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Highly Regio- and Stereoselective Oxidative Hydroacetoxylation of 1,2-Allenylic Sulfoxides via a Different Mechanism

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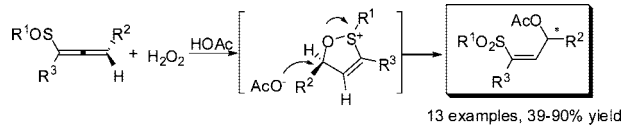


A highly regio- and stereoselective oxidative hydroacetoxylation of 1,2-allenylic sulfoxides affording 1-sulfonyl-1-alken-3-yl acetates in moderate to good yields was developed. Through the X-ray diffraction study, it was observed that the reaction may proceed via a 5-membered cyclic intermediate and the $^{-}$OAc attacks the chiral carbon atom, which is different from what was observed in our previous study.

Electrophilic additions of allenes[1,2] are synthetically useful in organic synthesis since two functionalities may be introduced within one operation. The most extensively studied one is the reaction of allenes with X_2 (X = Cl,[3,4a] Br,[3b,4] I,[4c,d,5] or IBr[4a]). Recently, we have developed highly regio- and stereoselective halohydroxylations of heteroatom substituted allenes, i.e., 1,2-allenyl sulfides,[5c,e,f] selenides,[5e,f] sulfoxides,[4c,5h,i] sulfones,[6a,b] phosphine oxides,[7] and butenolide-substituted allenes.[8] In all these reactions, the nature of the heteroatom or substituent in the allenes determines the stereoselectivity of the reaction: the reaction of sulfides or selenides affords *Z*-products while that of sulfoxides, sulfones, or phosphine oxides affords *E*-products. However, the reaction of heteroatom-substituted allenes with HX has not been studied yet. In this paper we wish to disclose our recent observation on the oxidative electrophilic hydroacetoxylation reaction of 1,2-allenyl sulfoxides with acetic acid affording 1-sulfonyl-1-alken-3-yl acetates highly regio- and stereoselectively.

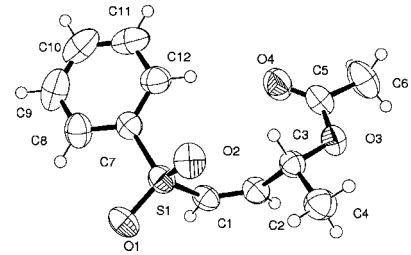
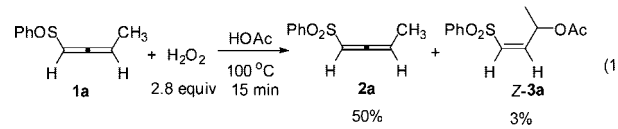


FIGURE 1. ORTEP representation of *Z*-**3a**.

In the previous work of our group, we synthesized 1,2-allenyl sulfones by the oxidation of 1,2-allenyl sulfides in HOAc with H_2O_2 (eq 1).[6c] In one case, the oxidation of 1,2-butadienyl sulfoxide **1a** with H_2O_2 in HOAc afforded the expected 1,2-butadienyl phenyl sulfone **2a** in 50% yield. In addition, 3-acetoxy-1(*Z*)-butenyl phenyl sulfone *Z*-**3a** was also isolated in 3% yield, unexpectedly. The structure of the product *Z*-**3a** was confirmed by the X-ray diffraction study (Figure 1).[9] By analyzing the structure of *Z*-**3a**, it is obvious that it is the oxidative hydroacetoxylation of the starting 1,2-allenyl sulfoxide **1a** and the *E*-stereoselectivity observed is similar to what was observed in the halohydroxylation of sulfoxides and sulfones.[4c,5i,6b] Thus, we started to study this type of transformation with H^{+} as the electrophile and acetate anion as the nucleophile.



No reaction was observed when water was used as the solvent (entry 1, Table 1). Further study indicated that conducting the reaction with different amounts of H_2O_2 (entries 2−5, Table 1) or at different concentrations (entries 6−9, Table 1) can obviously improve the yield of the allylic acetate *Z*-**3a**. *m*CPBA

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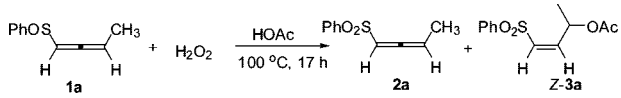
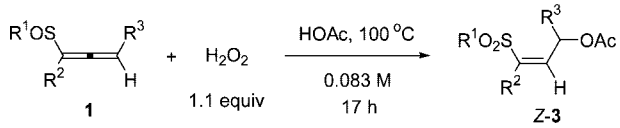
TABLE 1. Oxidative Electrophilic Hydroacetoxylation Reaction of 1,2-Butadienyl Phenyl Sulfoxide 1a with H_2O_2 in HOAc[a]



entry	[c] (mol/L)	H_2O_2 (equiv)	NMR yields **2a**	NMR yields *Z*-**3a**
1[b]	0.25	11	0	0
2	0.25	4.4	27	37
3	0.25	1.7	13	38
4	0.25	1.3	4	42
5	0.25	0.9	0	42
6	0.5	1.1	0	30
7	0.25	1.1	0	45
8	0.083	1.1	0	56 (53[c])
9	0.05	1.1	0	53
10	0.083	*d*	4	50
11	0.083	*e*	0	41

[a] The substrate **1a** (0.5 mmol) was dissolved in a half-volume of HOAc and heated to 100 °C, then a solution of H_2O_2 in the other half-volume of HOAc was added dropwise with stirring. The resulting mixture was heated at 100 °C for 17 h. [b] The reaction was carried out in water. [c] Isolated yield. [d] *m*CPBA was used as the oxidant. [e] *t*BuOOH was used as the oxidant.

TABLE 2. Oxidative Electrophilic Hydroacetoxylation Reaction of 1,2-Allenyl Sulfoxides 1 with H_2O_2 in HOAc[a]



entry	R^1	R^2	R^3	isolated yield of *Z*-**3**
1	Ph	H	CH_3 (**1a**)	53 (*Z*-**3a**)
2	Ph	H	H (**1b**)	50 (*Z*-**3b**)
3	Ph	H	C_2H_5 (**1c**)	55 (*Z*-**3c**)
4	Ph	H	*n*-C_4H_9 (**1d**)	54 (*Z*-**3d**)
5	Ph	H	*n*-C_5H_{11} (**1e**)	42 (*Z*-**3e**)
6	Ph	H	*n*-C_6H_{13} (**1f**)	40 (*Z*-**3f**)
7	Ph	H	*n*-C_7H_{15} (**1g**)	45 (*Z*-**3g**)
8	Ph	C_2H_5	CH_3 (**1h**)	80 (*Z*-**3h**)
9	Ph	*n*-C_4H_9	H (**1i**)	67 (*Z*-**3i**)
10	Ph	allyl	H (**1j**)	62 (*Z*-**3j**)
11	Ph	*n*-C_4H_9	Bn (**1k**)	73 (*Z*-**3k**)
12	*p*-BrC_6H_4	H	CH_3 (**1l**)	46 (*Z*-**3l**)
13	*p*-BrC_6H_4	C_2H_5	CH_3 (**1m**)	83 (*Z*-**3m**)

[a] The reaction was conducted by dissolving the substrate **1a** (0.5 mmol) in 3.0 mL of HOAc and heating to 100 °C. Then a solution of H_2O_2 in 3.0 mL of HOAc was added dropwise with stirring.

and *t*BuOOH gave inferior results (entries 10 and 11, Table 1). Finally it is observed that the best result was obtained when the reaction of **1a** (0.083 M in HOAc) with 1.1 equiv of H_2O_2 was conducted at 100 °C for 17 h affording *Z*-**3a** in 56% yield (entry 8, Table 1).

It was found that the reaction is quite general. Different R^1, R^2, and R^3 can be introduced to the starting 1,2-allenyl sulfoxides to afford differently substituted 3-acetoxy-1-alkenyl sulfones *Z*-**3** in moderate to good yields (Table 2). The structure of these products was further confirmed by the X-ray diffraction study of *Z*-**3h** (Figure 2).[10] The major byproducts are the corresponding 1,2-allenylsulfones. It should be noted that 3-phenyl-1,2-butadienyl phenyl sulfoxide and 3-ethyl-1,2-pentadienyl phenyl sulfoxide failed to afford the expected products.

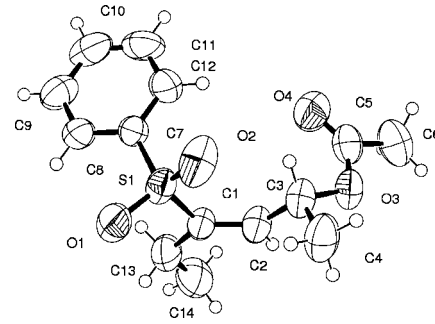
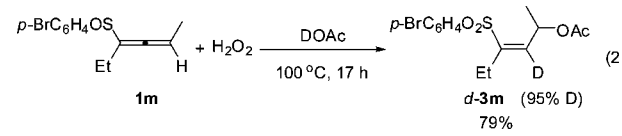
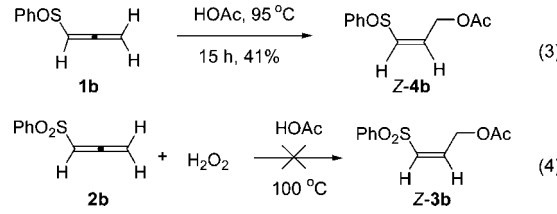


FIGURE 2. ORTEP representation of *Z*-**3h**.

To study the mechanism, DOAc was used as the solvent, and under the typical reaction conditions (1.1 equiv of H_2O_2 (30%), 100 °C, 17 h), 95% of D-incorporation was observed for the olefinic proton in compound *d*-**3m**, namely D^+ was connected to the center carbon atom of the allene moiety in the starting allene **1m** (eq 2).



Further study indicated that when **1b** was stirred for 15 h in HOAc at 95 °C in the absence of H_2O_2, sulfinylallyl acetate **4b** was formed in 41% isolated yield (eq 3). However, when 1,2-allenyl sulfone **2b** was stirred in HOAc at 100 °C, no reaction was observed with **2b** being recovered in 46% yield (eq 4). On the basis of these results, we reasoned that the reaction may first undergo hydroacetoxylation, which was followed by oxidation of the sulfoxide functionality.



To study the influence of the sulfoxide group on the stereoselectivity of the electrophilic addition process, we synthesized optically active substrate (*R*)-**1l** from (*R*)-3-butyn-2-ol. Under the standard conditions, the reaction afforded the expected product (*S*)-(*Z*)-**3l** in 41% yield. To determine the

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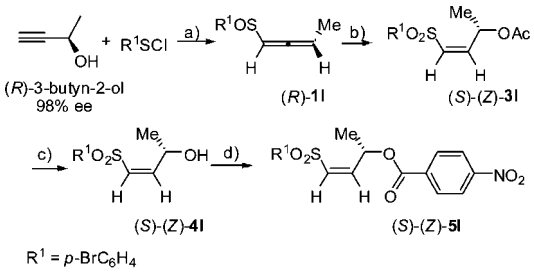
(9) Crystal data for compound *Z*-**3a**: $C_{12}H_{14}O_4S$, MW = 254.29, monoclinic, space group *C*2/*c*, final *R* indices [$I > 2\sigma(I)$], $R_1 = 0.0462$, $wR_2 = 0.0768$, *R* indices (all data) $R_1 = 0.0811$, $wR_2 = 0.0847$, $a = 20.253(2)$ Å, $b = 7.9925(8)$ Å, $c = 16.7147(18)$ Å, $\alpha = 90°$, $\beta = 109.567(2)°$, $\gamma = 90°$, $V = 2525.8(5)$ Å^3, $T = 296(2)$ K, $Z = 8$, reflections collected/unique 7232/2745 ($R_{int} = 0.0643$), number of observations [$I > 2\sigma(I)$] 1568, parameters 168. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center, CCDC 707622.

(10) Crystal data for compound *Z*-**3h**: $C_{14}H_{18}O_4S$, MW = 282.34, monoclinic, space group *P*2(1)/*c*, final *R* indices [$I > 2\sigma(I)$], $R_1 = 0.0664$, $wR_2 = 0.1588$, *R* indices (all data) $R_1 = 0.1147$, $wR_2 = 0.1824$, $a = 8.3591(13)$ Å, $b = 23.949(4)$ Å, $c = 8.0712(13)$ Å, $\alpha = 90°$, $\beta = 111.071(3)°$, $\gamma = 90°$, $V = 1507.7(4)$ Å^3, $T = 296(2)$ K, $Z = 4$, reflections collected/unique 8774/3276 ($R_{int} = 0.1402$), number of observations [$I > 2\sigma(I)$] 1695, parameters 184. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center, CCDC 707621.

SCHEME 1. Synthesis of Optically Active Derivatives (*S*)-(*Z*)-5l for the Determination of the Absolute Configuration of (*S*)-(*Z*)-3l[a]



[a] Reagents and conditions: (a) Et_3N, CH_2Cl_2, −78 °C, 10 min then CH_3I, rt, 65%, 98.2% ee (referred to the axial chirality); (b) H_2O_2, HOAc, 95 °C, 17 h, 41%, 94.8% ee; (c) K_2CO_3, MeOH, −30 °C, 4 h, 61%, 93.3% ee; (d) Et_3N, DMAP, 4-nitrobenzoyl chloride, CH_2Cl_2, rt, 12 h, 82%, 92.4% ee.

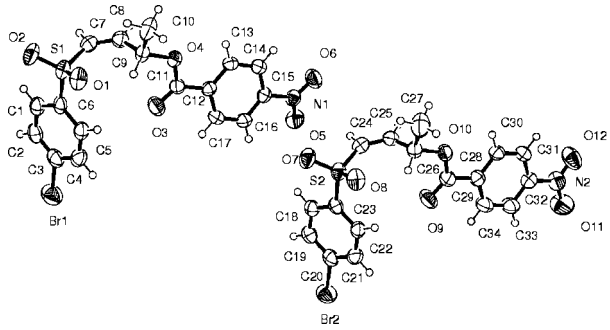


FIGURE 3. ORTEP representation of (*S*)-(*Z*)-**5l**.

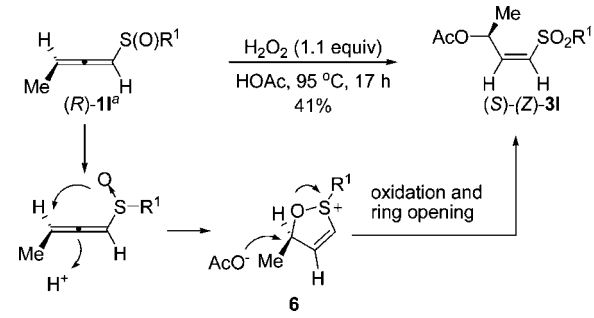
absolute configuration of this product, it was hydrolyzed and subsequently converted to its *p*-nitrobenzoate during which the absolute configuration should remain unchanged (Scheme 1).[11] The (*S*)-absolute configuration of this benzoate was then established by the X-ray diffraction study (Figure 3).[12] This result is very different from what was observed in the halohydroxylation of 1,2-allenyl sulfoxides and sulfones.[4c,5i,7]

On the basis of these results, we proposed a mechanism that is shown as follows: First, electrophilic addition of the proton with the relatively electron-rich carbon−carbon double bond in (*R*)-**1l** followed by intramolecular attack of the sulfinyl oxygen would afford the five-membered cyclic intermediate **6** determining the *Z*-selectivity in this addition reaction. S_N2 attack of CH_3COO^- at the allylic carbon atom instead of the sulfinyl group we observed before[4c,5i,7] results in the inversion of the chiral center (Scheme 2). Oxidation of the sulfoxide functionality by H_2O_2 forms the final product (*S*)-(*Z*)-**3l**.

On the basis of this observation, this reaction was used further for the preparation of optically active 3-acetoxy-1-butenyl sulfones **3f** and **3m** from the easily available optically active 1,2-allenyl sulfoxides[5b] **1f** and **1m** without obvious loss of the enantiopurity (Scheme 3).

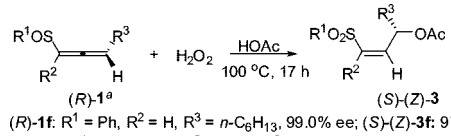
In conclusion, we have demonstrated that the reaction of 1,2-allenyl sulfoxides with HOAc in the presence of H_2O_2 afforded

SCHEME 2. Mechanism of the Oxidative Hydroacetoxylation of 1,2-Allenyl Sulfoxides[a]



[a] Referred to axial chirality.

SCHEME 3. Preparation of Optically Active 1-Sulfonyl-1-alken-3-yl Acetates[a]



(*R*)-**1f**: R^1 = Ph, R^2 = H, R^3 = n-C_6H_{13}, 99.0% ee; (*S*)-(*Z*)-**3f**: 97.9% ee, yield: 39%
(*R*)-**1m**: R^1 = p-BrC_6H_4, R^2 = C_2H_5, R^3 = CH_3, 95.1% ee; (*S*)-(*Z*)-**3m**: 94.8% ee, yield: 90%

[a] Referred to axial chirality.

3-sulfonylallylic acetates highly regio- and stereoselectively. The axial chirality can be transferred into the center chirality in the final products highly efficiently. Due to the highly loaded functionalities and the *Z* C═C bonds in the products, this reaction may be useful in organic synthesis.

General Experimental Methods

Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on instruments operating at 300 or 400 MHz. ^{13}C NMR were recorded at 75 or 100 MHz. Deuteriochloroform ($CDCl_3$) was used as solvent in all NMR experiments. Chemical shifts (δ) are given in parts per million (ppm). Infrared spectra were recorded on a FT-IR spectrometer. Mass spectra were carried out in EI mode. HRMS spectra were carried out in EI and MALDI mode. The enantiomeric excesse values (ee) were determined by HPLC analysis with chiral columns. Thin layer chromatography was performed on precoated glass back plates and visualized with UV light at 254 nm. Flash column chromatography was performed on silica gel (10−40 μm).

Synthesis of 4-(Phenylsulfonyl)but-3(*Z*)-en-2-yl acetate (*Z*-3a): Typical Procedure. To a solution of **1a** (88.7 mg, 0.5 mmol) in HOAc (3.0 mL) at 100 °C was added a solution of freshly ordered H_2O_2 (30%, 57 μL, d = 1.11 g/mL, 0.063 g, 0.56 mmol) in HOAc (3.0 mL) dropwise within 20 min. After being stirred at 100 °C for 17 h as monitored by TLC, the resulting mixture was quenched with 10 mL of an aqueous saturated solution of $NaHCO_3$, extracted with diethyl ether (15 mL × 3), washed with an aqueous saturated solution of $NaHCO_3$, and dried over anhydrous Na_2SO_4. After filtration and evaporation, column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1) afforded *Z*-**3a** (66.9 mg, 53%) as a solid, mp 88−89 °C (*n*-hexane/diethyl ether). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02−7.97 (m, 2 H), 7.65−7.59 (m, 1 H), 7.57−7.51 (m, 2 H), 6.44−6.36 (m, 1 H), 6.20−6.10 (m, 2 H), 2.01 (s, 3 H), 1.46 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 145.2, 140.2, 133.7, 129.2, 129.1, 127.6, 66.7, 20.9, 20.4; IR (KBr) ν (cm^{-1}) 3048, 3024, 2992, 2940, 1729, 1632, 1578, 1450, 1364, 1310, 1294, 1248, 1148, 1092, 1044; MS (70 eV, EI) *m*/*z* (%) 254 (M^+, 3.07), 43 (100). Anal. Calcd for $C_{12}H_{14}O_4S$: C, 56.68; H, 5.55. Found: C, 56.68; H, 5.52.

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(12) Crystal data for compound *Z*-**5l**: $C_{34}H_{28}Br_2N_2O_{12}S_2$, MW = 880.52, orthorhombic, space group $P2(1)2(1)2(1)$, final R indices [$I > 2\sigma(I)$], $R_1 = 0.0379$, $wR_2 = 0.0886$, R indices (all data) $R_1 = 0.0569$, $wR_2 = 0.0988$, $a = 6.7518(3)$ Å, $b = 17.3942(7)$ Å, $c = 31.4299(13)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, $V = 3691.2(3)$ Å^3, $T = 296(2)$ K, $Z = 4$, reflections collected/unique 42884/6492 ($R_{int} = 0.0479$), number of observations [$I > 2\sigma(I)$] 5154, parameters 469. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center, CCDC 707623.

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Supporting Information Available: Detailed experimental procedures and analytical data for all new products not listed in the text, ^{1}H and ^{13}C NMR spectra of all new compounds, and cif files for *Z*-**3a**, *Z*-**3h**, and (*S*)-*Z*-**5l**. This material is available free of charge via the Internet at http://pubs.acs.org.

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