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Reversed Stereoselectivity in Iodohydroxylation of Allenyl Sulfides. An Efficient Synthesis of (*Z*)-3-Organosulfur-2-iodo-2-propenols

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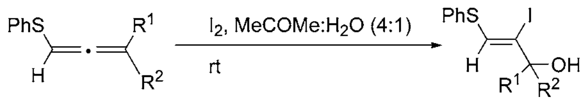
ABSTRACT



It is observed that the iodohydroxylation of 1,2-allenyl sulfides with I$_2$ and water in aqueous acetone showed *Z*-selectivity, which is opposite to that of the iodohydroxylation of 1,2-allenyl sulfoxides.

Allenes show unique reactivities in organic synthesis due to the presence of the cumulated C═C double bonds.[1] Recently, much attention has been paid to their reactivities.[2,3] On the other hand, addition reactions of a carbon−carbon multiple bond are synthetically attractive since two functional groups are introduced at the same time.[4] However, reports on the addition reaction of allenes[5] are limited due to the difficulty in controlling the regio- and stereoselectivity. Recently, we observed that (1) the regioselectivity of hydrohalogenation reaction of electron-deficient allenes leading to β,γ-unsaturated functionalized alkenes is controlled by the electronic effect of the electron-withdrawing group[6] and (2) the iodohydroxylation reaction of 1,2-allenyl sulfoxides exhibits excellent regio- and *E*-stereoselectivity.[7] In this paper, we

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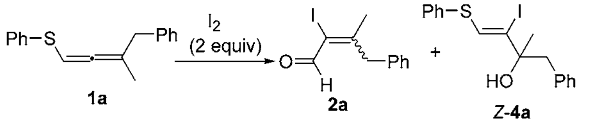
report our recent results of highly stereoselective iodohydroxylation of 1,2-allenyl sulfides.

The starting sulfides used in this study were prepared via the reduction of 1,2-allenyl sulfoxides, which are easily available from the reaction of progarylic alcohols with PhSCl. We started this research with the iodohydroxylation of 3-benzyl-1,2-butadienyl phenyl sulfide (**1a**) with I_2 and H_2O. Some typical results are summarized in Table 1. When we performed the iodohydroxylation under the same reaction conditions for 1,2-allenyl sulfoxides,[7] only a *Z*/*E* mixture of 2-iodo-2-propenal **2a** was obtained (entries 1 and 2, Table 1). The configuration of the C=C bond in **2a** was determined by the NOE study. This product must be formed via the 2,1-iodohydroxylation intermediate **3a** (path a, Scheme 1).

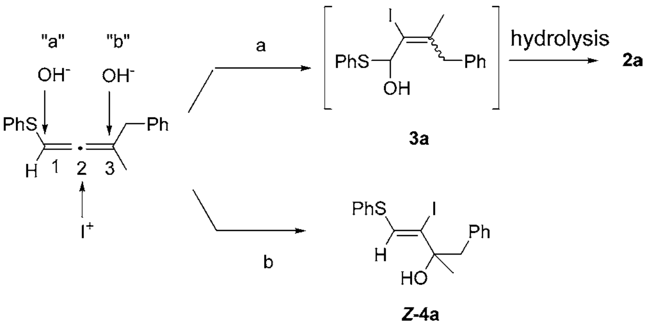
Table 1. Iodohydroxylation of 1,2-Butadienyl Phenyl Sulfide (**1a**)



entry	solvent	time (h)	*T* (°C)	yield of **2a** (*E*/*Z*)[a]	yield of (*Z*)-**4a** (%) (*Z*/*E*)[a]
1	$CH_3CN/H_2O = 4{:}1$	16	15	30 (1.08:1)	0
2	$CH_3CN/H_2O = 4{:}1$	16	28	16 (0.32/1)	0
3	acetone/$H_2O = 2{:}1$	10	0	8 (1.07/1)	50 (>99:1)
4[b]	acetone/$H_2O = 2{:}1$	10	0	22 (1.28/1)[c]	62 (>99:1)
5	acetone/$H_2O = 4{:}1$	11	15	16 (1.40/1)[c]	66 (>99:1)
6	acetone/$H_2O = 4{:}1$	13	28	16 (1.09/1)	68 (>99:1)
7	acetone/$H_2O = 2{:}1$	10.5	15	12 (1.07/1)	66 (>99:1)

[a] Isolated yield with the *Z*/*E* ratio determined by ^1H NMR spectra unless otherwise stated. [b] 4 equiv of I_2 was used. [c] The ratio was determined by isolation.

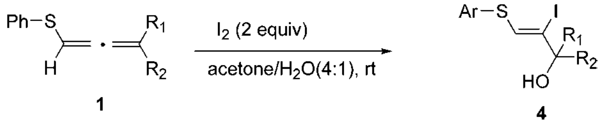
Scheme 1



However, it is interesting to observe that when the reaction was carried out in aqueous acetone the regioselectivity was reversed to a fairly high extent leading to the formation of synthetically useful 2,3-iodohydroxylation product *Z*-**4a** in 50% together with a 8% yield of **2a** (entry 3, Table 1). The best results in terms of the yield of Z-**4a** was obtained at room temperature in acetone/H_2O (4:1) (entry 6, Table 1).

Some typical results of the *Z*-iodohydroxylation of 1,2-allenyl sulfides are summarized in Table 2. It is obvious that the yields are from moderate to high with an excellent *Z*-selectivity, and both 3-mono- and 3,3-disubstituted allenyl sulfides reacted smoothly with I_2 in aqueous acetone. The stereoselectivity of this reaction was determined by the NOE experiment of (*Z*)-**4d** and the oxidation of (*Z*)-**4d** with *m*-CPBA in CH_2Cl_2 or H_2O_2 in HOAc to the corresponding sulfoxide (*Z*)-**5d** (Scheme 2).[7] It is obvious that the stereoselectivity is completely opposite to the results for the corresponding sulfoxides.[7]

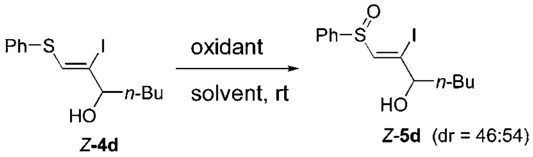
Table 2. Iodohydroxylation of 1,2-Allenyl Sulfides



entry	**1** R¹	**1** R²	time (h)	yield of **4**[a] (%)	*Z*/*E*
1	H	CH_3 (**1b**)	9	61 (**4b**)	97/3
2	H	*i*-Pr (**1c**)	10	56 (**4c**)	96/4
3	H	*n*-C_4H_9 (**1d**)	13.5	74 (**4d**)[b]	98/2
4	H	*n*-C_7H_{15} (**1e**)	9.5	67 (**4e**)[c]	96/4
5	H	Bn (**1f**)	9.5	65 (**4f**)[d]	96/4
6	CH_3	CH_3 (**1g**)	10.5	63 (**4g**)	94/6
7	CH_3	C_2H_5 (**1h**)	10	94 (**4h**)	94/6
8	CH_3	*i*-Bu(**1i**)	12	53 (**4i**)[e]	99/1
9	CH_3	*t*-C_4H_9 (**1j**)	9	85 (**4j**)	97/3
10	C_2H_5	C_2H_5 (**1k**)	8	72 (**4k**)	98/2
11	*n*-C_4H_9	*n*-C_4H_9(**1l**)	10	93 (**4l**)	95/5
12	*n*-C_5H_{11}	*n*-C_5H_{11}(**1m**)	10	80 (**4m**)	97/3

[a] Unless otherwise stated, the corresponding aldehyde **2** was isolated in a trace amount. [b] 14% of **2d** was isolated. [c] 18% of **2e** was isolated. [d] 18% of **2f** was isolated. [e] 14% of **2i** was isolated.

Scheme 2



oxidant	solvent	time (h)	yield of **5d** (%)
m-CPBA(1.1 equiv)	CH_2Cl_2	4	69
H_2O_2(4 equiv)	HOAC	36	71

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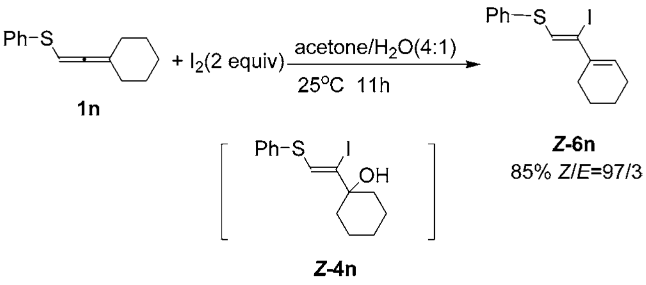
When we used **1n** as the starting allenyl sulfide, (*Z*)-1-(1′-cyclohexenyl)-1-iodo-2-(phenylsulfanyl)ethene **6n** was obtained via the dehydration of the iodohydroxylation product (*Z*)-**4n** (Scheme 3).

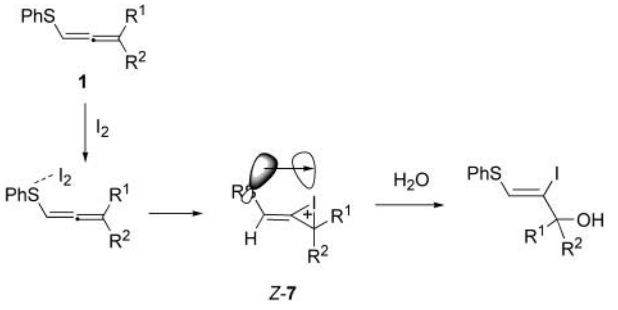
Scheme 3



It can be assumed that the lone electron pair of sulfur atom would interact with I_2 to form a molecular complex.[8] Intramolecular electrophilic delivery of I_2 to the C═C bond remote from the S group would form intermediate (*Z*)-**7**. Upon hydrolysis, the reaction affords (*Z*)-**4**. The regioselectivity may be attributed to the steric and electronic effect of R^1, R^2, and thiophenyl in the starting allenyl sulfides. The strong soft Lewis acid and base interaction between the positively charged iodine atom and S[9] in (*Z*)-**7** may be responsible for the stereoselectivity of this reaction (Scheme 4).

In conclusion, we have developed a highly regio- and stereoselective addition reaction of 1,2-allenyl sulfides with I_2 and H_2O. The *Z*-stereoselectivity for these reactions may be explained by the soft Lewis base and acid interaction between the sulfur atom and the positively charged iodine atom. The regioselectivity in these reactions may be controlled by the steric and electronic effects of substituents at the two terminals of allenes. Although the real nature controlling the stereoselectivity needs further attention, this reaction provides an efficient route to the Z-isomer of 3-organosulfur-2-iodo-2-propenols and may open up a new area for the control of selectivity in addition reactions of allenes. The scope of this reaction, the real nature of the *Z*-stereoselectivity, and the synthetic application of these reactions are currently being carried out in our laboratory.

Scheme 4



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

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