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Synthetic Methods

Highly Selective Thiiranation of 1,2-Allenyl Sulfones with Br_2 and $Na_2S_2O_3$: Mechanism and Asymmetric Synthesis of Alkylidenethiiranes**

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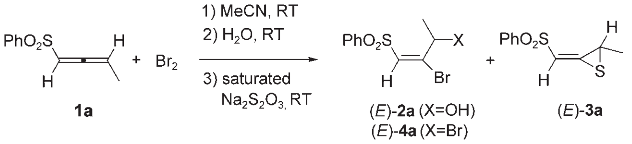
Electrophilic addition reactions of allenes have been explored in the search for highly selective reactions for organic synthesis.[1] We demonstrated the electrophilic halocyclization of allenes with a nucleophilic functionality.[2] On the basis of these observations, we developed highly regio- and stereoselective halohydroxylation reactions of heteroatom-substituted allenes, including 1,2-allenyl sulfides,[3] selenides,[4] and sulfoxides.[5] In these reactions, the stereoselectivity depends largely on the nature of the heteroatom: The reactions of sulfides or selenides afforded *Z* products, whereas sulfoxides reacted to give *E* products. However, under the reaction conditions used for the halohydroxylation of 1,2-allenyl sulfoxides,[5] no reaction was observed for 1,2-allenyl sulfones, probably as a result of the strong electron-withdrawing ability of the sulfone group.[6] Padwa and co-workers reported the electrophilic addition of Br_2 and I_2 to 1,2-propadienyl phenyl sulfone to give the corresponding *E*-2,3-dihalopropenyl phenyl sulfone with high stereoselectivity.[7] Furthermore, Braverman and co-workers reported the electrophilic addition of Br_2 to bisallenyl sulfones to form γ sultines.[8] Herein we disclose our recent observations on the electrophilic reaction of 1,2-allenyl sulfones with Br_2 and $Na_2S_2O_3$ to afford alkylidenethiiranes[9] with high regio- and stereoselectivity.

We initiated our study by attempting the reaction of 1,2-butadienyl phenyl sulfone (**1a**) with Br_2. We observed with interest that instead of the expected halohydroxylation product (*E*)-**2a**,[3–5] the reaction of **1a** with Br_2 (1.5 equiv) in MeCN in the presence of H_2O (2.0 equiv) afforded the 1-(phenylsulfonyl)methylene-2-methylthiirane (*E*)-**3a** in 56% yield together with the 2,3-dibromobutenyl sulfone (*E*)-**4a** (11%)[7] upon sequential quenching with water and aqueous $Na_2S_2O_3$ (Table 1, entry 1). A similar result was obtained in the absence of H_2O (Table 1, entry 2); with 2 equivalents of Br_2, (*E*)-**3a** and (*E*)-**4a** were formed in 67 and 9% yield, respectively (Table 1, entry 3). Finally, we observed that the reaction of **1a** with 2.5 equivalents of Br_2 in MeCN afforded (*E*)-**3a** in 70% yield as the only product (Table 1, entry 4).

Table 1: Electrophilic reaction of 1,2-butadienyl phenyl sulfone (**1a**) with Br_2.



Entry	H_2O [equiv]	Br_2 [equiv]	*t* [min]	Yield of **3a** [%]	Yield of **4a** [%]
1	2.0	1.5	60	56	11
2	0	1.5	60	56	11
3	0	2.0	60	67	9
4	0	2.5	15	70	–
5[a]	0	2.5	15	67	1.5

[a] The reaction was quenched directly with aqueous $Na_2S_2O_3$.

We found that the reaction was quite general: When different groups R^1, R^2, and R^3 were introduced, the reaction afforded substituted 1-sulfonyl alkylidenethiiranes (*E*)-**3** in moderate to good yields (Table 2). The structure of one of these products, (*E*)-**3m**, was confirmed by X-ray diffraction analysis (see the Supporting Information).[10] When the reaction of **1b** with Br_2 was quenched directly with saturated, aqueous $Na_2S_2O_3$, the yield was much lower (Table 2, entries 2 and 3).

As optically active 1,2-allenyl sulfones can be prepared very conveniently by a two-step procedure from readily available optically active propargylic alcohols,[11,5b] we also studied the possibility of using this reaction for the preparation of optically active 1-sulfonyl alkylidenethiiranes. The axial chirality in the 1,2-allenyl sulfones was transferred with high efficiency to the alkylidenethiiranes in the form of

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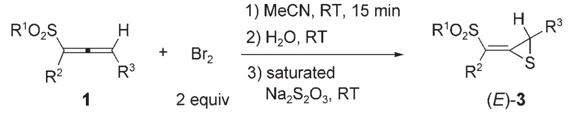
Supporting information for this article (including a typical experimental procedure and analytical data for all products not listed in the text) is available on the WWW under http://www.angewandte.org or from the author.

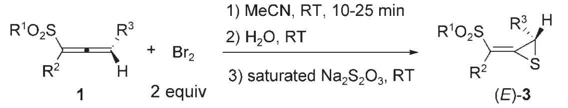
Table 2: Synthesis of 1-phenylsulfonylalkylidenethiiranes.



Entry	**1**	R^1	R^2	R^3	Yield of (*E*)-**3** [%]
1[a,b]	**1a**	Ph	H	CH_3	70 (**3a**)
2	**1b**	Ph	H	C_2H_5	70 (**3b**)
3[c]	**1b**	Ph	H	C_2H_5	55 (**3b**)
4	**1c**	Ph	H	*n*-C_3H_7	68 (**3c**)
5	**1d**	Ph	H	*n*-C_4H_9	71 (**3d**)
6	**1e**	Ph	H	*n*-C_5H_{11}	63 (**3e**)
7	**1f**	Ph	H	*n*-C_6H_{13}	69 (**3f**)
8	**1g**	Ph	H	Bn	72 (**3g**)
9	**1h**	Ph	*n*-C_4H_9	CH_3	80 (**3h**)
10	**1i**	Ph	*n*-C_4H_9	C_2H_5	67 (**3i**)
11	**1j**	Ph	*n*-C_4H_9	Bn	84 (**3j**)
12[d]	**1k**	Ph	C_2H_5	CH_3	84 (**3k**)
13[e]	**1l**	*p*-BrC_6H_4	C_2H_5	CH_3	61 (**3l**)
14[e]	**1m**	*p*-BrC_6H_4	H	CH_3	65 (**3m**)

[a] In this reaction 2.5 equivalents of Br_2 were used. [b] Reaction time: 10 min. [c] The reaction mixture was quenched directly with aqueous $Na_2S_2O_3$. [d] Reaction time: 20 min. [e] Reaction time: 25 min. Bn = benzyl.

Table 3: Synthesis of optically active 1-phenylsulfonylalkylidenethiiranes.



1 (*ee* [%])[a]	R^1	R^2	R^3	Yield of (*E*)-**3** [%]	*ee* [%][a]
(*R*)-**1f** (>99)	Ph	H	*n*-C_6H_{13}	58 ((*S*)-(*E*)-**3f**)	99
(*R*)-**1e** (99)	Ph	H	*n*-C_5H_{11}	62 ((*S*)-(*E*)-**3e**)	99
(*R*)-**1l** (96)	*p*-BrC_6H_4	C_2H_5	CH_3	74 ((*S*)-(*E*)-**3l**)	96
(*R*)-**1m** (99)	*p*-BrC_6H_4	H	CH_3	57 ((*S*)-(*E*)-**3m**)	99

[a] The *ee* values were determined by HPLC on a chiral phase (see the Supporting Information for details).

central chirality (Table 3). The absolute configuration of the products was determined by X-ray diffraction analysis of (*S*)-(*E*)-**3m**[12] by using the bromine atom in the molecule as a reference (Figure 1).

To study the mechanism of the reaction and the origin of the regio- and stereoselectivity, 1,2-butadienyl *p*-bromophenyl sulfone (**1l**) was prepared. The treatment of **1l** with Br_2 (2.0 equiv) under the standard reaction conditions afforded the expected product (*E*)-**3l** in 61% yield (Table 2, entry 13). However, a five-membered intermediate **5l** with Br_3^- as the counter ion could be isolated with careful handling after the treatment of **1l** with Br_2 (2.0 equiv). The structure of this intermediate was established by X-ray diffraction analysis of its *trans* isomer (Figure 2).[13] The treatment of **5l** (*cis*/*trans* 1:1) with H_2O in MeCN followed by the addition of saturated aqueous $Na_2S_2O_3$ afforded cleanly (*E*)-**3l** as a single product (Scheme 1).

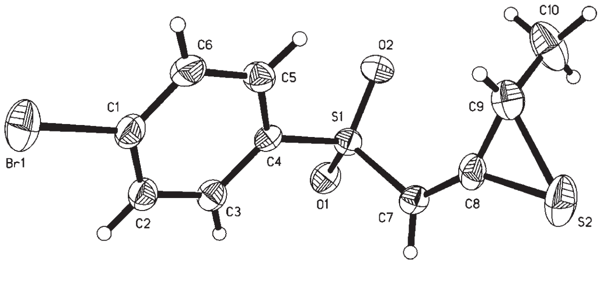


Figure 1. ORTEP representation of (*S*)-(*E*)-**3m**.

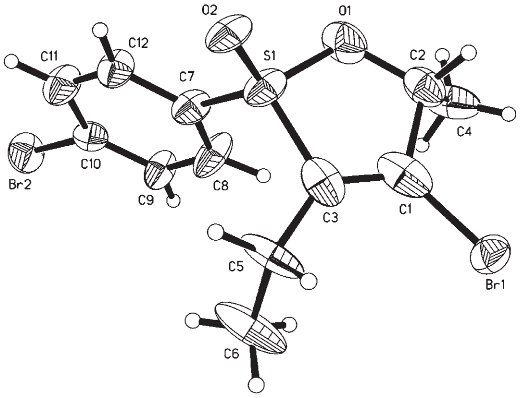
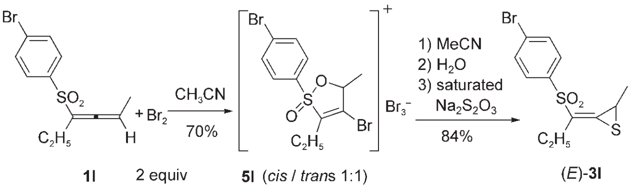


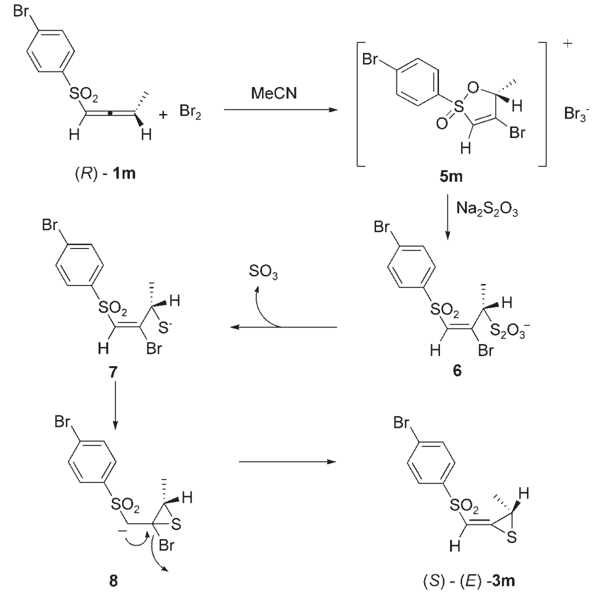
Figure 2. ORTEP representation of *trans*-**5l**.



Scheme 1. Identification of the intermediate **5l** in the thiiranation of **1l** with Br_2 and $Na_2S_2O_3$.

We propose a mechanism for this transformation on the basis of the results shown in Scheme 1 and the steric outcome presented in Table 3 and Figure 1 (Scheme 2): The electrophilic addition of Br_2 to (*R*)-**1m** in MeCN may afford the 5-membered-ring intermediate **5m**, which may be attacked by $S_2O_3^{2-}$ with ring opening to afford the acyclic intermediate **6**. The release of a molecule of SO_3 would afford the 2-bromoallylic sulfide **7**, which would undergo intramolecular conjugated addition and elimination to afford (*S*)-(*E*)-**3m**. The stereoselectivity of this reaction is determined by the intermediacy of **5** and the stereospecific nature of the addition–elimination reaction of **7**.

In conclusion, we have demonstrated that the reaction of 1,2-allenyl sulfones with Br_2 followed by sequential treatment with H_2O and an aqueous solution of $Na_2S_2O_3$ affords 1-sulfonyl alkylidenethiiranes with high regio- and stereoselectivity. Axial chirality in the allenes can be converted efficiently into central chirality in the final products. This reaction should be useful in organic synthesis because



Scheme 2. Proposed mechanism of the stereoselective thiiranation of 1,2-allenyl sulfones with Br_2 and $Na_2S_2O_3$.

optically active starting allenes, which are readily available from propargylic alcohols, are transformed into densely functionalized products.

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[10] Crystal data for (*E*)-**3m**: $C_{10}H_9BrO_2S_2$, $M_r = 305.20$, monoclinic, $P2(1)/n$, $Mo_{K\alpha}$ radiation, final R indices ($I > 2\sigma(I)$): $R1 = 0.0531$, $wR2 = 0.1244$, $a = 11.4801(16)$, $b = 7.8884(11)$, $c = 12.9888(17)$ Å, $\beta = 95.286(2)°$, $V = 1171.3(11)$ Å^3, $Z = 4$, number of reflections (measured/unique): 6774/2648 ($R_{int} = 0.1155$), number of observations: 1764 ($I > 2\sigma(I)$), 145 parameters. CCDC-614240 (±-(*E*)-**3m**), CCDC-629979 ((*S*)-(*E*)-**3m**), and CCDC-614242 (*trans*-**51**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[11] Optically pure allenyl sulfones were synthesized by the oxidation of chiral allenyl sulfoxides with *m*-chloroperbenzoic acid in an ice bath. For the synthesis of chiral allenyl sulfoxides, see reference [5b].

[12] Crystal data for (*S*)-(*E*)-**3m**: $C_{10}H_9BrO_2S_2$, $M_r = 305.20$, monoclinic, $P2(1)/n$, $Mo_{K\alpha}$ radiation, final R indices ($I > 2\sigma(I)$): $R1 = 0.0614$, $wR2 = 0.1552$, $a = 11.0171(16)$, $b = 5.0148(8)$, $c = 21.889(3)$ Å, $\beta = 93.672(3)°$, $V = 1206.9(3)$ Å^3, $Z = 4$, number of reflections (measured/unique): 7157/4737 ($R_{int} = 0.0762$), number of observations: 2877 ($I > 2\sigma(I)$), 273 parameters; see reference [10].

[13] Crystal data for *trans*-**51**: $C_{12}H_{13}Br_5O_2S$, $M_r = 620.83$, monoclinic, $P2(1)/n$, $Mo_{K\alpha}$ radiation, final R indices ($I > 2\sigma(I)$), $R_1 = 0.0763$, $wR2 = 0.1752$, $a = 15.211(7)$, $b = 8.598(4)$, $c = 15.846(7)$ Å, $\beta = 118.082(7)°$, $V = 1828.4(14)$ Å^3, $Z = 4$, number of reflections (measured/unique): 9294/3410 ($R_{int} = 0.1718$), number of observations: 1375 ($I > 2\sigma(I)$), 184 parameters; see reference [10].