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Tetrahedron Letters 45 (2004) 6063–6065
Tetrahedron Letters

Convenient stereoselective synthesis of 3-hydroxy-2-iodo-2(*E*)-alkenyl sulfides via iodohydroxylation of 1,2-allenyl sulfoxides in the presence of BnSH

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Received 29 March 2004; revised 21 May 2004; accepted 26 May 2004

Abstract—The iodohydroxylation of 1,2-allenyl sulfoxides with I_2 in the presence of BnSH affords 3-hydroxy-2-iodo-2(*E*)-alkenyl sulfides in good yields and selectivities. The stereochemistry for the products of this transformation is opposite to what was obtained from the iodohydroxylation of 1,2-allenyl sulfides. Based on the results of some control experiment, a mechanism was proposed.

The electrophilic or nucleophilic addition reaction of allenes is versatile providing that the regio- and stereoselectivity can be addressed since two functionalities can be introduced into the final products in one 'operation'. Recently, we have demonstrated the regioselective nucleophilic addition of electron-deficient allenes.[1] Quite recently we also observed the regio- and stereoselective halohydroxylation reaction of 1,2-allenyl sulfoxides,[2] sulfides[3] and selenides.[4] In these reactions, the presence of sulfinyl group or organosulfur/selenium group is important for the unique stereoselectivity of the halohydroxylation reaction. In this paper we wish to report our recent observation on the iodohydroxylation of the readily available 1,2-allenyl sulfoxides *in the presence of benzyl thiol* affording 3-hydroxy-2-iodo-2(*E*)-alkenyl sulfides, the C=C bond configuration of which is opposite to what was synthesised via the iodohydroxylation of 1,2-allenyl sulfides.[3]

We initiated this study with the notion that the cyclic intermediate **2**[2] involved in the electrophilic *E*-halohydroxylation of 1,2-allenyl sulfoxides may react with nucleophiles to produce **3**-type products with the stereoselectivity defined by the participation of the sulfoxide functionality (Scheme 1).[2,5]

As a first try, we treated 1,2-propadienyl phenyl sulfoxide **1a**[6] with benzyl thiol and I_2 in *anhydrous* MeCN. Some typical results are summarised in Table 1. It is a surprise for us that with 1.2 equiv of I_2 and 1 equiv of BnSH, besides the iodohydroxylation product **5a**, *E*-3-phenylthio-2-iodopropenol **4a** was isolated in 37% yield with an *E*/*Z* ratio of 96/4 as the major product (Table 1, entry 1). The formation of **3**-type product (Nu = SBn) was not observed. In the absence of BnSH the reaction in MeCN afforded *E*-**5a** as the major product (Table 1, entry 2).[2] After some screening it was clear that *E*-**4a** can be formed in 50% yield with 1.5 equiv of I_2 and 1 equiv of BnSH (Table 1, entry 3). The stereochemistry of *E*-**4a** was determined by the NOE study and comparison with the authentic sample of the *Z*-isomer.[3]

In order to see the generality of this interesting transformation, some differently substituted 1,2-alkadienyl sulfoxides[6] were prepared and the corresponding reaction with I_2 in the presence of 1 equiv of BnSH were studied. Some typical results are shown in Table 2. From Table 2, the following points should be noted: (1) the reaction is general since it proceeded well with unsubstituted 3-mono, 3,3-disubstituted and 1,3,3-trisubstituted 1,2-alkadienyl sulfoxides; (2) the

Keywords: Allenes; Sulfoxides; Iodohydroxylation.
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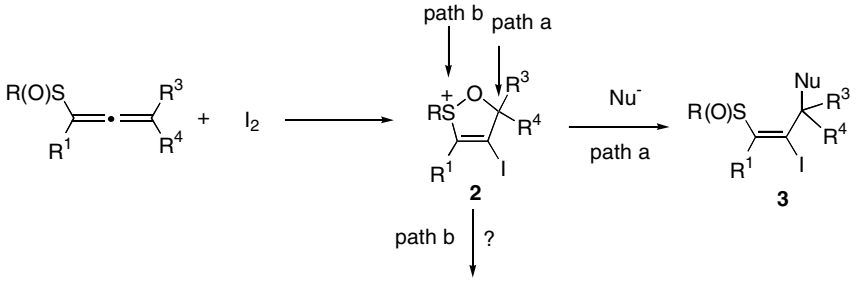
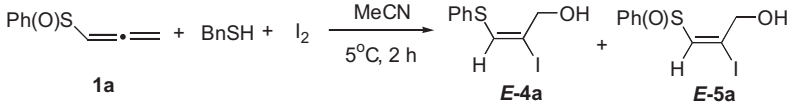
0040-4039/$ - see front matter © 2004 Published by Elsevier Ltd.
doi:10.1016/j.tetlet.2004.05.160



Scheme 1.

Table 1. The reaction of propadienyl sulfoxide **1a** with I_2 in the presence of BnSH



1a ***E*-4a** ***E*-5a**

Entry	I_2 (equiv)	$PhCH_2SH$ (equiv)	Yield of **4a** (%)	E/Z	Yield of *E*-**5a** (%)[a]
1	1.2	1	37	96/4	3
2	1.5	0	14	96/4	58
3	1.5	1	50	94/6	3
4	2	1	42	80/20	5
5[b]	0	1	0	0	0
6	1.5	0.5	38	74/26	43
7	1.5	1.2	32	80/20	3
8	1.5	0.75	55	60/40	6
9	1.5	2	19	99/1	1
10[c]	1.5	BnSSBn	35	99/1	33

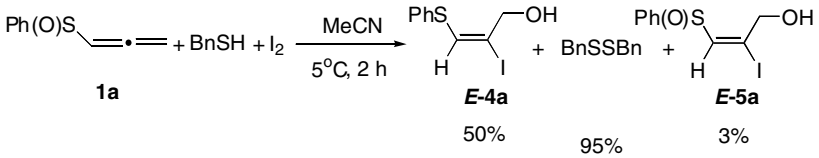
[a] Isolated yield.
[b] The reaction was conducted at 15 °C.
[c] No BnSH was added. **1a** was recovered in 21% yield.

stereoselectivity for the formation of *E*-**4** is high with the E/Z ratio ranging from 94/6 ~ 99/1; (3) the reaction is very fast even at −40 °C (Table 2, entries 4–9).

This method provides a complimentary method for the stereoselective synthesis of both isomers of 3-phenylthio-2-iodo-2-alkenols.[8] In order to study the mechanism we tried to look for the product derivated from BnSH. Actually, we isolated BuSSBu as a light yellow solid in 95% yield after the reaction.

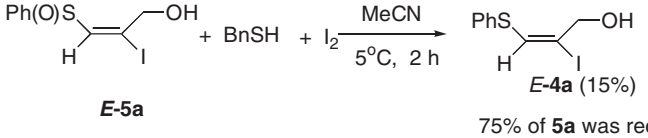
Although the reduction of sulfoxides by thiols is known,[9] only 15% of *E*-**4a** was obtained with 75% of *E*-**5a** recovered when *E*-**5a** and I_2 were treated under a set of similar condition, indicating that *E*-**4a** was not formed from the in situ reduction of **5a** (Eq. 2).

Thus, a rationale for this transformation was proposed (Scheme 2). The reaction of the cyclic intermediate **2** (R = Ph) with BnSH afforded cationic allylic alcohol **6**, which would lead to the formation of the final sulfide **4** and BnS^+. The reaction of BnS^+ with BnSH would form BnSSBn.[10] Control experiments show that BnSSBn can also induce this transformation, however, sulfide *E*-**4a** and sulfoxide *E*-**5a** were formed in a ratio of 1:1 indicating that the in situ formed BnSSBn is, at least, not the



1a ***E*-4a** ***E*-5a**
50% 95% 3%

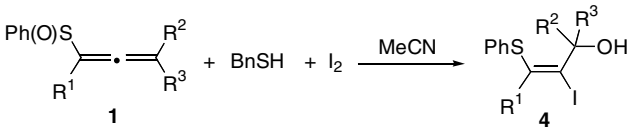
(1)



***E*-5a** ***E*-4a** (15%)
75% of **5a** was recovered

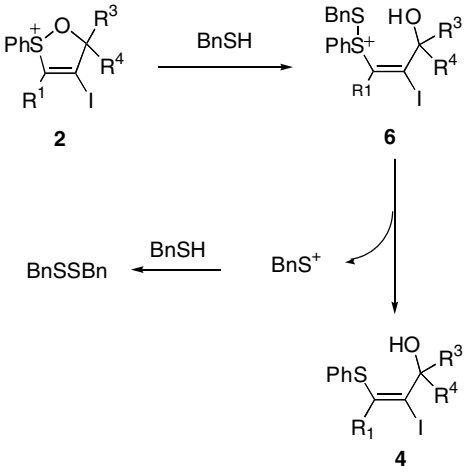
(2)

Table 2. Synthesis of 3-hydroxy-2-iodo-2(*E*)-alkenyl sulfides[7]



Entry	1			I_2 (equiv)	Condition[a]	Temp (°C)	Time (h)	Yield of 4[b] (%)	*E*/*Z* of 4
	R^1	R^2	R^3						
1	H	H	H	1.5	A	5	2	50 (**4a**)	94/6
2	H	H	*n*-C_4H_9	1.5	B	−20	0.5	65 (**4b**)	95/5
3	H	H	*n*-C_7H_{15}	1.5	B	−20	1.5	67 (**4c**)	96/4
4	H	CH_3	CH_3	1.2	B	−40	0.2	74 (**4d**)	94/6
5	H	Et	C_2H_5	1.2	B	−40	0.3	78 (**4e**)	94/6
6	H	Et	Ph	1.2	B	−40	0.25	59 (**4f**)	99/1
7	H	CH_3	*i*-C_4H_9	1.2	B	−40	0.3	72 (**4g**)	98/2
8	H	$(CH_2)_5$		1.2	B	−40	0.15	79 (**4h**)	99/1
9	*n*-C_4H_9	CH_3	CH_3	1.2	B	−40	0.3	79 (**4i**)	99/1
10	H	H	*i*-C_3H_7	1.5	B	−20	0.8	80 (**4j**)	97/3

[a] Condition A: A solution of **1** (0.5 mmol) in *anhydrous* MeCN (4 mL) was treated with I_2 (190.5 mg, solid) for 5 min followed by the addition of solution of BnSH (0.5 mmol) in MeCN (2 mL) with stirring; condition B: to a solution of **1** (0.4 mmol) and BnSH (0.4 mmol) in *anhydrous* MeCN (3.6 mL) was added a solution of I_2 (0.48 mmol) in anhydrous MeCN (2.4 mL).
[b] Isolated yield.



Scheme 2.

main reagent responsible for this transformation (Table 1, entry 10).

In conclusion, an interesting *E*-iodohydroxylation of 1,2-allenyl sulfoxides leading to 3-hydroxy-2-iodo-2(*E*)-alkenyl sulfides was observed. Although the real mechanism needs further attention, this study may open up a new area for the highly selective halohydroxylation of heteroatom-substituted allenes. Further studies in this area are being pursued in our laboratory.

Acknowledgements

Financial supports from the National Natural Science Foundation of China, the Major State Basic Research Development Program (Grant No. G2000077500), and Cheung Kong Scholar Programme are greatly appreciated. S.M. is jointly appointed by Zhejiang University and Shanghai Institute of Organic Chemistry. This work was conducted at Zhejiang University.

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7. *E*-**4a**: Oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.38 (m, 5H), 6.96 (s, 1H), 4.39 (s, 2H), 2.18 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.7, 133.0, 130.2, 129.7, 128.0, 99.6, 66.2; IR (neat) ν (cm^{-1}) 3383, 1666, 1580, 1528, 1478, 1439; MS (70 eV, EI) *m*/*z* (%): 292 (M^+, 92.72), 111 (100); Anal. Cacld for C_9H_9SOI: C, 37.00, H, 3.11; Found: C, 37.24, H, 3.17.
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