

# Unique Selectivity of Iodohydroxylation Reaction of Allenyl Phenyl Sulfoxides in Aqueous MeCN. A Stereodefined Synthesis of (*E*)-2-Iodo-3-hydroxy-1-alkenyl Sulfoxides

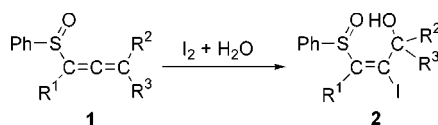
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## ABSTRACT



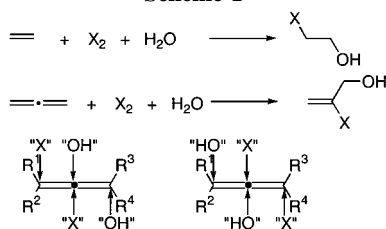
Iodohydroxylation reaction of allenyl phenyl sulfoxides with I<sub>2</sub> can smoothly proceed to generate (*E*)-2-iodo-3-hydroxy-1-alkenyl sulfoxides with excellent regio- and stereoselectivity in high or excellent yields. The configuration of *E*-2a was determined by the X-ray diffraction study.

Halohydroxylations of carbon–carbon double bond are one of the most important methods of providing  $\beta$ -halogen-substituted alcohols,<sup>1</sup> since two functional groups, i.e., -X and -OH, are introduced into substrates at the same time (Scheme 1). However, for allenes, the regio- and stereo-

the iodohydroxylation of a series of allenyl phenyl sulfoxides affording the stereodefined (*E*)-2-iodo-3-hydroxy-1-alkenyl phenyl sulfoxides in high yields.

During the course of our study on the chemistry of allenes,<sup>3</sup> we have developed the highly selective hydrohalogenation reactions of electron-deficient 1,2-allenes.<sup>4</sup> In our continuous effort toward the highly selective addition reaction of allenes, it is interesting to observe that the addition reaction of (1,2-propadienylsulfenyl)benzene (**1a**) with I<sub>2</sub> unexpectedly afforded the iodohydroxylation product (*E*)-3-(phenylsulfinyl)-2-iodopropenol (*E*-2a) with excellent regio- and stereoselectivity albeit in low yield; the formation of the corre-

Scheme 1



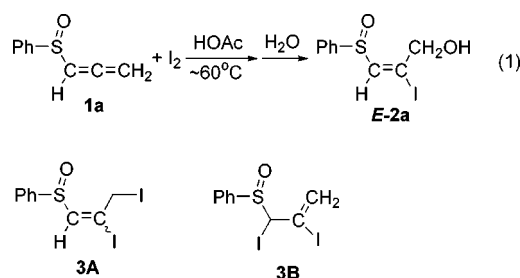
selectivity would be a formidable challenge to make this type of methodology synthetically attractive<sup>2</sup> unless a factor is introduced to control the selectivity! In this Letter, we wish to report the first protocol for such highly regio- and stereoselective chemical transformations by introducing a sulfinyl group into allenes to ensure high selectivities, i.e.,

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sponding diiodides **3A** and **3B** was not observed (Scheme 2). The structure of *E*-**2a** was unambiguously established by the X-ray diffraction study.

Scheme 2



With the unique selectivity observed for the formation of *E*-**2a**, we tried to optimize the conditions of this iodohydroxylation reaction of **1a** using iodine in  $MeCN-H_2O$  (7:1). The results are summarized in Table 1. When 2.0 equiv

**Table 1.** Reaction of (1,2-Propadienylsulfinyl)benzene (**1a**) with  $I_2/H_2O$  in Aqueous  $MeCN^a$

entry	$I_2^b$	additives	time (h)	temp ( $^\circ C$ )	yield (%) <sup>c</sup>	<b>1a</b> <sup>d</sup> (%)
1	1.0		5	rt	49	34
2	2.0		4	rt	66	0
3	2.0	$K_2CO_3$	4	rt	3.9	84
4	1.5	LiOAc	4	55	62	29
5	2.0	$NaHCO_3$	2.5	65	64	0
6	2.0	LiOAc	5	rt	69	18
7 <sup>e</sup>	2.0	LiOAc	0.2	55	60	0
8	2.4	LiOAc	1	55	96	0

<sup>a</sup> The reaction of allenic sulfoxide (**1a**, 1 mmol) with  $I_2$  was carried out in  $MeCN-H_2O$  (2 mL/0.3 mL). <sup>b</sup> Equivalents of iodine used. <sup>c</sup> Isolated yield based on **1a**. <sup>d</sup> Yield of recovered **1a**. <sup>e</sup> Only 4.0 equiv of  $H_2O$  used.

of iodine was used, the reaction was complete in aqueous  $MeCN$  within 4 h to afford the product *E*-**2a** in 66% yield (entry 2, Table 1) together with some byproducts of low polarity. Since the iodohydroxylation product (*E*-**2a**) and HI were formed at the same time, and allenyl phenyl sulfoxides are sensitive to even a small amount of strong acids (such

as  $HX$ ),<sup>5</sup> bases were added to neutralize the in situ generated HI. The result with  $K_2CO_3$  was not satisfactory (entry 3, Table 1). After trial and error, we found that LiOAc showed the best result with the exclusive formation of *E*-**2a** in 69% at rt, but 18% of starting material was recovered (entry 6, Table 1). When the reaction was heated to  $55^\circ C$  using 2.0 equiv of  $I_2$ , *E*-**2a** was formed in 96% yield within 1 h (entry 8, Table 1). The reaction did not go to completion with 1.5 equiv of  $I_2$  even after 4 h at  $55^\circ C$  (entry 4, Table 1). In addition, the utilization of 4.0 equiv of water accelerated the reaction but the yield was lower (entry 7, Table 1).

Thus, we studied the iodohydroxylation of a series of allenyl phenyl sulfoxides. Some typical results are summarized in Table 2. The following points are noteworthy:

**Table 2.** The Reaction of Allenyl Phenyl Sulfoxides with  $I_2/H_2O$  in Aqueous  $MeCN^a$

entry	$R^1$	$R^2$	$R^3$	$I_2^c$	time (h)	yield (%) <sup>d</sup>
1 <sup>b</sup>	H	H	H ( <b>1a</b> )	2.4	1	96
2	Ph	H	H ( <b>1b</b> )	1.6	2.2	79
3	<i>n</i> -Bu	H	H ( <b>1c</b> )	1.6	1.5	82
4	H	H	<i>t</i> -Bu ( <b>1d</b> )	1.2	3.2	87
5	H	Me	Me ( <b>1e</b> )	1.2	0.5	87
6	H		$(CH_2)_5$ ( <b>1f</b> )	1.2	0.3	74
7	<i>n</i> -Bu	Me	Me ( <b>1g</b> )	1.2	1.3	88

<sup>a</sup> The reaction was carried out using allenyl phenyl sulfoxide (0.5 mmol),  $I_2$  (see Table 2), and LiOAc (1 mmol) in  $MeCN-H_2O$  (1 mL, v/v = 7:1) at room temperature. <sup>b</sup> The reaction was carried out at  $55^\circ C$ . <sup>c</sup> Equivalents of iodine used. <sup>d</sup> Isolated yield of *E*-**2** based on **1**.

(1) The iodohydroxylation reactions of *C*-aryl- or *C*-alkyl-substituted allenyl phenyl sulfoxides were faster than that of the unsubstituted **1a**, and the reactions finished in from 0.3 to 3.2 h at room temperature (compare entries 2–7 with 1, Table 2). (2) The yields of the corresponding products **2** are high yields and the regio- and stereoselectivity of this reaction are excellent. (3) When **1d** with a de ratio of 93:7 was used the corresponding iodohydroxylation product *E*-**2d** was formed in the same diastereomeric ratio as determined by  $^1H$  NMR spectra and HPLC (entry 4, Table 2).

Generally the iodohydroxylation of carbon–carbon double bond directly using  $I_2$  and  $H_2O$  is difficult.<sup>6</sup> Reaction of allenes or 2,3-allenic esters with halogens was known to form

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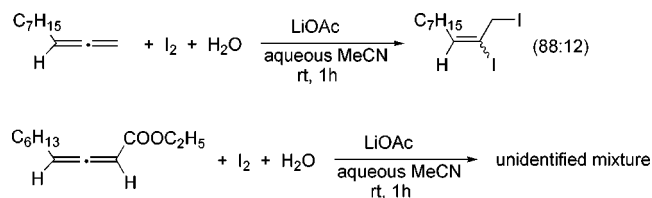
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dihalogenation products.<sup>7</sup> Even under our reaction conditions, the diiodination product 1,2-diiodo-2-decene with a configurationally isomeric ratio of 88:12 was formed (Scheme 3). The introduction of the sulfinyl group must be the key for the control of selectivities.

Scheme 3



In conclusion, we have observed the unique regio- and stereoselectivity in the iodohydroxylation reaction of allenyl phenyl sulfoxides, which provides an efficient entry to (*E*)-2-iodo-3-hydroxy-1-alkenyl sulfoxides. Because of the easy availability of the starting materials,<sup>8</sup> simple/convenient

operation, and ready elaboration of the functional groups in the products,<sup>9</sup> the reaction shows its broad utility in organic synthesis. In addition, with different nucleophiles and a search for different groups which are capable of controlling the pertinent selectivities, this protocol will open up a new area for the highly selective synthesis of functionalized stereodefined alkenes. Further studies on the scope, the mechanism of iodohydroxylation of 1,2-allenic sulfoxides, and the synthetic applications of this reaction are being carried out in our laboratory.

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**Supporting Information Available:** Typical experimental procedure and analytical data for all the products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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