

Control of regio- and stereoselectivity in electrophilic addition reactions of allenes*

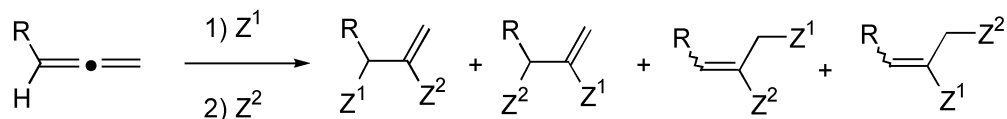
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Abstract: The halohydroxylation reaction of 1,2-allenyl sulfoxides exhibits *E*-selectivity while those of analogous sulfides and selenides show *Z*-selectivity. Rationales for the stereoselectivities are proposed. The reaction of 2,3-allenols with X⁺ affords 3-halo-2,5-dihydrofurans or 3-halo-3-enals depending on the nature of the alcohols.

Keywords: allenes; selectivity; electrophilic addition; halohydroxylation; 1,2-shift.

Allenes are a class of compounds with unique reactivity [1]. Recently, we have observed nice reactivity as well as selectivity in transition metal-catalyzed or -mediated reaction of functionalized allenes [2,3]. On the other hand, the electrophilic addition reaction of allenes [4,5], which introduces two functionalities within one operation, would be synthetically attractive if the issues of regio- and stereoselectivity can be properly addressed (Scheme 1).

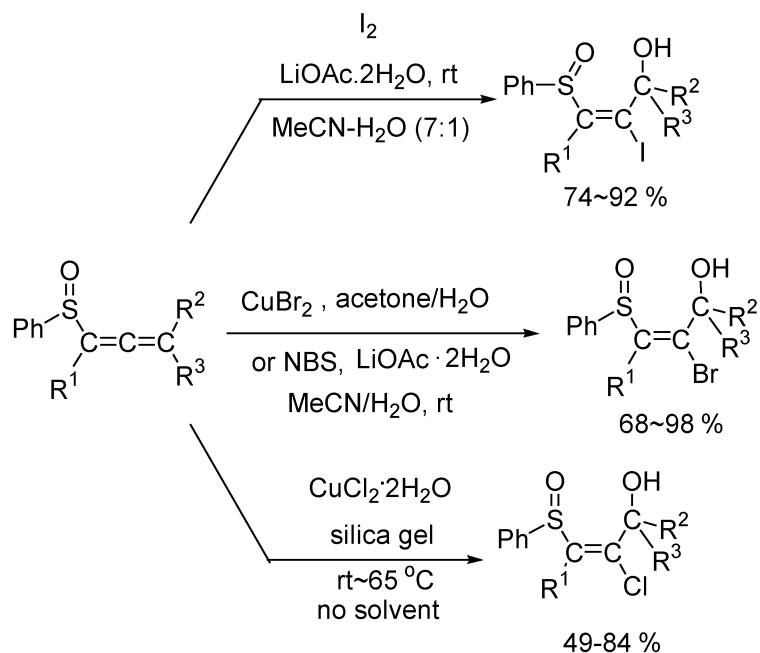


Z¹ = reagent No. 1, Z² = reagent No. 2

Scheme 1

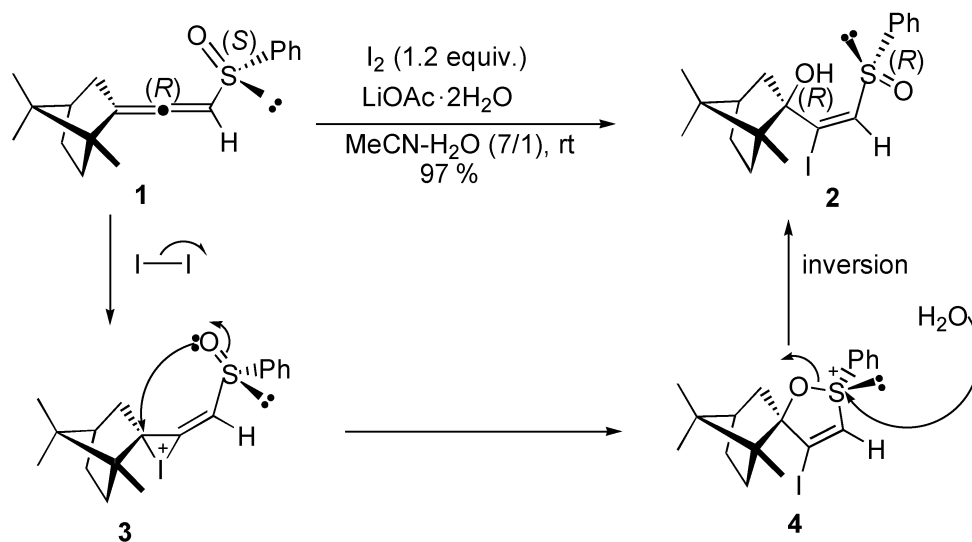
In 2000, we observed a highly regio- and stereoselective halohydroxylation of 1,2-allenyl sulfoxides with X⁺ and water. The reaction shows excellent regioselectivity with the X attacks on the middle carbon atom while the OH group connects to the terminal carbon atom of the allene moiety remote from the sulfinyl group and *E*-stereoselectivity. With I₂, CuBr₂, NBS, or CuCl₂, the iodo-, bromo-, or chloro-analogs can be prepared in high yields within a couple of hours (Scheme 2) [5].

*Paper based on a presentation at the 16th International Conference on Organic Synthesis (ICOS-16), 11–15 June 2006, Mérida, Yucatán, México. Other presentations are published in this issue, pp. 153–291.



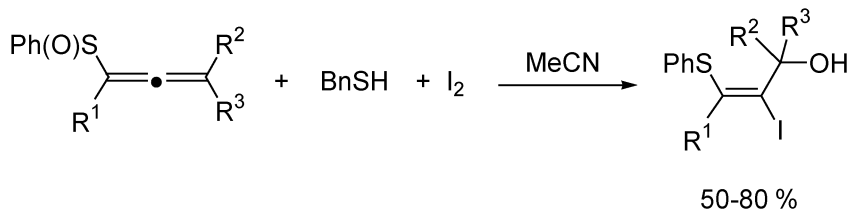
Scheme 2

By examining the stereochemical information of both the optically active starting material **1** and the corresponding product **2**, it was observed that the absolute configuration of the sulfur atom was inverted after the reaction. Thus, a rationale involving the cyclic intermediates **3** and **4** for this transformation was proposed as shown in Scheme 3 [6]. The regioselectivity was determined by the interaction of I_2 with the relatively electron-rich C–C double bond while the stereoselectivity may be explained by the intermediacy of **4** (Scheme 3).



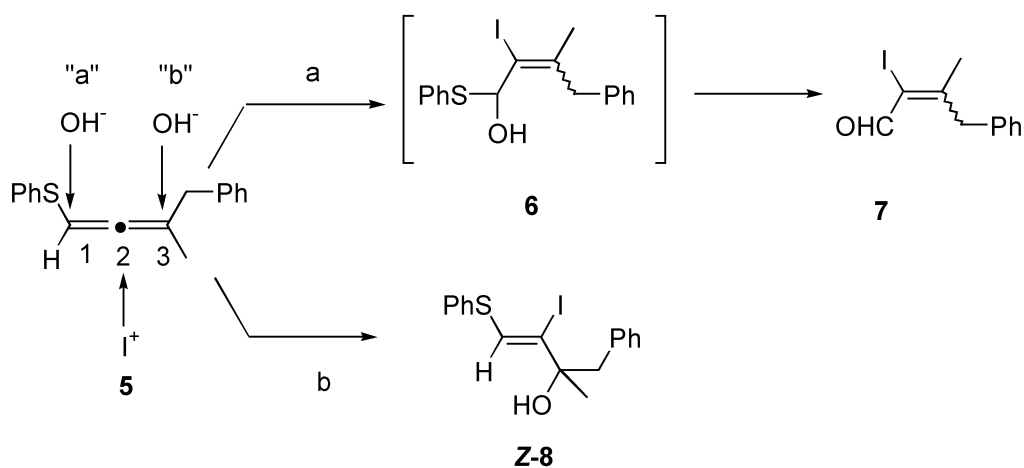
Scheme 3

In the presence of BnSH, the iodohydroxylation of 1,2-allenyl sulfoxides afforded 3-hydroxy-2-iodo-2(*E*)-alkenyl sulfides (Scheme 4) [7]. In this reaction, the sulfoxide functionality was reduced to sulfide. The oxygen atom in the sulfoxide functionality may form the hydroxyl group with BnSH being converted to BnSSBn.



Scheme 4

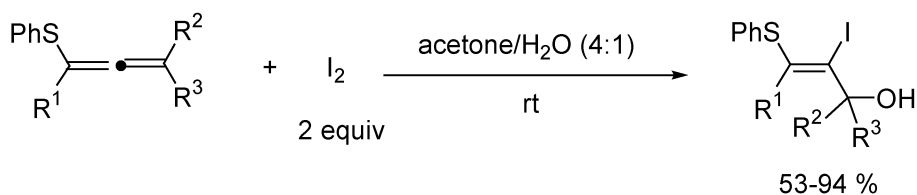
Furthermore, the halohydroxylation of 1,2-allenyl sulfide **5** with I_2 in aqueous MeCN afforded 2-iodo-3-methyl-4-phenyl-2-butenal **7** in 30 % with a *E/Z* ratio of 1.08:1 as the identified product. This product was formed via the iodohydroxylation of the C–C double bond connected with PhS. Further screening led to the observation of a dramatic solvent effect, i.e., the reaction in aqueous acetone afforded the expected iodohydroxylation product *Z*-**8** in 66 % yield together with a 12 % yield of aldehyde **7**. It should be noted that the C–C double bond in product **8** is in *Z*-configuration (Scheme 5).



Solvent	time (h)	7 (<i>E/Z</i>)	8 (<i>Z/E</i>)
MeCN:H ₂ O (4:1)	16	30 (1.08:1)	0
Acetone:H ₂ O (2:1)	10.5	12 (1.07:1)	66 (>99:1)

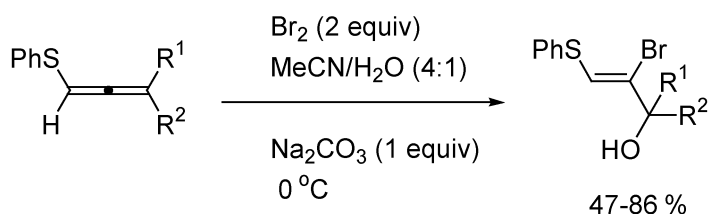
Scheme 5

Under these reaction conditions, differently substituted 1,2-allenyl sulfides afforded 2-iodo-3-hydroxy-1(*Z*)-alkenyl phenyl sulfides in good yields highly stereoselectively (Scheme 6) [8].



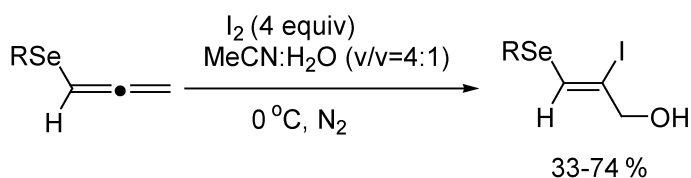
Scheme 6

The corresponding bromohydroxylation can be accomplished in aqueous MeCN (MeCN:H₂O = 4:1) in the presence of Na₂CO₃ (1 equiv) (Scheme 7) [9].



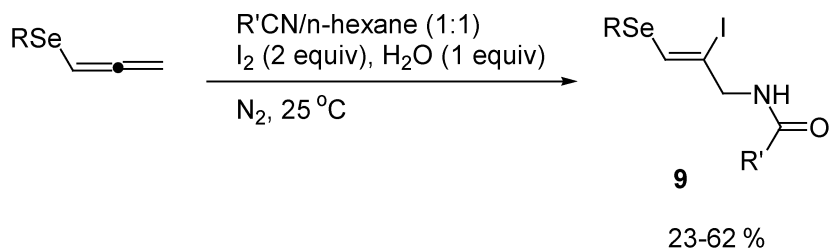
Scheme 7

Under similar reaction conditions, this reaction can be extended to the iodohydroxylation of 1,2-allenyl selenides (Scheme 8) [10].



Scheme 8

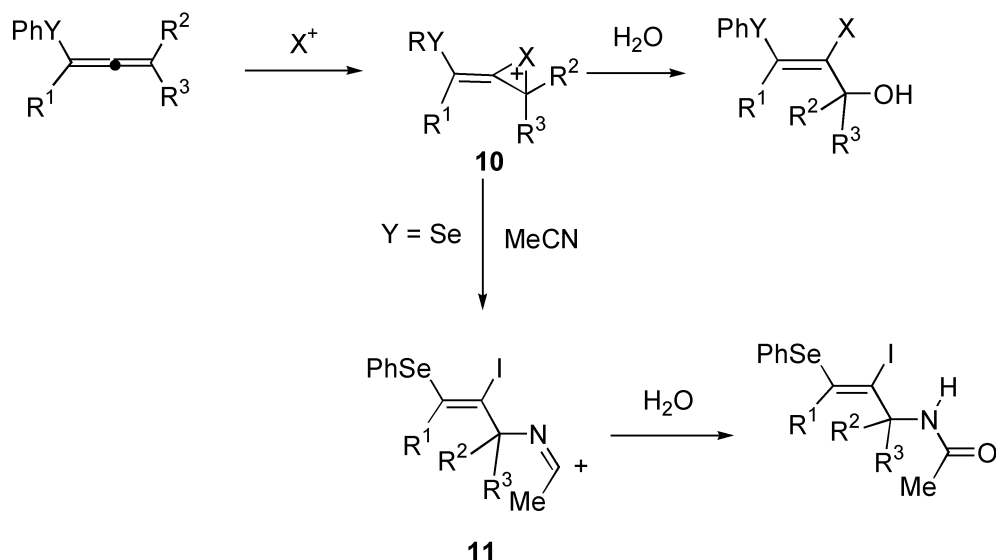
Using MeCN/hexane (1:1) as the solvent and a limited amount of H₂O, MeCN may participate in the reaction to afford the four-component reaction products *N*-(2(*Z*)-iodo-3-seleno)-2-propenyl amides **9** (Scheme 9) [10].



Scheme 9

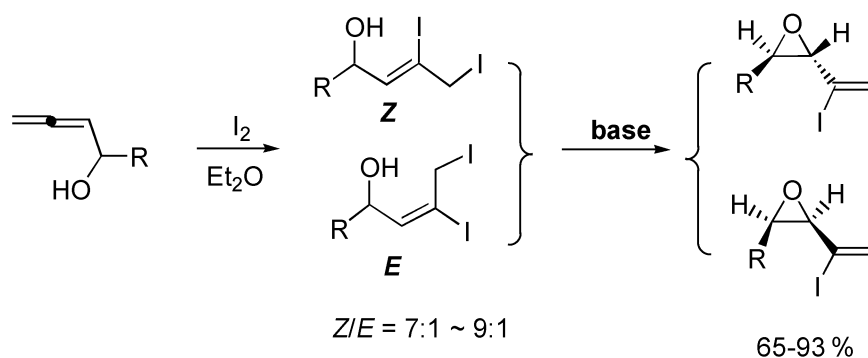
The soft Lewis acid–base interaction between X⁺ and S or Se may determine the *Z*-stereoselectivity observed in the halohydroxylation of 1,2-allenyl sulfides and selenides. In the presence of a lim-

ited amount of water, the intermediate **10** would react with MeCN first, followed by the reaction with water to afford amides (Scheme 10).



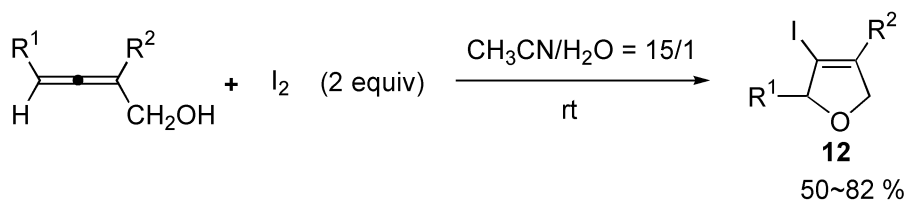
Scheme 10

In 1993, Friesen et al. reported that the electrophilic addition reaction of 2,3-allenols with I_2 afforded an *E/Z* mixture of 4-hydroxy-2-iodo-2(*Z*)-alkenyl iodides, which upon treatment with a base afforded 1-iodovinyl epoxides (Scheme 11) [11].



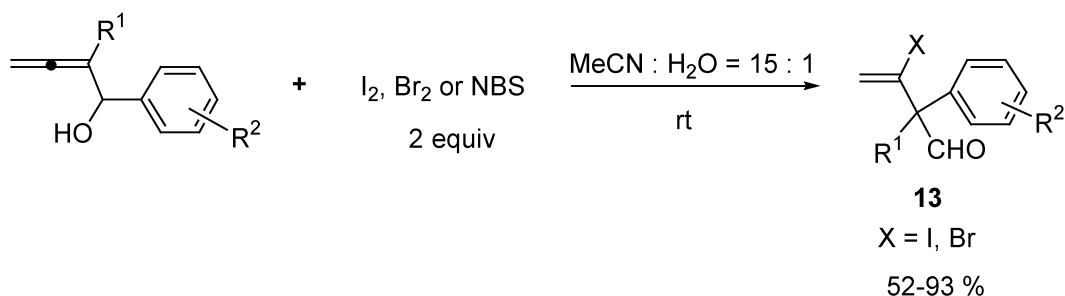
Scheme 11

Based on the above results, we showed strong interest in using the established procedure to control the selectivity of electrophilic addition of 2,3-allenols with X^+ . In fact, when primary 2,3-allenols were treated with I_2 , 3-iodo-2,5-dihydrofurans **12** were formed in 50~82 % yields in aqueous MeCN (Scheme 12).



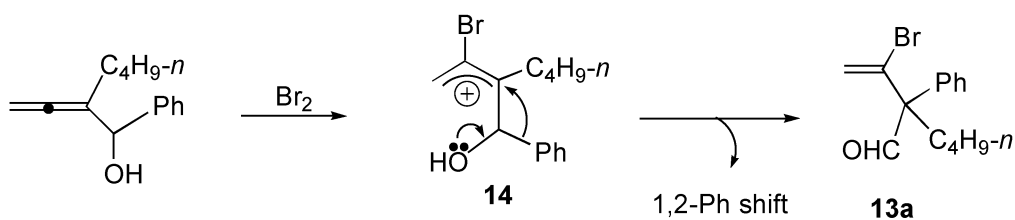
Scheme 12

However, when 1-aryl-2,3-allenols were applied under the same reaction conditions, instead of forming the corresponding 5-membered products, 2-aryl-3-halo-3-alkenals **13** were formed in high yields cleanly when R^2 is H or an electron-donating group (Scheme 13) [12]. Owing to the fact that one C–C double bond remained after reaction may also easily interact with Br_2 , the yields of aldehydes **13** ($\text{X} = \text{Br}$) are higher with NBS.



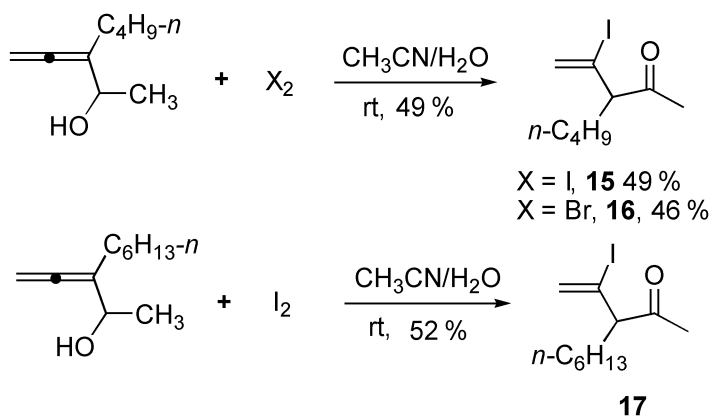
Scheme 13

The aldehyde **13a** may be formed by the 1,2-phenyl shift reaction of cationic 2-bromo- π -allylic intermediate **14** (Scheme 14).



Scheme 14

It is interesting to observe that the corresponding reaction of 3-alkyl-3,4-pentadien-2-ols with I_2 or Br_2 afforded 4-halo-4-en-2-ones **15–17**, which must be formed by the 1,2-H shift of **14**-type intermediates (Scheme 15) [12].



Scheme 15

In conclusion, the regio- and stereoselectivity of electrophilic addition reactions of allenes with a functionality of sulfoxide, sulfide, or selenide depend largely on the reaction conditions applied and the nature of these functionalities. Reaction products of I_2 , Br_2 , or NBS with 2,3-allenols are determined by the substituent of the carbon atom connected with the hydroxyl group. Further studies are required to reveal the real mechanism of these reactions.

ACKNOWLEDGMENTS

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