

Synthetic Methods

Highly Selective Thiirane of 1,2-Allenyl Sulfones with Br₂ and Na₂S₂O₃: 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 Br₂ and I₂ 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 Br₂ to bisallenyl sulfones to form γ sultines.^[8] Herein we disclose our recent observations on the electrophilic reaction of 1,2-allenyl sulfones with Br₂ and Na₂S₂O₃ 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 Br₂. We observed with interest that instead of the expected halohydroxylation product (*E*)-**2a**,^[3–5] the reaction of **1a** with Br₂ (1.5 equiv) in MeCN in the presence of H₂O (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 Na₂S₂O₃ (Table 1, entry 1). A similar result was obtained in

Table 1: Electrophilic reaction of 1,2-butadienyl phenyl sulfone (**1a**) with Br₂.

Entry	H ₂ O [equiv]	Br ₂ [equiv]	<i>t</i> [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 Na₂S₂O₃.

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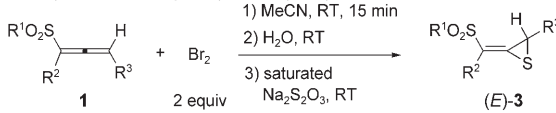
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Supporting information for this article (including a typical experimental procedure and analytical data for all products not listed in the text) is available on the WWW under <http://www.angewandte.org> or from the author.

the absence of H₂O (Table 1, entry 2); with 2 equivalents of Br₂, (*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 Br₂ in MeCN afforded (*E*)-**3a** in 70 % yield as the only product (Table 1, entry 4).

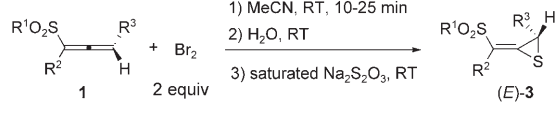
We found that the reaction was quite general: When different groups R¹, R², and R³ were introduced, the reaction afforded substituted 1-sulfonyl alkylidenethiiranes (*E*)-**3** in moderate to good yields (Table 2). The structure of one of these products, (*E*)-**3m**, was confirmed by X-ray diffraction analysis (see the Supporting Information).^[10] When the reaction of **1b** with Br₂ was quenched directly with saturated, aqueous Na₂S₂O₃, 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

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 ₂ H ₅	70 (3b)
3 ^[c]	1b	Ph	H	C ₂ H ₅	55 (3b)
4	1c	Ph	H	<i>n</i> -C ₃ H ₇	68 (3c)
5	1d	Ph	H	<i>n</i> -C ₄ H ₉	71 (3d)
6	1e	Ph	H	<i>n</i> -C ₅ H ₁₁	63 (3e)
7	1f	Ph	H	<i>n</i> -C ₆ H ₁₃	69 (3f)
8	1g	Ph	H	Bn	72 (3g)
9	1h	Ph	<i>n</i> -C ₄ H ₉	CH ₃	80 (3h)
10	1i	Ph	<i>n</i> -C ₄ H ₉	C ₂ H ₅	67 (3i)
11	1j	Ph	<i>n</i> -C ₄ H ₉	Bn	84 (3j)
12 ^[d]	1k	Ph	C ₂ H ₅	CH ₃	84 (3k)
13 ^[e]	1l	<i>p</i> -BrC ₆ H ₄	C ₂ H ₅	CH ₃	61 (3l)
14 ^[e]	1m	<i>p</i> -BrC ₆ H ₄	H	CH ₃	65 (3m)

[a] In this reaction 2.5 equivalents of Br₂ were used. [b] Reaction time: 10 min. [c] The reaction mixture was quenched directly with aqueous Na₂S₂O₃. [d] Reaction time: 20 min. [e] Reaction time: 25 min. Bn = benzyl.

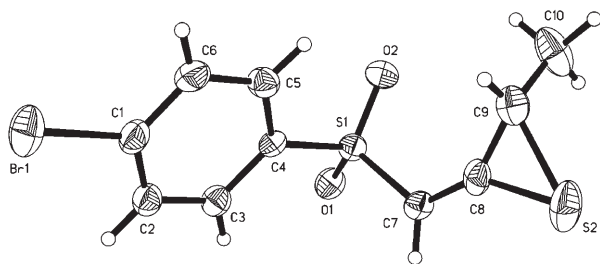
Table 3: Synthesis of optically active 1-phenylsulfonylalkylidenethiiranes.


1 (<i>ee</i> [%]) ^[a]	R ¹	R ²	R ³	Yield of (E)-3 [%]	<i>ee</i> [%] ^[a]
(<i>R</i>)-1f (> 99)	Ph	H	<i>n</i> -C ₆ H ₁₃	58 ((<i>S</i>)-(E)-3f)	99
(<i>R</i>)-1e (99)	Ph	H	<i>n</i> -C ₅ H ₁₁	62 ((<i>S</i>)-(E)-3e)	99
(<i>R</i>)-1l (96)	<i>p</i> -BrC ₆ H ₄	C ₂ H ₅	CH ₃	74 ((<i>S</i>)-(E)-3l)	96
(<i>R</i>)-1m (99)	<i>p</i> -BrC ₆ H ₄	H	CH ₃	57 ((<i>S</i>)-(E)-3m)	99

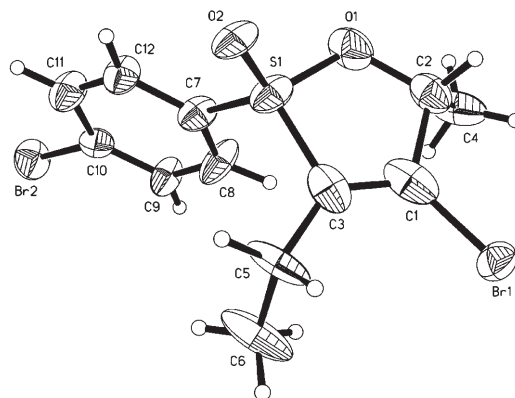
[a] The *ee* values were determined by HPLC on a chiral phase (see the Supporting Information for details).

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).

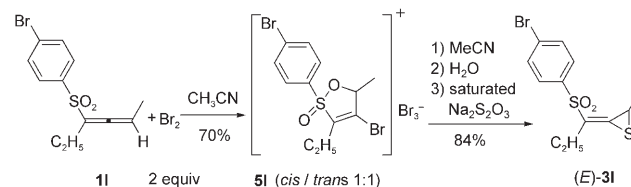
To study the mechanism of the reaction and the origin of the regio- and stereoselectivity, 1,2-butadienyl *p*-bromophenyl sulfone (1l) was prepared. The treatment of 1l with

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

Br₂ (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 Br₃[−] as the counter ion could be isolated with careful handling after the treatment of 1l with Br₂ (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*

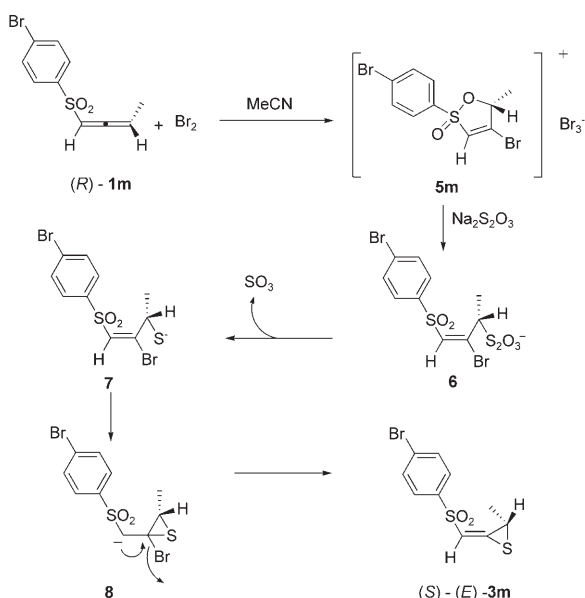
**Figure 2.** ORTEP representation of *trans*-5l.

1:1) with H₂O in MeCN followed by the addition of saturated aqueous Na₂S₂O₃ afforded cleanly (*E*)-3l as a single product (Scheme 1).

**Scheme 1.** Identification of the intermediate 5l in the thiirane of 1l with Br₂ and Na₂S₂O₃.

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 Br₂ to (*R*)-1m in MeCN may afford the 5-membered-ring intermediate 5m, which may be attacked by S₂O₃^{2−} with ring opening to afford the acyclic intermediate 6. The release of a molecule of SO₃ 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 Br₂ followed by sequential treatment with H₂O and an aqueous solution of Na₂S₂O₃ 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 thiirane addition of 1,2-allenyl sulfones with Br_2 and $\text{Na}_2\text{S}_2\text{O}_3$.

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

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- [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: $\text{C}_{10}\text{H}_9\text{BrO}_2\text{S}_2$, $M_r = 305.20$, monoclinic, $P2(1)/n$, $\text{MoK}\alpha$ radiation, final R indices ($I > 2\sigma(I)$): $R_1 = 0.0614$, $wR_2 = 0.1552$, $a = 11.0171(16)$, $b = 5.0148(8)$, $c = 21.889(3)$ Å, $\beta = 93.672(3)^\circ$, $V = 1206.9(3)$ Å³, $Z = 4$, number of reflections (measured/unique): 7157/4737 ($R_{\text{int}} = 0.0762$), number of observations: 2877 ($I > 2\sigma(I)$), 273 parameters; see reference [10].
- [13] Crystal data for trans-51: $\text{C}_{12}\text{H}_{13}\text{Br}_3\text{O}_2\text{S}$, $M_r = 620.83$, monoclinic, $P2(1)/n$, $\text{MoK}\alpha$ radiation, final R indices ($I > 2\sigma(I)$): $R_1 = 0.0763$, $wR_2 = 0.1752$, $a = 15.211(7)$, $b = 8.598(4)$, $c = 15.846(7)$ Å, $\beta = 118.082(7)^\circ$, $V = 1828.4(14)$ Å³, $Z = 4$, number of reflections (measured/unique): 9294/3410 ($R_{\text{int}} = 0.1718$), number of observations: 1375 ($I > 2\sigma(I)$), 184 parameters; see reference [10].