Mechanistic studies of a Pummerer-type reaction in acyclic and rigid cyclic sulfoxides induced by ketene *tert*-butyldimethylsilyl methyl acetal

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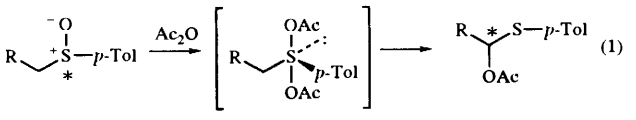
The Pummerer-type reaction of acyclic and rigid cyclic sulfoxides with ketene *tert*-butyldimethylsilyl methyl acetal **2** in the presence of a catalytic amount of zinc iodide in acetonitrile has been shown to proceed with highly stereoselective deprotonation of the α-methylene proton. A plausible reaction mechanism involving an *anti* elimination process is proposed based on an isotope labelling experiment using *syn*- and *anti*-[α-$^2H_1$]benzyl methyl and [α-$^2H_1$]benzyl *tert*-butyl sulfoxides.

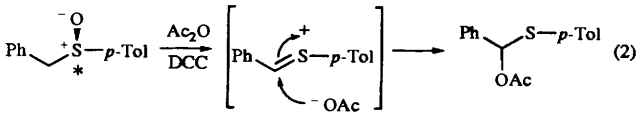
The Pummerer reaction of sulfoxides is a useful method for the synthesis of α-substituted sulfides[1] and has attracted considerable synthetic and mechanistic attention.[2] The stereoselective Pummerer reaction of optically active sulfoxides,[3–7] which is one of the self-immolative-type asymmetric transformations,[8] is of considerable interest, because it could provide a means of synthesizing chiral, non-racemic α-substituted sulfides. Although detailed studies of the Pummerer reaction using ^{18}O tracer experiments[9] showed intermolecular rearrangements to be involved, the whole mechanism is still unclear, especially in the reaction of chiral, non-racemic acyclic sulfoxides. In the late 1970s, the first asymmetric Pummerer reaction of chiral, non-racemic acyclic sulfoxides was independently reported by Oae and co-workers[5] and Mikolajczyk *et al.*[6] [eqn. (1)]. The extent of asymmetric transformation, however,



(1)

R = CN,[5] PO(OMe)$_2$[6] sulfurane < 30% ee

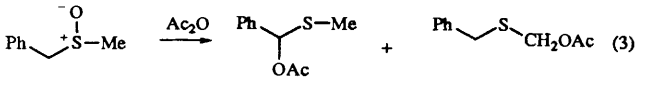
never exceeded 30% ee probably owing to the formation of a sulfurane intermediate by reaction with the generated acetate anion. Although the stereoselectivity was improved up to 70% ee by the addition of 1,3-dicyclohexylcarbodiimide (DCC) as an effective scavenger of acetic acid, the chemical yield decreased to 10%,[7] and the Pummerer reaction of chiral, non-racemic benzyl tolyl sulfoxide *R*-**1a** in the presence of DCC gave only a racemic adduct *via* the sulfonium intermediate [eqn. (2)].[10]



(2)

R-**1a** racemic

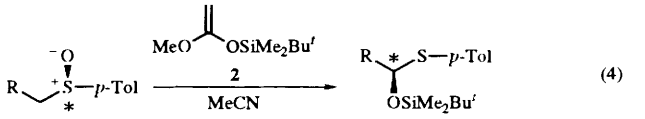
Wolfe and Kazmaier studied diastereotopic selectivity in the deprotonation step of *syn*- and *anti*-[α-$^2H_1$]benzyl methyl sulfoxides under normal Pummerer conditions.[11] According to their paper, little selectivity was observed because of competing epimerization at the sulfur *via* the sulfurane intermediate. Furthermore, regioselectivity was not evident in the reaction, *i.e.* the Pummerer reaction of benzyl methyl sulfoxide **1b** gave two regioisomers [acetoxy(phenyl)methyl methyl sulfide and acetoxymethyl benzyl sulfide] in a ratio of 45:55 in 39% yield [eqn. (3)]. Several years ago, we reported a novel silicon-



(3)

1b

induced Pummerer-type reaction of sulfoxides using ketene *tert*-butyldimethylsilyl methyl acetal **2**, which gave α-siloxy sulfides under mild conditions.[12] Recently, we reported the first highly asymmetric transformation of chiral, non-racemic acyclic sulfoxides *R*-**1c** leading to enantiomerically enriched α-siloxy sulfides *R*-**3** in high yields [eqn. (4)] using our silicon-



(4)

R-**1c** *R*-**3**

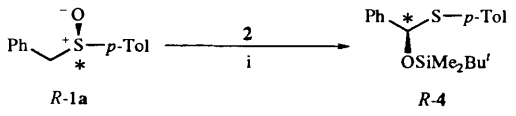
induced Pummerer-type reaction[13] and very recently communicated mechanistic studies of the asymmetric Pummerer-type reaction using a deuterium-labelling experiment.[14] We now present a full account of our mechanistic studies of the Pummerer-type reaction of acyclic sulfoxides and additional studies on rigid cyclic sulfoxides.

Pummerer-type reaction of acyclic sulfoxides with ketene *tert*-butyldimethylsilyl methyl acetal 2

Although a standard Pummerer reaction of chiral, non-racemic benzyl tolyl sulfoxide *R*-**1a** using acetic anhydride–DCC gave a racemic α-acetoxy sulfide,[10] treatment of the chiral, non-racemic *R*-**1a** with the acetal **2** using our silicon-induced Pummerer-type reaction[13] gave an 87% yield of enantiomerically enriched α-siloxy sulfide *R*-**4** {70% ee, $[\alpha]_D^{22}$ +24.6 (acetone)}† (Scheme 1). The enantiomeric purity was determined using Daicel CHIRALPAK AS as the chiral HPLC column.

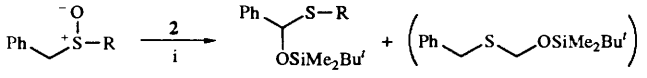
Next, we investigated the reaction of benzyl methyl sulfoxide **1b** and benzyl *tert*-butyl sulfoxide **5**, and the corresponding α-deuteriated compounds (**8a,b**)[15] with the acetal **2** and found that deprotonation of the α-proton occurred with both high regio- and diastereo-selectivity, the latter being dependent on the deprotonation step. Treatment of **1b** with **2** gave α-siloxy sulfide **6a** accompanied by a small amount of the regioisomer, benzyl α-siloxymethyl sulfide **7**. Similarly, the sulfoxide **5** was converted into the α-siloxyl sulfide **6b** in high yield (Scheme 2).

† Absolute stereochemistry of *R*-**5** was tentatively assigned from ref. 13.



R-1a *R*-4

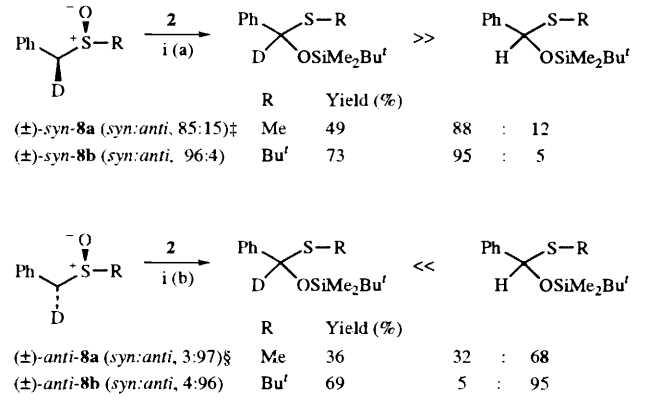
Scheme 1 *Reagents and conditions:* i, cat. ZnI_2, MeCN, 0 °C–room temp., 3–5 h



1b R = Me **6a** R = Me, 61% 7 2%
5 R = Bu^t **6b** R = Bu^t, 75%

Scheme 2 *Reagents and conditions:* i, cat. ZnI_2, MeCN, 0 °C–room temp., 0.5–4 h

Highly diastereospecific deprotonation of the α-methylene proton was observed in both *syn*- and *anti*-[α-$^2H_1$]benzyl methyl (**8a**)‡§[16] and [α-$^2H_1$]benzyl *tert*-butyl (**8b**)[15] sulfoxides. Both *syn*-**8a** and **8b** were converted into the corresponding [α-$^2H_1$]-α-siloxy sulfides with the loss of the α-proton, in contrast to the results obtained with *anti*-**8a** and **8b** which were converted into the α-siloxy sulfides with the loss of the α-deuterium, since the influence of isotope effect was quite low (Scheme 3). The stereogenicity of the sulfur atom was significant in the deprotonation step.

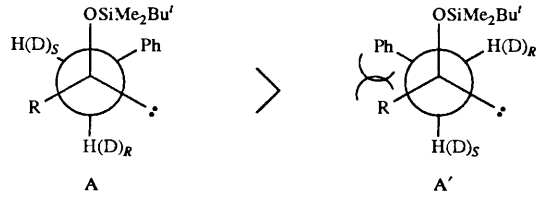


	R	Yield (%)			
(±)-*syn*-**8a** (*syn*:*anti*, 85:15)‡	Me	49	88	:	12
(±)-*syn*-**8b** (*syn*:*anti*, 96:4)	Bu^t	73	95	:	5

	R	Yield (%)			
(±)-*anti*-**8a** (*syn*:*anti*, 3:97)§	Me	36	32	:	68
(±)-*anti*-**8b** (*syn*:*anti*, 4:96)	Bu^t	69	5	:	95

Scheme 3 Silicon-induced Pummerer-type reaction of α-deuteriated sulfoxides (**8a** and **8b**). *Reagents and conditions:* i, cat. ZnI_2, MeCN, 0 °C room temp., (a) 1–6 h; (b) 1–12 h.

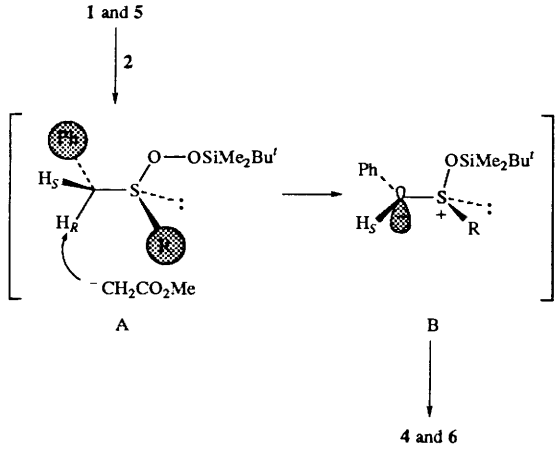
Finally, we experimented on this reaction with a mixture of *syn* and *anti* deuteriated sulfoxides. The starting mixture of chiral, optically active sulfoxides (**1a**:**1d**:**1e**:**1f**, 15:50:24:11) was prepared from *R*-**1a** by the reported method.[16] The stereochemistries of **1d** and **1e** were determined by the ^1H NMR chemical shift of the methylene proton in $CDCl_3$ (**1d**: δ 3.96; **1e**: δ 4.08). The sulfoxides **1a**,**d**–**f** were treated with **2** under the same conditions. The reaction was monitored by TLC and stopped at about 50% conversion. The recovered sulfoxides were found to have a different ratio of isomers, **1a**:**1d**:**1e**:**1f** 3:15:50:32 and the deuterium content of **4** was 77%. In this experiment, discrimination was observed between the two monodeuteriated sulfoxides **1d** and **1e**. Thus, the Pummerer-type reaction of **1d** occurred much faster than that of **1e** under these conditions. The isotope effect leads to a decrease in the rate of α-hydrogen abstraction from **1e**. This result suggested that **4** was produced with preferential loss of the sulfinyl *pro*-*R*-hydrogen in *R*-**1a** (Scheme 4).



A A′

Fig. 1

The following mechanism is proposed to explain the present results (Scheme 5). Silylation of sulfoxides with the acetal **2**

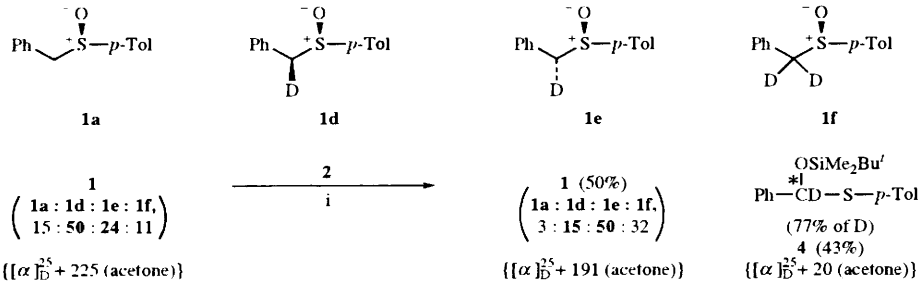


A B

Scheme 5

affords two conformers (**A** and **A′**) in which the siloxy group and the hydrogen (or deuterium) have an antiperiplanar relationship (Fig. 1). Conformer **A** is much more stable than conformer **A′** because of a gauche interaction between the phenyl group and the R group in conformer **A′**. Thus, **A** may yield an anion intermediate (**B**) through abstraction of the *pro*-*R**-hydrogen or deuterium (antiperiplanar hydrogen) with an ester enolate

‡ A small amount of **1b** (7%) and double labelled **1b** [$PhCD_2S(O)Me$, 12%] were present.
§ A small amount of **1b** (19%) and double labelled **1b** [$PhCD_2S(O)Me$, 6%] were present.



1a **1d** **1e** **1f**

1 (**1a**:**1d**:**1e**:**1f**, 15:50:24:11) {[α]$_D^{25}$ + 225 (acetone)}

1 (50%) (**1a**:**1d**:**1e**:**1f**, 3:15:50:32) {[α]$_D^{25}$ + 191 (acetone)}

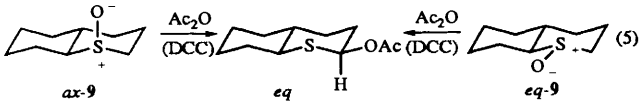
OSiMe$_2$Bu^t | Ph—CD—S—*p*-Tol (77% of D) **4** (43%) {[α]$_D^{25}$ + 20 (acetone)}

Scheme 4 Kinetic resolution of **1** with **2**. *Reagents and conditions:* i, cat. ZnI_2, MeCN, room temp., 3 h.

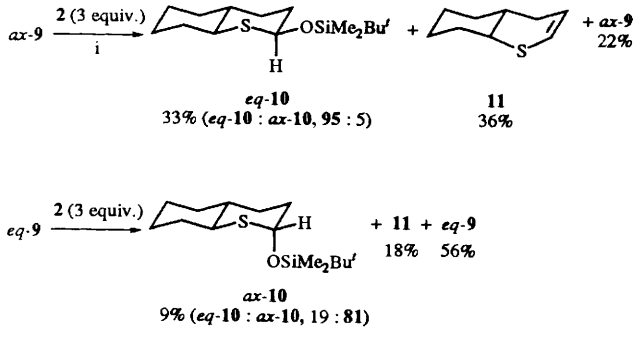
generated from the opposite face of the sulfoxide oxygen, and the siloxy group may be forced to attack the α-position as soon as the anion intermediate **B** undergoes *anti*-elimination resulting in the production of α-siloxy sulfides. Although the exact reaction process for the attack of siloxy anion on the α-carbon is not clear, it might be explained by attack on the same face as the sulfinyl oxygen as discussed in a previous paper.[13]

Pummerer-type reaction in rigid cyclic sulfoxides with the ketene acetal 2

Among several Pummerer reactions of cyclic sulfoxides,[17] a clear-cut stereoselective Pummerer reaction has been reported by Oae *et al.* in the reaction of conformationally rigid *trans*-1-thiadecalin 1-axial and 1-equatorial sulfoxides (*ax*-**9** and *eq*-**9**). In this reaction, treatment of *ax*-**9** and *eq*-**9** with acetic anhydride in the absence or presence of DCC gave the equatorial α-acetoxy sulfide in each case *via* a *trans* E-2 type elimination [eqn. (5)].[17a] In contrast to Oae's findings, an



extremely high retention of the stereochemistry of the starting sulfoxides was observed in the silicon-induced Pummerer-type reaction of both sulfoxides, *ax*-**9** and *eq*-**9**. Thus, treatment of *ax*-**9** with 3 equiv. of **2** gave the equatorial α-siloxy sulfide *eq*-**10** accompanied by the volatile olefinic sulfide **11**. In the case of *eq*-**9**, the reaction proceeded very slowly and *ax*-**10** was



Scheme 6 *Reagents and conditions:* i, cat. ZnI_2, MeCN, 65 °C, 48 h

stereoselectively obtained accompanied by a substantial amount of recovered *eq*-**9** and **11** (Scheme 6).

To clarify the reaction mechanism, the deprotonation step of the α-hydrogen was examined. The [α-$^2H_1$] sulfoxides (*ax*-[$^2H_1$]-**9** and *eq*-[$^2H_1$]-**9** for the isotope studies were prepared by a modification of Oae's methods. The deuterium content of all sulfoxides [$^2H_1$]-**9** and α-siloxy sulfides [$^2H_1$]-**10** was determined from the 500 MHz ^1H NMR spectra. Treatment of *ax*-[$^2H_1$]-**9** with **2** gave *eq*-**10** stereoselectively with retention of the α-hydrogen in the product. Upon treatment of *eq*-[$^2H_1$]-**9** with **2**, the [α-$^2H_1$] sulfide *ax*-[$^2H_1$]-**10** was obtained predominantly with retention of the α-deuterium label in the product (Scheme 7). Isotope studies strongly suggested a stereospecific *trans* E-2 type elimination similar to Oae's results, although the stereochemistry of the products was entirely different from that found by them. This difference cannot be explained in terms of the absence of sulfurane. It may involve a different contribution of the ion-pair or radical-pair intimacy and its lifetime (the very tight nature of the ion-pair or radical pair and very rapid recombination).[13]

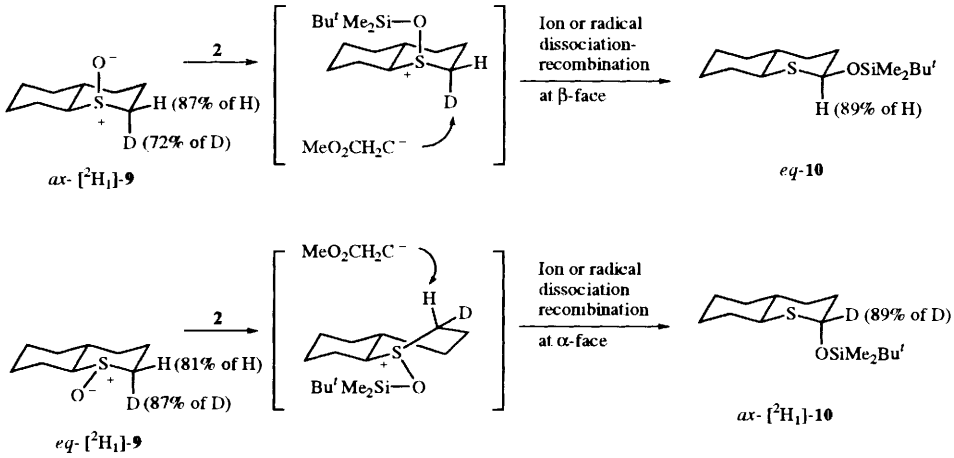
Conclusions

The first stereoselective deprotonation of the α-proton from both acyclic and rigid cyclic sulfoxides¶ was observed in a silicon-induced Pummerer-type reaction by a deuterium labelling experiment. Thus, the antiperiplanar proton or deuterium adjacent to the siloxy group was stereoselectively abstracted and subsequently the siloxy group was shifted to the α-carbon with retention of the stereochemistry on the sulfur atom.

Experimental

All mp's were determined on a Yanaco micro melting apparatus and are uncorrected. IR absorption spectra were recorded on JASCO HPIR-102 and Shimadzu FTIR-8100 spectrophotometers with $CHCl_3$ as solvent. ^1H NMR spectra were measured on JEOL JNM-FX90Q (90 MHz), JEOL JNM-EX270 (270 MHz) and JEOL JNM-GX500 (500 MHz) spectrometers with $CDCl_3$ as solvent and with tetramethylsilane as an internal standard unless otherwise noted. *J* Values are given in Hz. Mass spectra (MS) and high-resolution MS were obtained from

¶ Although a clear-cut example of *anti*-elimination in the normal Pummerer reaction was suggested by Oae *et al.*, it is limited only to a rigid six-membered thiane 1-oxide; ref. 17*a*.



Scheme 7

ESCO EMD-05A and JEOL JMS-D300 mass spectrometers. Optical rotations were measured in 1 dm cells of 1 cm^3 capacity with a Perkin-Elmer 241 instrument; $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. E. Merck silica gel 60 (70–230 mesh ASTM) for column chromatography and E. Merck precoated TLC plates with silica gel F_{254} for preparative TLC (PLC) were used. Organic layers were dried with anhydrous Na_2SO_4. All starting sulfoxides were prepared by the reported methods.[11,15,17a,18]

(*R*)-*tert*-Butyldimethylsiloxy(phenyl)methyl 4-methylphenyl sulfide *R*-4

To a solution of the sulfoxide *R*-**1a** (192.5 mg, 0.837 mmol) and ZnI_2 (26.8 mg, 0.0840 mmol) in dry MeCN at room temperature was added ketene *tert*-butyldimethylsilyl methyl acetal **2** (472.1 mg, 2.511 mmol) dropwise. The reaction mixture was stirred for 3 h under nitrogen, and then the mixture was poured into saturated aqueous sodium hydrogen carbonate and repeatedly extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried and evaporated. The residue was purified by silica gel column chromatography (2.5% AcOEt–hexane) to give *R*-**4** (250.2 mg, 87%, 70% ee) as an oil; $[\alpha]_D^{22}$ +24.6 (*c* 1.29, acetone); ν_{max}/cm^{-1} 3021, 1599 and 1491; δ_H 0.16, −0.08 (each 3 H, each s, $SiMe_2$), 0.83 (9 H, s, SiBu^t), 2.33 (3 H, s, Me), 6.10 (1 H, s, PhC*H*) and 7.09–7.36 (m, 9 H, ArH); *m*/*z* 287 (M^+ − Bu^t) [Found: (M^+ − Bu^t), 287.0957. $C_{16}H_{19}OSSi$ requires *M*, 287.0927].

General procedure for the Pummerer-type reaction of *O*-silylated ketene acetal 2 with benzyl methyl sulfoxides 1b, *syn*-8a and *anti*-8a

To a solution of the sulfoxide (0.2 mmol) and ZnI_2 (0.02 mmol) in dry MeCN at 0 °C was added *tert*-butyldimethylsilyl methyl acetal **2** (0.6 mmol) dropwise. The reaction mixture was stirred for 1 h under nitrogen, and then the mixture was poured into saturated aqueous sodium hydrogen carbonate and repeatedly extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried and evaporated. The residue was purified by PLC to give the corresponding α-siloxy sulfide **6a**, **7** in yields between 44 and 63%.

***tert*-Butyldimethylsiloxy(phenyl)methyl methyl sulfide 6a and benzyl *tert*-butyldimethylsiloxymethyl sulfide 7.** (*i*) **1b** (28.0 mg, 0.182 mmol), **2** (103 mg, 0.545 mmol) and ZnI_2 (5.8 mg, 0.0182 mmol) gave an inseparable mixture of **6a** and **7** (30.7 mg, 63%) (**6a**:**7**, 97:3) as an oil; ν_{max}/cm^{-1} 2859 and 1472; δ_H 0.07 and 0.18 (each 3 H, each s, $SiMe_2$), 0.93 (9 H, s, SiBu^t), 1.95 (97/100 × 3 H, s, Me), 4.67 (3/100 × 2 H, s, PhC*H*), 5.95 (97/100 × 1 H, s, PhC*H*) and 7.14–7.45 (5 H, m, ArH); *m*/*z* 268 (M^+) (Found: M^+, 268.1319. $C_{14}H_{24}OSSi$ requires *M*, 268.1318).

(*ii*) *syn*-**8a** {29.2 mg, 0.188 mmol; a mixture of **1b**, *syn*-**8a**, *anti*-**8a** and [$^2H_2$]-**1b** (7:69:12:12)}, **2** (106.3 mg, 0.565 mmol) and ZnI_2 (6.0 mg, 0.0188 mmol) gave an inseparable mixture of **6a**, [$^2H_1$]-**6a** and **7** (26.8 mg, 53%), (**6a**:[$^2H_1$]-**6a**:**7**, 11:82:7) as an oil; ν_{max}/cm^{-1} 2859 and 1472; δ_H 0.07 and 0.18 (each 3 H, each s, $SiMe_2$), 0.93 (9 H, s, SiBu^t), 1.95 (93/100 × 3 H, s, Me), 4.67 (7/100 × 2 H, s, PhC*H*), 5.96 (11/100 × 1 H, s, PhC*H*) and 7.20–7.46 (5 H, m, ArH). [$^2H_1$]-**6a**; *m*/*z* 212 (M^+ − Bu^t) [Found: (M^+ − Bu^t), 212.0682. $C_{10}H_{14}DOSSi$ requires *M*, 212.0676].

(*iii*) *anti*-**8a** {31.8 mg, 0.205 mmol, a mixture of **1b**, *syn*-**8a**, *anti*-**8a** and [$^2H_2$]-**1b** (19:2:73:6)}, **2** (116.0 mg, 0.615 mmol) and ZnI_2 (6.5 mg, 0.0205 mmol) gave an inseparable mixture of **6a**, [$^2H_1$]-**6a** and **7** (23.2 mg, 44%), (**6a**:[$^2H_1$]-**6a**:**7**, 56:26:18) as an oil; ν_{max}/cm^{-1} 2859 and 1472; δ_H 0.06, 0.18 (each 3 H, each s, $SiMe_2$), 0.93 (9 H, s, SiBu^t), 1.95 (82/100 × 3 H, s, Me), 4.67 (18/100 × 2 H, s, PhC*H*), 5.95 (56/100 × 1 H, s, PhC*H*) and 7.23–7.46 (5 H, m, ArH).

General procedure for the Pummerer-type reaction of *O*-silylated ketene acetal 2 with benzyl *tert*-butyl sulfoxides 5, *syn*-8b and *anti*-8b

To a solution of the sulfoxide (0.2 mmol) and ZnI_2 (0.02 mmol) in dry MeCN at 0 °C, was added *tert*-butyldimethylsilyl methyl acetal **2** (0.6 mmol) dropwise. The reaction mixture was stirred for 4–12 h under nitrogen, and then the mixture was poured into saturated aqueous sodium hydrogen carbonate and repeatedly extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried and evaporated. The residue was purified by PLC to give the corresponding α-siloxy sulfide **6b** in yields between 69 and 75%.

***tert*-Butyl *tert*-butyldimethylsiloxy(phenyl)methyl sulfide 6b.** (*i*) **5** (36 mg, 0.184 mmol), **2** (103.5 mg, 0.551 mmol) and ZnI_2 (5.7 mg, 0.0184 mmol) gave, after 4 h, **6b** (42.4 mg, 75%) as an oil; ν_{max}/cm^{-1} 2963 and 1471; δ_H −0.23 and 0.13 (each 3 H, each s, $SiMe_2$), 0.89 (9 H, s, SiBu^t), 1.42 (9 H, s, SBu^t), 6.10 (1 H, s, PhC*H*) and 7.24–7.43 (5 H, m, ArH); *m*/*z* 310 (M^+) (Found: M^+, 310.1785. $C_{17}H_{30}OSSi$ requires *M*, 310.1785).

(*ii*) *syn*-**8b** [31.3 mg, 0.159 mmol; a mixture of *syn*-**8b** and *anti*-**8b** (96:4)], **2** (89.7 mg, 0.477 mmol) and ZnI_2 (5.1 mg, 0.0159 mmol) gave, after 6 h, an inseparable mixture of **6b** and [$^2H_1$]-**6b** (36.3 mg, 73%) (**6b**:[$^2H_1$]-**6b**, 5:95) as an oil; ν_{max}/cm^{-1} 2963 and 1472; δ_H −0.23 and 0.12 (each 3 H, each s, $SiMe_2$), 0.88 (9 H, s, SiBu^t), 1.41 (9 H, s, SBu^t), 6.10 (5/100 × 1 H, s, PhC*H*) and 7.24–7.43 (5 H, m, ArH); *m*/*z* 311 (M^+) (Found: M^+, 311.1845. $C_{17}H_{29}DOSSi$ requires *M*, 311.1846).

(*iii*) *anti*-**8b** [30.0 mg, 0.152 mmol; a mixture of *syn*-**8b** and *anti*-**8b** (4:96)], **2** (85.9 mg, 0.457 mmol) and ZnI_2 (4.8 mg, 0.0152 mmol) gave, after 12 h, an inseparable mixture of **6b** and [$^2H_1$]-**6b** (32.3 mg, 69%) (**6b**:[$^2H_1$]-**6b**, 95:5) as an oil; ν_{max}/cm^{-1} 2961 and 1462; δ_H −0.23 and 0.13 (each 3 H, each s, $SiMe_2$), 0.89 (9 H, s, SiBu^t), 1.42 (9 H, s, SBu^t, 6.10 (95/100 × 1 H, s, PhC*H*) and 7.24–7.43 (5 H, m, ArH).

[α-$^2H_1$]Benzyl 4-methylphenyl sulfoxides 1d,e

To a solution of (*R*)-benzyl 4-methylphenyl sulfoxide *R*-**1a** (96.0 mg, 0.417 mmol) in dry THF (9 cm^3) at 0 °C, was added butyllithium (1.6 mol dm^{-3} in hexane; 0.287 cm^3, 0.459 mmol) dropwise. The reaction mixture was stirred for 20 min under nitrogen, and then D_2O was added. The mixture was poured into saturated aqueous ammonium chloride and repeatedly extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried and evaporated. The residue was recrystallized from CH_2Cl_2–hexane to give the monodeuteriated sulfoxides **1d,e** (93%); $[\alpha]_D^{25}$ +225 (*c* 0.55, acetone). The sulfoxide was a mixture of **1a**, **1d**, **1e** and **1f** (15:50:24:11). For **1d** and **1e**: *m*/*z* 231 (M^+) (Found: M^+, 231.0859. $C_{14}H_{13}DOS$ requires *M*, 231.0828); for **1f**: *m*/*z* 232 (M^+) (Found: M^+, 232.0909. $C_{14}H_{12}D_2OS$ requires *M*, 232.0891).

Pummerer-type reaction of *O*-silylated ketene acetal 2 with [α-$^2H_1$]benzyl 4-methylphenyl sulfoxides 1d,e

To a solution of benzyl 4-methylphenyl sulfoxides **1d,e** {23.9 mg, 0.10 mmol, 91.7% ee, $[\alpha]_D^{25}$ +225.4 (*c* 0.55, acetone)} and ZnI_2 (3.2 mg, 0.010 mmol) in dry MeCN at room temperature, was added *tert*-butyldimethylsilyl methyl acetal **2** (29.5 mg, 0.155 mmol) dropwise. The reaction mixture was stirred for 3 h under nitrogen. The reaction was monitored by TLC. When the reaction reached about 50% conversion, the mixture was poured into saturated aqueous sodium hydrogen carbonate and repeatedly extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried and evaporated. The residue was purified by PLC to give the corresponding α-siloxy sulfide **4** and [$^2H_1$]-**4** (17.7 mg, 43%), (**4**:[$^2H_1$]-**4**, 23:77) and recovered starting material **1d,e** {10.3 mg, $[\alpha]_D^{25}$ +191.3 (*c* 0.40, acetone)} as an oil; $[\alpha]_D^{22}$ +20.3 (*c* 1.29, acetone); δ_H −0.16 and −0.08 (each 3 H, each s, $SiMe_2$), 0.83 (9 H, s, SiBu^t), 2.33 (3 H,

s, Me), 6.10 (23/100 × 1 H, s, PhC*H*) and 7.09–7.36 (9 H, m, ArH). [$^2H_1$]-**4**: *m/z* 288 (M^+ − Bu^t) [Found: (M^+ − Bu^t), 288.0986. $C_{16}H_{18}$DOSSi requires *M*, 288.0989]. Recovered starting material **1d,e** was a mixture of **1a**, **1d**, **1e** and **1f** (3:15:50:32).

General procedure for the Pummerer-type reaction of *O*-silylated ketene acetal 2 with thiadecalin oxides *ax*-9, *eq*-9 ‖

To a solution of sulfoxide **9** (0.3 mmol) and ZnI_2 (0.03 mmol) in dry MeCN at room temperature, was added *tert*-butyldimethylsilyl methyl acetal **2** (0.9 mmol) dropwise. The reaction mixture was warmed to 65 °C, after which it was stirred for 48 h under nitrogen and then evaporated. The residue was purified by PLC to give the corresponding α-siloxy sulfides *ax*-**10**, *eq*-**10**, olefin **11** and the starting sulfoxide **9**.

***eq*-2-*tert*-Butyldimethylsiloxythiadecalin *eq*-10.** *ax*-**9** (49.9 mg, 0.290 mmol), **2** (163.6 mg, 0.870 mmol) and ZnI_2 (9.3 mg, 0.029 mmol) gave a mixture of *ax*-**10**, *eq*-**10** and **11** (36.2 mg, *ax*-**10**:*eq*-**10**:**11**, 5:95:110) and *ax*-**9** (11.2 mg, 22%). *eq*-**10** was isolated in a pure state by PLC as an oil; ν_{max}/cm^{-1} 1472, 1464 and 1449; δ_H 0.05 and 0.06 (each 3 H, each s, $SiMe_2$), 0.83 (9 H, s, $SiBu^t$), 0.7–1.7 (12 H, m), 1.97–2.09 (1 H, m), 2.35–2.42 (1 H, m) and 4.74 (1 H, dd, *J* 3.7 and 10.1, *ax*-2-H); *m/z* 286 (M^+) (Found: M^+, 286.1768. $C_{15}H_{30}OSSi$ requires *M*, 286.1784).

***ax*-2-*tert*-Butyldimethylsiloxythiadecalin *ax*-10.** *eq*-**9** (50.5 mg, 0.294 mmol), **2** (165.8 mg, 0.882 mmol) and ZnI_2 (9.4 mg, 0.029 mmol) gave a mixture of *ax*-**10**, *eq*-**10** and **11** (11.6 mg, *ax*-**10**:*eq*-**10**:**11**, 81:19:200) and *eq*-**9** (28.4 mg, 56%). *ax*-**10** was isolated in a pure state by PLC as an oil; ν_{max}/cm^{-1} 1449, 1262 and 1100; δ_H 0.02, 0.07 (each 3 H, each s, $SiMe_2$), 0.84 (9 H, s, $SiBu^t$), 0.8–2.0 (13 H, m), 2.70–2.77 (1 H, m) and 4.89 (1 H, br s, *eq*-2-H); *m/z* 286 (M^+) (Found: M^+, 286.1784. $C_{15}H_{30}OSSi$ requires *M*, 286.1784).

[2-*ax*-$^2H_1$]Thiadecalin 1-*ax*-oxide *ax*-[$^2H_1$]-9

To a solution of *ax*-**9** (872 mg, 5.07 mmol) in THF (20 cm^3) at −78 °C, was added butyllithium (1.6 mol dm^{-3} in hexane; 3.5 cm^3, 5.60 mmol) dropwise. The reaction mixture was stirred for 1 h under nitrogen, then quenched with CD_3OD (1.0 cm^3). After 1 h, D_2O (0.1 cm^3) was added to this solution. The mixture was warmed to room temperature, then poured into saturated aqueous ammonium chloride and repeatedly extracted with CH_2Cl_2. The combined organic layers were dried with anhydrous $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography (3% MeOH–AcOEt) to give *ax*-[$^2H_1$]-**9** (393 mg, 45%) as white crystals, mp 87 °C (cyclohexane); ν_{max}/cm^{-1} 2930 and 1027; δ_H 0.8–2.4 (14 H, m), 2.3–2.4 (28/100 × 1 H, m, *ax*-2-H) and 3.04 (87/100 × 1 H, br s, *eq*-2-H).

[2-ax-$^2H_1$]Thiadecalin 1-*eq*-oxide *eq*-[$^2H_1$]-9

To a solution of *eq*-**9** (900 mg, 5.23 mmol) in THF (20 cm^3) at −78 °C, was added butyllithium (1.6 mol dm^{-3} in hexane; 3.6 cm^3, 5.75 mmol) dropwise. The reaction mixture was stirred for 1 h under nitrogen, then quenched with D_2O. The mixture was warmed to room temperature then poured into saturated aqueous ammonium chloride and repeatedly extracted with CH_2Cl_2. The combined organic layers were dried with anhydrous $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography (3% MeOH–AcOEt) to give *eq*-[$^2H_1$]-**9** (850 mg, 94%) as white crystals, mp 71 °C (cyclohexane); ν_{max}/cm^{-1} 2930 and 1035; δ_H 0.8–2.5 (14 H, m), 2.5–2.6 (13/100 × 1 H, m, *ax*-2-H), 3.30 (81/100 × 1 H, br s, *eq*-2-H).

‖ Thiadecalin = 3,4,4a,5,6,7,8,8a-octahydro-2*H*-thiachromene.

General procedure for the Pummerer-type reaction of *O*-silylated ketene acetal 2 with [$^2H_1$]thiadecalin oxides *ax*-[$^2H_1$]-9, *eq*-[$^2H_1$]-9

To a solution of the sulfoxide [$^2H_1$]-**9** (0.4 mmol) and ZnI_2 (0.04 mmol) in dry MeCN at room temperature, was added ketene *tert*-butyldimethylsilyl methyl acetal **2** (1.2 mmol) dropwise. The reaction mixture was warmed to 65 °C, after which it was stirred for 48 h under nitrogen and then evaporated. The residue was purified by PLC to give the corresponding α-siloxy sulfide **10**.

(*i*) *ax*-[$^2H_1$]-**9** (75.0 mg, 0.434 mmol), **2** (244.4 mg, 1.30 mmol) and ZnI_2 (13.8 mg, 0.043 mmol) gave *eq*-**10** (35.2 mg, 28%) as an oil; δ_H 0.05 and 0.06 (each 3 H, each s, $SiMe_2$), 0.83 (9 H, s, $SiBu^t$), 0.7–1.7 (12 H, m), 1.97–2.09 (1 H, m), 2.35–2.42 (1 H, m) and 4.74 (89/100 × 1 H, dd, *J* 3.7 and 10.1, *ax*-2-H); *m/z* 230 (M^+ − Bu^t) [Found: (M^+ − Bu^t), 230.1141. $C_{11}H_{20}$DOSSi requires *M*, 230.1145]. There was 11% ^2H at *ax*-2 H, which was determined by ^1H NMR.

(*ii*) *eq*-[$^2H_1$]-**9** (72.7 mg, 0.420 mmol), **2** (236.9 mg, 1.26 mmol) and ZnI_2 (13.4 mg, 0.042 mmol) gave *ax*-**10** (10.7 mg, 9%) as an oil; δ_H 0.03 and 0.07 (each 3 H, each s, $SiMe_2$), 0.84 (9 H, s, $SiBu^t$), 0.8–2.0 (13 H, m), 2.70–2.77 (1 H, m), 4.89 (11/100 × 1 H, br s, *eq*-2-H); *m/z* 230 (M^+ − Bu^t) [Found: (M^+ − Bu^t), 230.1139. $C_{11}H_{20}$DOSSi requires *M*, 230.1145]. There was 89% ^2H at *eq*-2H, which was determined by ^1H NMR.

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References

1 R. Pummerer, *Ber. Dtsch. Chem. Ges.*, 1909, **42**, 2282; 1910, **43**, 1401; L. Horner and P. Kaiser, *Justus Liebigs Ann. Chem.*, 1959, **626**, 19; L. Horner, *Justus Liebigs Ann. Chem.*, 1960, **631**, 198.
2 Reviews, see: T. Durst, *Adv. Org. Chem.*, 1969, **6**, 285; T. Numata and S. Oae, *Yuki Gosei Kagaku Kyokai Shi*, 1977, **35**, 726 (*Chem. Abstr.*, 1978, **88**, 5639s); J. P. Marino, *Topics in Sulfur Chemistry*, ed. A. Senning, George Thieme Publishers, Stuttgart, 1976, vol. 1, p.1; T. Numata, *Yuki Gosei Kagaku Kyokai Shi*, 1978, **36**, 845 (*Chem. Abstr.*, 1979, **90**, 136847x); S. Oae, T. Numata and T. Yoshimura, *Heterosulphonium Salts*, in *The Chemistry of the Sulphonium Group*, eds. C. J. M. Stirling and S. Patai, Wiley, New York, 1981, part 2, ch. 15.
3 J. E. McCormick and R. S. McElhinney, *J. Chem. Soc., Chem. Commun.*, 1969, 171; S. Glue, I. T. Kay and M. R. Kipps, *J. Chem. Soc., Chem. Commun.*, 1970, 1158.
4 B. Stridsberg and S. Allenmark, *Acta Chem. Scand., Ser. B*, 1974, **28**, 591; 1976, **30**, 219; S. Wolfe, P. M. Kazmaier and H. Auski, *Can. J. Chem.*, 1979, **57**, 2404; T. Kaneko, Y. Okamoto and K. Hatada, *J. Chem. Soc., Chem. Commun.*, 1987, 1511.
5 T. Numata and S. Oae, *Tetrahedron Lett.*, 1977, 1337; T. Numata, O. Itoh and S. Oae, *Chem. Lett.*, 1977, 909.
6 M. Mikolajczyk, A. Zatorski, S. Grzejszczak, B. Costisella and W. Midura, *J. Org. Chem.*, 1978, **43**, 2518.
7 T. Numata, O. Itoh and S. Oae, *Tetrahedron Lett.*, 1979, 1869; T. Numata, O. Itoh, T. Yoshimura and S. Oae, *Bull. Chem. Soc. Jpn.*, 1983, **56**, 257.
8 K. Mislow, *Introduction to Stereochemistry*, W. A. Benjamin, New York, 1965.
9 Reviews, see: S. Oae and T. Numata, *The Pummerer Type of Reactions*, in *Isotopes in Organic Chemistry*, eds. E. Buncel and C. C. Lee, Elsevier, New York, 1980, vol. 5, ch. 2; O. D. Lucchi, U. Miotti and G. Modena, *Org. React.*, 1990, **40**, 157.
10 O. Itoh, T. Numata, T. Yoshimura and S. Oae, *Bull. Chem. Soc. Jpn.*, 1983, **56**, 266.
11 S. Wolfe and P. M. Kazmaier, *Can. J. Chem.*, 1979, **57**, 2388, 2397.
12 Y. Kita, H. Yasuda, O. Tamura, F. Itoh and Y. Tamura, *Tetrahedron Lett.*, 1984, **25**, 4681; Y. Kita, O. Tamura, H. Yasuda, F. Itoh and Y. Tamura, *Chem. Pharm. Bull.*, 1985, **33**, 4235; Y. Kita, O. Tamura, F. Itoh, H. Yasuda, T. Miki and Y. Tamura, *Chem. Pharm. Bull.*, 1987, **35**, 562.

13 Y. Kita, N. Shibata and N. Yoshida, *Tetrahedron Lett.*, 1993, **34**, 4063; Y. Kita, N. Shibata, N. Yoshida and S. Fujita, *J. Chem. Soc., Perkin Trans. 1*, 1994, 3335.
14 Y. Kita, N. Shibata, N. Yoshida, S. Fukui and C. Fujimori, *Tetrahedron Lett.*, 1994, **35**, 2569.
15 K. Nakamura, M. Higaki, S. Adachi, S. Oka and A. Ohno, *J. Org. Chem.*, 1987, **52**, 1414. Deuterium contents of all sulfoxides and α-siloxy sulfides were determined by 200, 250 and 270 MHz ^{1}H NMR spectra.
16 M. Nishio, *Chem. Commun.*, 1968, 562. The *pro-R*-proton in *R*-benzyl *p*-chlorophenyl sulfoxide appeared at a higher field in $CDCl_3$.
17 (*a*) S. Oae, O. Itoh, O. Numata and O. Yoshimura, *Bull. Chem. Soc. Jpn.*, 1983, **56**, 270; (*b*) T. Masuda, T. Numata, N. Furukawa and S. Oae, *J. Chem. Soc., Perkin Trans. 2*, 1978, 1302; (*c*) M. Bhupathy and T. Cohen, *Tetrahedron Lett.*, 1987, **28**, 4793; (*d*) F. S. Gonzalez and P. G. Mendoza, *Carbohydr. Res.*, 1988, **183**, 227.
18 K. Mislow, M. M. Green, P. Laur, J. T. Malillo, T. Simmons and A. L. Ternay, *J. Am. Chem. Soc.*, 1965, **87**, 1958.

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