Stereocontrolled synthesis of either *trans*- or *cis*-trimethylsilylvinyloxiranes *via* sulfonium ylides

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trans- or _cis_-β-Trimethylsilylvinyloxiranes are prepared by the reaction of aldehydes with a 3-trimethylsilylated dimethylsulfonium allylide under phase-transfer conditions or with a preformed 3-trimethylsilylated diphenylsulfonium allylide in the presence of LiBr, both in excellent yields and high stereoselectivity.

Among various functionalized oxiranes, vinyloxirane has proven to be one of the most important ones. It is not only because this type of chemically active substances can undergo various chemical transformations and a variety of rearrangements,[1] but also because that the α,β-unsaturated epoxide is a structural unit in many natural products.[2] For its versatile chemical properties,vinyloxirane has been extensively used as an intermediate in the synthesis of biologically significant molecules.[3] At present, the preparation of vinyloxiranes requires strict reaction conditions and a multi-step sequence or troublesome operations are often adopted.[4] S, As and Te allylides[5] have been used to prepare vinyloxiranes, *trans*-epoxides from allylic sulfonium[5a–c] and arsonium[5d] ylides. Products derived from telluronium[5e] ylides have preferentially a *cis*-configuration. Because of the known [2,3]-σ-rearrangement,[6] allylic sulfonium ylides have found very limited applications in the preparation of vinyloxiranes. The successful use of a non-rearrangeable 3-trimethylsilylated dimethylsulfonium allylide, generated by the deprotonation of the sulfonium salt **2**, in the preparation of vinylaziridines[7] encouraged us to use **2** as the ylide precursor in the preparation of vinyloxiranes. Here we report a stereocontrolled synthesis of either of the *trans*- or *cis*-β-trimethylsilylvinyloxiranes, eqns. (1) and (2).

Under extremely mild conditions, aldehydes **1** reacted smoothly with a silylated dimethylsulfonium allylide, produced *in situ* from the sulfonium salt **2**[8] by solid KOH in acetonitrile, to furnish the *trans*-isomer-enriched epoxide **3** in excellent yields, eqn. (1). In the presence of LiBr, **1** reacted with a preformed ylide, generated *in situ* from the sulfonium salt **4**[9] and $KN(SiMe_3)_2$ in THF at low temperature, to give epoxide **3** in excellent yields and with very high *cis* selectivity, eqn. (2). The results are summarized in Table 1.

The reactions shown in eqns. (1) and (2) provide high stereoselectivity for the preparation of either the *trans*- or *cis*-β-trimethylsilylvinyloxiranes in excellent yields. To our knowledge, both stereoisomers of vinyloxirane have not been obtained using the same ylide type. In addition, epoxidation with sulfonium ylides has never been found to give preferentially the *cis*-isomers.

It should be pointed out that the addition of LiBr in the low temperature reaction [eqn. (2)] is crucial. Otherwise, an epoxide with a ratio of *trans*:*cis* = 2:1 would be obtained. The dramatic lithium salt effect was also observed in ylide cyclopropanation reactions.[10] The presence of a trimethylsilyl group did improve the *trans*/*cis* selectivity of the products. All recorded results for the preparation of simple vinyl-substituted epoxides by way of S, As and Te allylides were shown to give low *trans*/*cis* selectivity. Any attempts to use sulfonium salt **4** instead of sulfonium salt **2** in the phase-transfer reaction or use of **2** instead of **4** in the low temperature reaction would result in epoxides with a ratio of *trans*:*cis* = 2:1. The high stereoselectivity exhibited in this work is therefore noteworthy.

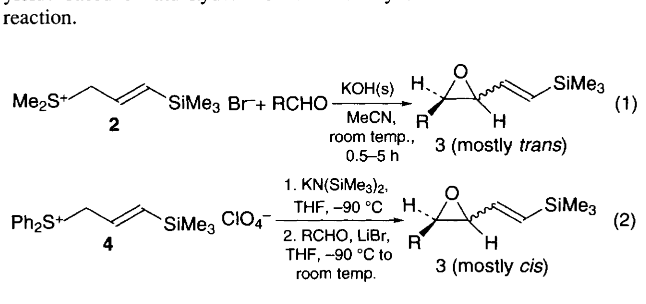
The possible pathway to achieve either *trans*- or *cis*-epoxides under different conditions might be postulated as shown in Scheme 1.

On using sulfonium salt **2** under phase-transfer conditions, the reaction proceeded *via* an intermediate **A** which is more stable than intermediate **B** and then furnish the thermodynamically stable *trans* epoxides. With the sulfonium salt **4** (R′ = Ph in transition state **a** or **b**), the lithium salt changed the reaction path by coordination with both the substrate and ylide through a halogen bridge.[11] The reaction proceeds *via* the more

Table 1 Preparation of either *trans*- or *cis*-β-trimethylsilylvinyloxiranes **3** *via* sulfonium ylides

Entry	Salt/reaction condition[a]	R	Yield (%)[b]	*trans*/*cis*[c]
1	2/A	*p*-ClC_6H_4	95	98/2
2	**4**/B	*p*-ClC_6H_4	96	6/94
3	2/A	Ph	91	87/13
4	**4**/B	Ph	96	15/85
5	2/A	*p*-BrC_6H_4	91	82/18
6	**4**/B	*p*-BrC_6H_4	95	14/86
7	2/A	4-biphenyl	84	80/20
8	**4**/B	4-biphenyl	93	7/93
9	2/A	3-pyridyl	91	87/13
10	**4**/B	3-pyridyl	81	5/95
11	2/A	2-naphthyl	84	80/20
12	**4**/B	2-naphthyl	92	8/92
13	2/A	*p*-FC_6H_4	88	98/2
14	**4**/B	*p*-FC_6H_4	88	12/88
15	2/A	cyclohexyl	[d]	—
16	**4**/B	cyclohexyl	85	20/80

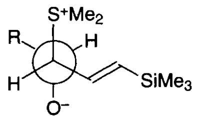
[a] General procedure for Condition A. Aldehyde (**1**, 1.0 equiv.) and sulfonium salt (**2**, 1.2 equiv.) were placed in acetonitrile (4 ml). Powdered potassium hydroxide (1.2 equiv.) was subsequently added under stirring. After the reaction was complete, column chromatography (pentane:ethyl acetate = 100:1 as eluent) gave the pure product; Condition B. A solution of $KN(SiMe_3)_2$ (1.2 equiv.) in THF was introduced through a syringe to a solution of the sulfonium salt (**4**, 1.2 equiv.) in THF (5 ml) at −90 °C under N_2. After stirring for 5 min, aldehyde (**1**, 1.0 equiv.) and LiBr (1.0 equiv.) in THF (2 ml) were added and the mixture was allowed to warm to room temp. over 2–3 h. Work-up was accomplished as described above. [b] Isolated yields based on aldehyde. [c] Determined by 300 MHz ¹H NMR. [d] No reaction.

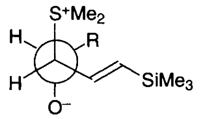


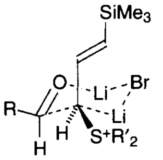
Scheme 1

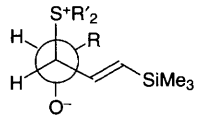
favourable transition state **a**, where Ph_2S^+ is bulkier than $CH{=}CHSiMe_3$ and in an equatorial orientation, rather than in an unfavourable axial orientation (transition state **b**), to give an unstable intermediate **c** followed by an immediate *anti*-elimination of Ph_2S to furnish *cis*-epoxides. When using sulfonium salt **2** instead of **4** at low temperature in the presence of LiBr, $CH{=}CHSiMe_3$ was slightly larger than SR'_2 (R′ = Me) and transition state **b** ($CH{=}CHSiMe_3$ situated preferentially in an equatorial orientation) was more favourable than transition state **a** (R′ = Me). The favourable intermediate **d** from transition state **b** was therefore predominant and would lead to epoxides with a *trans*:*cis* ratio of 2:1.

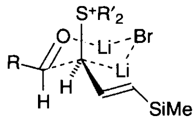
The compatibility of a wide range of substrates, *i.e.* aryl, heteroaryl and aliphatic aldehydes, excellent yields, high stereoselectivity and the expected variety of chemical transformations of the product suggest that the present method would be potentially useful for the synthesis of complex molecules.

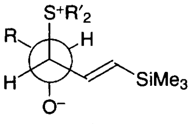

Intermediate **A**


Intermediate **B**


R′ = Ph or Me
Transition state **a**


Intermediate **c**


R′ = Ph or Me
Transition state **b**


Intermediate **d**

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8 Prepared by a method similar to ref. 6.

9 Prepared by a method similar to ref. 5*a* but using $AgClO_4$ instead of $AgBF_4$.

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