, 8 mol%) in acetic acid, and various alkynes 6 were examined.^{12,13} The procedure could stereoselectively give the corresponding (E)- β -haloalkenyl sulfones 7 from terminal or internal alkynes 6 (Table 3, entries 1-6). The sulfonylation proceeded anti-selectively.

Strangely, the reaction using 4-octyne afforded (E)-4-bromo-5-(4-tolylthio)-4-octene in 32% yield, and the formation of the expected alkenyl sulfone 7db was only 5% yield (Table 3, entry 7). On the other hand, diphenyl acetylene was lower reactivity (Table 3, entry 8).

To investigate reaction mechanisms, sulfonylations in the absence of oxygen were carried out. When a mixture of styrene 1a with 4-MeC₆H₄SO₂Na (2b) was treated under nitrogen atmosphere, the corresponding alkenyl sulfone **3ab** was obtained in 27% yield (Scheme 2). Similarly, in



Scheme 2 Sulfonylation of alkene or alkyne in the absence of oxygen

D 1 -	<u> </u>	R ³ SO ₂ Na, KX cat. Cul-bpy (8 mol%)	×	$X \to R^2$	
R'=	<u> </u>	AcOH, air, 100 °C	R ^T SC 7	D_2R^3	
Entry	6	7	Time (h)	Yield of 7 (%) ^b	
1	Ph	Ph SO ₂ Ph	18	63	
2		Br Ph $SO_2C_6H_4Me-4$ 7ab	18	52	
3		Ph SO ₂ Me	18	74	
4		Ph SO ₂ Me	18	51	
5	<i>n-</i> C ₆ H ₁₃ ── ─	^{Br} <i>n</i> -C ₆ H ₁₃ SO ₂ C ₆ H ₄ Me 7bb	18 >-4	30	
6	Ph	Ph SO ₂ C ₆ H ₄ Me-4	18	71	
7	n-Pr	<i>n</i> -Pr <i>n</i> -Pr <i>s</i> O ₂ C ₆ H ₄ Me	18	5°	
8	Ph— — —Ph	$\begin{array}{c} \textbf{7db} \\ \textbf{Br} & \textbf{Ph} \\ \textbf{Ph} & \textbf{SO}_2 C_6 H_4 Me-4 \\ \textbf{7eb} \end{array}$	18	trace	

 Table 3
 Copper-Catalyzed Synthesis of Alkenyl Sulfones from Alkynes^a

^a Conditions: The mixture of **6** (0.3 mmol), R^3SO_2Na **2** (0.33 mmol), KX (0.33 mmol), and CuI–bpy (1:1, 0.024 mmol) in AcOH (0.3 mL) was stirred at 100 °C.

^b Isolated yields after silica gel chromatograpy.

 $^{\rm c}$ (*E*)-4-Bromo-5-(4-tolylthio)-4-octene was also obtained in 32% yield.

the reaction using 1-phenyl-1-propyne (**6c**), the yield of (*E*)- β -bromoalkenyl sulfone **7cb** was 20% (Scheme 2). These experiments suggest that oxygen is necessary for promotions of these procedures. In addition, it seems that disproportionations of copper complexes also proceed.^{9,14}

From these results, reaction mechanisms are considered as follows (Scheme 3). At first step, after Cu(II) was produced by the oxidation of Cu(I) or the disproportionation, sulfonyl radicals or cations were afforded by Cu(II).¹⁵ Consequently, herein produced sulfonyl activators afford-

ed (*E*)-alkenyl sulfones via *anti* additions to alkenes and eliminations of HI or (*E*)- β -haloalkenyl sulfones via *anti* additions to alkynes.



Scheme 3 A plausible reaction mechanism

In conclusion, preparation of alkenyl sulfoxides was conveniently achieved via a copper-catalyzed oxidation of sulfinic acid sodium salts in air. The reaction using alkenes afforded (*E*)-alkenyl sulfones. Furthermore, the employment of alkynes gave (*E*)- β -haloalkenyl sulfones.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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- (11) **Typical Procedure of Alkenyl Sulfones Using Alkenes** To a mixture of CuI (4.6 mg, 0.024 mmol), bpy (3.7 mg, 0.024 mmol), PhSO₂Na (**2a**, 59.4 mg, 0.33 mmol), and KI (24.9 mg, 0.15 mmol) in DMSO (0.15 mL) and AcOH (0.15 mL) was added styrene **1a** (31.2 mg, 0.3 mmol), and the mixture was stirred at 100 °C for 18 h in air. After the residue was dissolved in Et₂O, the solution was washed with sat. NaHCO₃, H₂O, and sat. NaCl and dried over anhyd MgSO₄. Chromatography on silica gel (30% Et₂O–hexane) gave phenyl (*E*)-2-phenylethenyl sulfone (**3aa**, 68.7 mg, 94%). ¹H NMR (270 MHz, CDCl₃): δ = 7.96–7.93 (m, 2 H), 7.68 (d, *J* = 15.5 Hz, 1 H), 7.58–7.30 (m, 8 H), 6.87 (d, *J* = 15.5 Hz, 1 H). ¹³C NMR (67.5 MHz, CDCl₃): δ = 142.4, 140.6,

133.3, 132.2, 131.1, 129.3, 128.9, 128.5, 127.6, 127.2. IR (CHCl₃): 3061, 3025, 1613, 1447, 1306 cm⁻¹. Anal. Calcd for $C_{14}H_{12}O_2S$: C, 68.83; H, 4.95. Found: C, 68.75; H, 5.13.

- (12) The stereochemistry of these compounds was determined by the comparison with references or authentic samples. Compounds **7cb**, **7db**, (*Z*)-**3hb**, and (*Z*)-**3ib** were prepared by oxidation of the corresponding alkenyl sulfides using MCPBA. For the preparation of alkenyl sulfides, see: Taniguchi, N. *Tetrahedron* **2009**, *65*, 2782; see ref. 15a.
- (13) Typical Procedure of β-Haloalkenyl Sulfones Using Alkynes
 - To a mixture of CuI (4.6 mg, 0.024 mmol), bpy (3.7 mg, 0.024 mmol), PhSO₂Na (**2a**, 59.4 mg, 0.33 mmol), and KBr (39.3 mg, 0.33 mmol) in AcOH (0.3 mL) was added phenylacetylene **1a** (30.6 mg, 0.3 mmol), and the mixture was stirred at 100 °C for 18 h in air. After the residue was dissolved in Et₂O, the solution was washed with sat. NaHCO₃, H₂O, and sat. NaCl and dried over anhyd MgSO₄. Chromatography on silica gel (40% Et₂O–hexane) gave (*E*)-1-phenylsulfonyl-2-bromo-2-phenylethene (**7aa**, 60.7 mg, 63%). ¹H NMR (270 MHz, CDCl₃): δ = 7.61–7.51 (m, 3 H), 7.42–7.30 (m, 7 H), 7.17 (s, 1 H). ¹³C NMR (67.5 MHz, CDCl₃): δ = 140.2, 138.7, 135.9, 134.1, 133.5, 130.4, 128.9, 128.5, 127.9, 127.7. IR (CHCl₃): 3056, 1611, 1590, 1446, 1324 cm⁻¹. Anal. Calcd for C₁₄H₁₁O₂SBr: C, 52.03; H, 3.43. Found: C, 51.42; H, 3.17.
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