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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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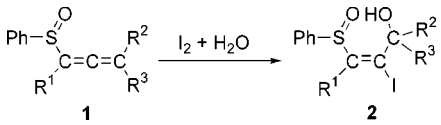
ABSTRACT



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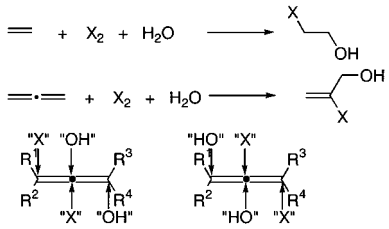
Iodohydroxylation reaction of allenyl phenyl sulfoxides with I_2 can smoothly proceed to generate (*E*)-2-iodo-3-hydroxy-1-alkenyl sulfoxides with excellent regio- and stereoselectivity in high or excellent yields. The configuration of *E*-2a was determined by the X-ray diffraction study.

Halohydroxylations of carbon−carbon double bond are one of the most important methods of providing β-halogen-substituted alcohols,[1] 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 stereoselectivity would be a formidable challenge to make this type of methodology synthetically attractive[2] *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., the iodohydroxylation of a series of allenyl phenyl sulfoxides affording the stereodefined (*E*)-2-iodo-3-hydroxy-1-alkenyl phenyl sulfoxides in high yields.

Scheme 1



During the course of our study on the chemisty of allenes,[3] we have developed the highly selective hydrohalogenation reactions of electron-deficient 1,2-allenes.[4] In our continuous effort toward the highly selective addition reaction of allenes, it is interesting to observe that the addition reaction of (1,2-propadienylsulfinyl)benzene (**1a**) with I_2 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-

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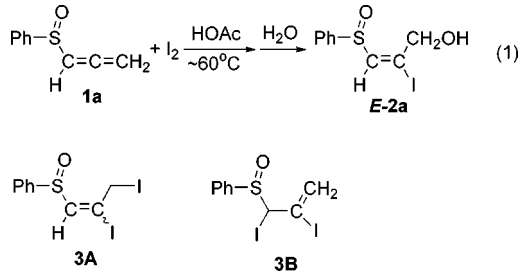
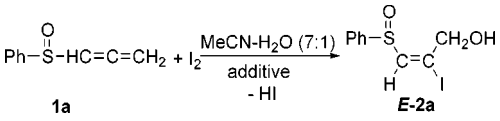
sponding diiodides **3A** and **3B** was not observed (Scheme 2). The structure of *E*-**2a** was unambiguously established by the X-ray diffraction study.

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 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),[5] 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 °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 °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).

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

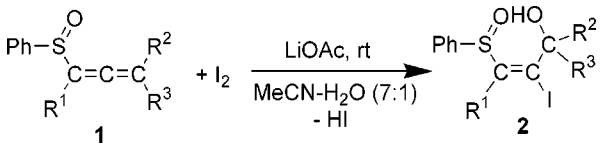


entry	I_2[b]	additives	time (h)	temp (°C)	yield (%)[c]	**1a**[d] (%)
1	1.0		5	rt	49	34
2	2.0		4	rt	66	0
3	2.0	K_2CO_3	4	rt	3.9	84
4	1.5	LiOAc	4	55	62	29
5	2.0	$NaHCO_3$	2.5	65	64	0
6	2.0	LiOAc	5	rt	69	18
7[e]	2.0	LiOAc	0.2	55	60	0
8	**2.4**	**LiOAc**	**1**	**55**	**96**	**0**

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

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]



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

[a] 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. [b] The reaction was carried out at 55 °C. [c] Equivakents of iodine used. [d] 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.[6] Reaction of allenes or 2,3-allenic esters with halogens was known to form

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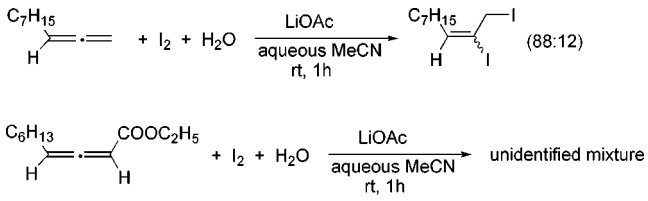
dihalogenation products.[7] Even under our reaction conditions, the diiodination product 1,2-diiodo-2-decene with a configurationally isomeric ratio of 88:12 was formed (Scheme 3). The introduction of the sulfinyl group must be the key for the control of selectivities.

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,[8] simple/convenient operation, and ready elaboration of the functional groups in the products,[9] 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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