Novel Transformation of β-Keto Sulfoxides to Unsaturated β-Keto Sulfides

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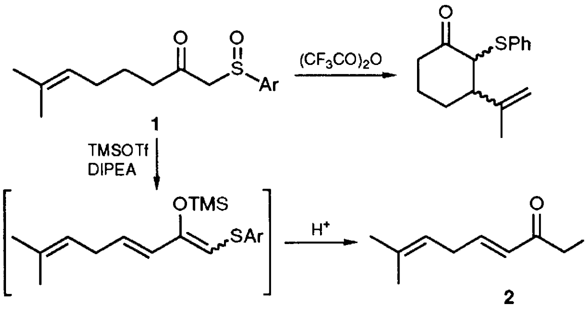
Reaction of β-keto sulfoxides with trimethylsilyl trifluoromethanesulfonate in the presence of diisopropylethylamine afforded the corresponding (1*E*,3*E*)-1-phenylthio-2-(trimethylsilyloxy)-1,3-diene derivatives which underwent hydrolysis to furnish 1-phenylthio-alk-3-en-2-one derivatives in high yields.

β-Keto sulfoxides are useful synthetic intermediates; a variety of methods, including the Pummerer reaction, reduction and alkylation, may be used for transformation of the sulfoxide functionality which eventually leads to sulfur-free compounds.[1] As a part of our continuing synthetic studies using sulfur compounds,[2] we examined the reactivity of the unsaturated β-keto sulfoxide **1** *via* the corresponding thionium cation and observed that **1** underwent cyclisation with trifluoroacetic anhydride[3] to give cyclohexanone derivatives. In contrast with these findings, reaction of **1** with trimethylsilyl trifluoromethanesulfonate (TMSOTf) in the presence of tertiary amine bases took a completely different pathway which led to the formation of the α,β-unsaturated β-keto sulfide **2** in 45% yield after silica gel chromatography (Scheme 1). TLC monitoring implied that **2** was the hydrolysed product of the initially formed silyl enol ether. Here we report this novel and facile transformation of β-keto sulfoxides into α,β-unsaturated β-keto sulfides.

β-Keto sulfoxides **3** were routinely prepared from esters and the lithium carbanion of methyl phenyl sulfoxide. Among the several conditions examined, the best results were obtained when **3** was treated with TMSOTf (3 equiv.) and diisopropylethylamine (DIPEA) (4 equiv.) in dichloromethane at room temperature. Thus, the reaction of **3a** under these conditions for 2 h, followed by alkaline aqueous work-up, gave the (1*E*,3*E*)-hexadiene **4a** in quantitative yield (Scheme 2).† The *E* configuration of the C-3, C-4 double bond in **4a** was assigned on the basis of the observed coupling constant (*J* 15.4 Hz in C_6D_6) for the vinylic signals. The *E* configuration of the silyl enol ether moiety was determined from the comparison of the chemical shift (δ 5.45) of the C-1 vinylic proton with that (δ 5.39) of the *Z*-silyl enol ether (**Z-4**) derived from the β-keto sulfide **5a**.[4]



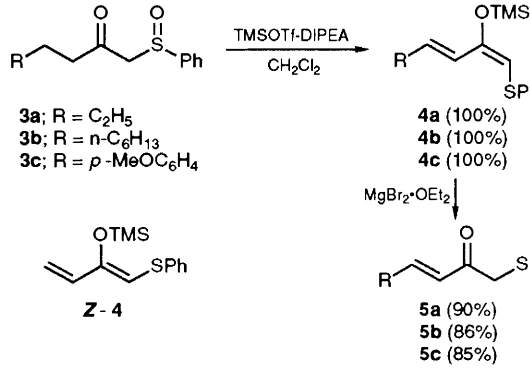
Scheme 1

The rather labile diene **4a** reacted with $MgBr_2{\cdot}Et_2O$ in dichloromethane to afford (*E*)-1-phenylthiohex-3-ene-2-one **5a** in 90% yield; hydrolysis using aqueous mineral acids or fluoride ion was unsatisfactory. Other examples are shown in Scheme 2. In an attempt to extend this method, the reaction of β-keto sulfoxides having an alkyl branch at the γ or δ position was examined; these reactions were extremely slow, resulting in the low yields.

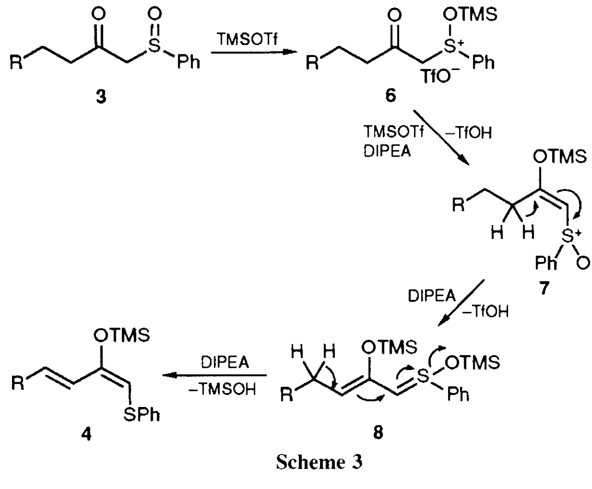
The use of iodotrimethylsilane–DIPEA[5] or TMSOTf–triethylamine was also successful for the present transformation but a significant amount of the sulfide derived from direct reduction of the sulfinyl moiety was formed in addition to **4**. It is noted that **4** was not formed in the absence of tertiary amines. Furthermore, replacement of TMSOTf with chlorotrimethylsilane resulted in complete recovery of the starting sulfoxides.

Thus, the formation of **4** may be accounted for by oxidation of the γ and δ positions with concomitant reduction of the sulfoxide. A plausible pathway may involve the conversion of the siloxy sulfonium triflate **6** into the intermediate silyl enol ether **7**. Subsequent double deprotonation from the γ and δ positions assisted by the sulfur moiety would result in the formation of **4** as shown in Scheme 3.

The present procedure can also be extended to prepare 2-(trimethylsilyloxy)-trienyl sulfides from α,β-unsaturated β-keto sulfoxides. The sulfoxides **9a** and **9b**, obtained by oxidation of **5a** and **5b** respectively with *m*-chloroperbenzoic



Scheme 2



Scheme 3

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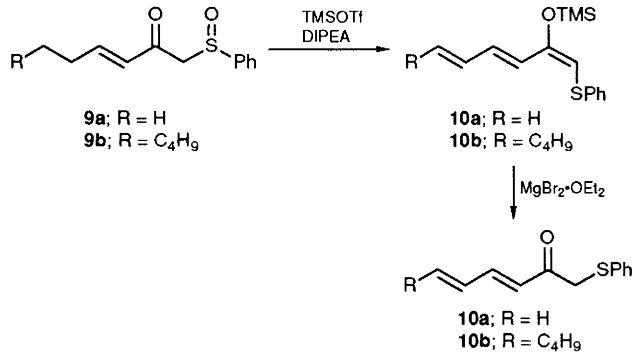
† All new compounds described here show satisfactory spectral, microanalytical and/or high-resolution mass data.

General procedure: to a cold (0 °C) solution of **3a** (1.343 g, 5.99 mmol) and diisopropylethylamine (4.2 ml, 24 mmol) in dry dichloromethane (3 ml) was added trimethylsilyl trifluoromethanesulfonate (0.5 mol l^{-1} in dichloromethane; 36 ml, 18 mmol) under N_2. After being stirred for 2 h at room temperature, the solution was poured into cold aqueous $NaHCO_3$ and extracted with diethyl ether–hexanes (1 : 1). The combined organic layers were washed with water and brine, and dried over anhydrous Na_2SO_4. Evaporation of the solvent left 1.676 g (100%) of **4a** which was homogeneous by TLC and spectral analysis. The silyl enol ether **4a** (1.04 g, 3.34 mmol) was treated with $MgBr{\cdot}Et_2O$ (980 mg) in dichloromethane (25 ml) for 3.5 h. Usual aqueous work-up and purification of the oily residue by chromatography (Florisil, EtOAc–hexanes) gave 695 mg (90% yield) of **5a**.



Scheme 4

acid (MCPBA), were treated with TMSOTf and DIPEA under the same conditions as described above, providing the corresponding trienes **10a** and **10b** in almost quantitative yields.‡ Reaction with $MgBr_2 \cdot Et_2O$ gave the dienyl β-keto sulfides **11a** and **11b**, in 48 and 58% yields, respectively (Scheme 4). The low yields for the latter step may be due to the instability of the products under these conditions.

In conclusion, we have shown a novel transformation of β-keto sulfoxides in which the change of the valence state of the sulfinyl moiety participates in the introduction of unsaturation at the γ,δ-positions beyond the β-carbonyl moiety. Furthermore, the present method is applicable to the preparation of dienyl carbonyl derivatives.

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‡ The stereochemistry of **10a** and **10b** could not be determined. However, we assume **10a** and **10b** are all *E* from the analogy with **4** and the stereochemistry of **11**. It is noted that the yields of the hydrolysis step were considerably higher (⩾72%) when the products were isolated as the corresponding sulfoxides after oxidation with MCPBA. **11a**: ^1H NMR (250 MHz, $CDCl_3$) δ 3.79 (s, 2H), 5.57 (d, *J* 10.5, 1H), 5.66 (d, *J* 17.0, 1H), 6.43 (d, *J* 15.5, 1H), 6.46 (dt, *J* 17.0, 10.5, 1H), 7.18 (dd, *J* 15.5, 10.5, 1H) and 7.2–7.4 (m, 5H). **11b**: ^1H NMR (250 MHz, C_6D_6) δ 0.80 (br t, *J* 6.8, 3H), 1.1–1.3 (m, 4H), 1.82 (q, *J* 10.6, 2H), 3.43 (s, 2H), 5.69 (dt, *J* 15.1, 6.8, 1H), 5.87 (dd, *J* 15.1, 10.6, 1H), 6.21 (d, *J* 15.3, 1H), 7.21 (dd, *J* 15.3, 10.6, 1H) and 6.8–7.4 (m, 5H). All *J* values are in Hz.