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Tin-Pummerer Rearrangement in the Synthesis of *O,S*-Acetal Derivatives

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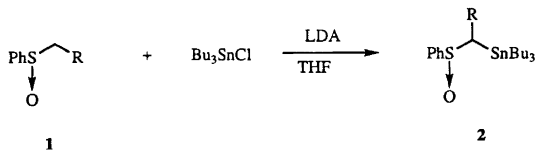
α-Thioalkyl esters and carbonates have been prepared by a tin-Pummerer rearrangement in reactions of α-stannylated sulfoxides with acid chlorides or chloroformates, respectively. Acid chlorides have a higher reactivity than chloroformates in this reaction.

We have previously shown that α-oxygenated sulfides are precursors for α-halo ethers,[1] α-haloalkyl esters[2] and α-haloalkyl carbonates.[3] The α-oxygenated sulfide precursors for the α-halo ethers and the α-halo esters are readily prepared by reacting α-halo sulfides with alkoxides or carboxylates, respectively. A similar approach to α-thioalkyl carbonates, i.e., reaction of an α-halo sulfide with the anion of a monoester of carbonic acid, does not work because of the low nucleophilicity of carbonate anions.

α-Thioalkyl carbonates can be prepared by reacting monothioacetals with chloroformates.[3] This method can, however, only be used to prepare α-thioalkyl carbonates that are unsubstituted or substituted with an electron-withdrawing substituent, at the acylal carbon. Hemithioacetals substituted with an electron-donating group at the acetal carbon have low stability and readily revert to the corresponding thiol and aldehyde. Attempts to use *O*-silylated hemithioacetals in this reaction led only to the formation of monothio carbonates.[3]

The Pummerer rearrangement can be used to make α-oxygenated sulfides,[4] and Pohmakotr *et al.* have shown that 1-alkoxycarbonyloxy-1-phenylthiocyclopropanes, as well as other cyclopropane derivatives, can be prepared from α-stannyl sulfoxides by a tin-Pummerer rearrangement.[5] In this communication we report that the method can be extended to other α-stannyl sulfoxides.

The α-stannylated sulfoxides **2** were prepared by reacting the sulfoxides **1** with LDA (lithium diisopropylamide) at −78 °C in THF, followed by tributylstannyl chloride (Scheme 1). Both normal addition, i.e., addition of the stannyl chloride to a solution of the α-lithio sulfoxide, and reversed addition were tried (Table 1). The reversed addition gave a slightly better yield



1 2

Scheme 1.

(73–78%) than the normal addition (61–66%) in the case of methyl phenyl sulfoxide (**1**, R = H), while the opposite was true for ethyl phenyl sulfoxide (**1**, R = Me): reversed addition 65% and normal addition 72%. In the synthesis of **2b** the diastereomeric ratio was 7:1 (^{1}H NMR) using reversed addition, while it was close to 1:1 for the normal addition. Both α-metallation and alkylation of α-metallated sulfoxides are known to be highly stereoselective.[6] Thus some diastereoselectivity was to be expected in the alkylation of ethyl phenyl sulfoxide. That no diastereoselectivity was observed for the normal addition, may be due to an isomerization taking place under the basic conditions of the normal addition protocol.

The Pummerer rearrangement of the sulfoxides **2** with acid chlorides (Scheme 2) gave moderate to good yields of the α-acyloxy sulfides **3** (Table 2, entries 1–5). The yields were reduced when chloroformates were used as electrophiles (Table 2, entries 6–9), especially with the sulfoxide **2b** (Table 2, entry 8 and 9). The difference in reactivity between acid chlorides and chloroformates, might be either a reflection of the reactivity of these electrophiles towards the sulfoxide oxygen or the nucleophilicity of carboxylate anions contra carbonate anions. In hydrolysis reactions acid chlorides are more reactive than chloroformates.[7] As seen from Table 2, the reaction with chloroformates required substantially longer reaction times than the acid chlorides.

In the reaction between **2a** and ethyl chloroformate

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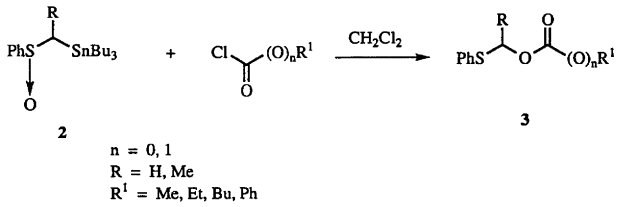
Table 1. Preparation of α-stannylated sulfoxides **2** by reaction of the sulfoxides **1** with LDA and tributylstannyl chloride.

Entry	Product	R	Conditions	Yield (%)	Diastereomeric ratio
1	**2a**	H	Reversed addition, −78 °C	73–78	—
2	**2a**	H	Normal addition, −78 °C	61–66	—
3	**2b**	Me	Reversed addition, −78 °C to 5 °C	65	7:1
3	**2b**	Me	Normal addition, −78 °C to 5 °C	72	1:1

Table 2. Preparation of α-thioalkyl ester (**3a–e**) and α-thioalkyl carbonates (**3f–i**) by reaction of the sulfoxides **2** with acid chlorides or chloroformates, respectively.

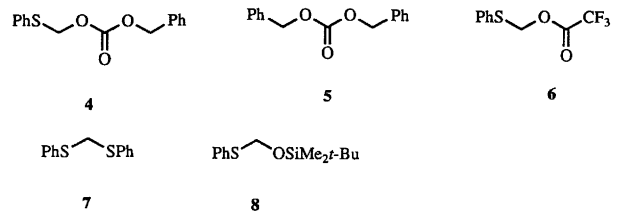
Entry	Product	*n*	R	R^1	Conditions	Yield (%)
1	**3a**	0	H	Me	R.t., 30 min	77
2	**3b**	0	H	Et	Reflux, 1 h	66
3	**3c**	0	H	Ph	0 °C, 30 min +r.t., 90 min	76
4	**3d**	0	Me	Me	0 °C, 20 min	46
5	**3e**	0	Me	Et	0 °C, 20 min	61
6	**3f**[3]	1	H	Et	Reflux, 36 h	37
7	**3g**[3]	1	H	Bu	Reflux, 44 h	40
8	**3h**[3]	1	Me	Et	Reflux, 22 h	19
9	**3i**[3]	1	Me	Bu	Reflux, 48 h	25



Scheme 2.

(entry 6) chloromethyl phenyl sulfide was isolated (11%) as a by-product. ^{1}H NMR spectroscopy of the crude product also indicated that some thioanisole had been formed in the reaction. The reaction products were the same whether the reaction was performed with or without a base [0.1 mol equiv. DMAP (4-dimethylamino-pyridine)].

The reaction of **2a** with benzyl chloroformate gave a nearly 1:1 mixture of the α-thioalkyl carbonate **4** and dibenzyl carbonate **5** (Scheme 3). These two compounds could not be separated by TLC, but dibenzyl carbonate was isolated by preparative GLC. The formation of dialkyl carbonates was observed in other reactions as well. Heating butyl chloroformate with the α-thioalkyl carbonate **3g** at 50 °C in dichloromethane for 58 h, gave



Scheme 3.

only recovered starting materials, indicating that the dialkyl carbonates are not formed from the products.

A number of electrophiles other than those mentioned in Scheme 2 were reacted with the sulfoxide **2a**. Phenyl isocyanate and dimethylcarbamoyl chloride gave only recovered starting material together with methyl phenyl sulfoxide after heating for about 50 h at 50 °C. In the reaction of **2a** with methane- or toluene-sulfonyl chloride, all starting materials were consumed, but only complex reaction mixtures resulted.

Acetic anhydride does not react with 1-tributylstannyl-1-phenylsulfinyl-cyclopropane.[5] We found that the more reactive trifluoroacetic anhydride reacted with the sulfoxide **2a** even at −78 °C, to give a mixture (9:1) of the rearranged product **6** and methyl phenyl sulfoxide (5–10% of the starting material was methyl phenyl sulfoxide). Also, triflic anhydride reacted at −78 °C with **2a**, but the only product isolated from this reaction was the *S,S*-acetal **7**. *tert*-Butyldimethylsilyl chloride gave the silylated *O,S*-acetal **8**[8] in 45% yield (89% pure by GC).

Experimental

The NMR spectra were recorded in $CDCl_3$ at 200 MHz (^{1}H) and at 50 MHz (^{13}C). The chemical shifts are given in ppm downfield from tetramethylsilane. The mass spectra, under electron impact conditions, were recorded at 70 eV ionizing energy. Methane was used for chemical ionization (CI); the spectra are presented as *m/z* (% rel. int.).

Phenylsulfinylmethyl(tributyl)stannane[9] (**2a**). Butyllithium in hexane (3.55 ml 1.7 M, 6.04 mmol) was added dropwise to diisopropylamine (0.925 ml, 6.54 mmol) in

THF (30 ml) at −78 °C under N_2 and the mixture was stirred for 30 min. Methyl phenyl sulfoxide (841 mg, 6.01 mmol) in THF (10 ml) was added dropwise and the mixture stirred for 1 h before being added dropwise (by cannula) to a solution of tributyltin chloride (1.98 g, 6.07 mmol) in THF (30 ml) at −78 °C under N_2. The mixture was stirred for 1 h before being added dropwise to 10% ammonium chloride at 0 °C and extracted with diethyl ether. The organic phase was washed with saturated sodium bicarbonate and dried (K_2CO_3). The crude product was purified by rapid flash chromatography[10] on silica gel using diethyl ether for elution. The product thus obtained usually contained 5–10 mol% (by ^{1}H NMR) of methyl phenyl sulfoxide. Yield 1.89 g (73%). ^{1}H NMR: δ 0.7–1.6 (m, Bu), 2.64 and 2.78 (AB system, *J* 11.8 Hz, CH_2SO), 7.4–7.7 (m, Ph). ^{13}C NMR: δ 11.4, 14.3, 27.7, 29.4, 40.9, 123.2, 128.5, 129.9, 147.5. MS (CI): 431/430/429/428/427 (3/3/5/2/3, *M*), 401 (3), 400 (3), 399 (3), 398 (3), 397 (2), 373 (100), 372 (37), 371 (69), 370 (27), 369 (42), 343 (11), 341 (8), 291 (54), 290 (19), 289 (41), 288 (14), 287 (24), 235 (17), 233 (15), 175 (13), 141 (17), 123 (35).

1-Phenylsulfinylethyl(tributyl)stannane (**2b**). Butyllithium in hexane (2.15 ml 1.7 M, 3.66 mmol) was added dropwise to diisopropylamine (0.570 ml, 4.03 mmol) in THF (15 ml) at −78 °C under N_2, and the mixture was stirred for 30 min. Ethyl phenyl sulfoxide[11] (564 mg, 3.66 mmol) in THF (5 ml) was added dropwise and the mixture was stirred for 1 h before being added dropwise (by cannula) to a solution of tributyltin chloride (1.19 g, 3.66 mmol) in THF (15 ml) at −78 °C under N_2. The mixture was stirred overnight (17 h), during which time the temperature reached 5 °C, and was worked up as described for **2a**. Yield: 1.06 g (65%) as a mixture of diastereoisomers. ^{1}H NMR: δ 0.7–1.7 (m, Bu and Me), 2.57 (q, *J* 7.2 Hz, CH) and 2.87 (q, *J* 7.6 Hz, CH), 7.4–7.7 (m, Ph).

(Phenylthio)methyl acetate[12] (**3a**). Acetyl chloride (100 µl, 1.41 mmol) was added to a solution of phenylsulfinylmethyl(tributyl)stannane (454 mg, 1.06 mmol) in dichloromethane (3 ml) under N_2 at ambient temperature. The mixture was stirred for 30 min and the solvent evaporated off. The residue was dissolved in diethyl ether and cooled to 0 °C. Excess aqueous potassium fluoride was added and the mixture was stirred for 30 min and filtered. The filter was washed through with diethyl ether and the aqueous layer separated. The organic layer was washed with water and dried ($MgSO_4$). The crude product was purified by flash chromatography on silica gel using ethyl acetate–hexane (15:85) for elution. Yield 149 mg (77%). ^{1}H NMR: δ 2.11 (CH_3), 5.41 (CH_2), 7.2–7.5 (m, Ph). ^{13}C NMR: δ 21.1, 68.0, 127.3, 129.1, 130.2, 134.7, 170.2. MS: 182 (8, *M*), 152 (6), 123 (4), 110 (38), 109 (7), 77 (4), 43 (100).

(Phenylthio)methyl propionate (**3b**). Propionyl chloride (156 µl, 1.79 mmol) was added to a solution of phenylsulfinylmethyl(tributyl)stannane (589 mg, 1.37 mmol) in dichloromethane (4 ml). The mixture was stirrred under N_2 for 1 h at 40–45 °C and worked up as described for **3a**. Yield 177 mg (66%), liquid. ^{1}H NMR: δ 1.16 (t, *J* 7.5 Hz, CH_3), 2.38 (q, *J* 7.5 Hz, CH_2CH_3), 5.43 (s, SCH_2O), 7.2–7.5 (m, Ph). ^{13}C NMR: δ 8.9, 27.7, 67.9, 127.3, 129.1, 130.3, 134.8, 173.7. MS: 196 (12, *M*), 166 (15), 123 (7), 110 (22), 109 (7), 77 (6), 57 (100).

(Phenylthio)methyl benzoate[2] (**3c**). Benzoyl chloride (187 µl, 1.61 mmol) was added to a solution of phenylsulfinylmethyl(tributyl)stannane (575 mg, 1.34 mmol) in dichloromethane (4 ml) at 0 °C. The mixture was stirred under N_2 for 30 min at 0 °C and then at ambient temperature for 1.5 h and worked up as described for **3a.** Ethyl acetate–hexane (1:7) was used for chromatography. Yield 250 mg (76%). ^{1}H NMR: δ 5.66 (s, CH_2), 7.2–7.65 and 8.0–8.1 (m, 8 H and m, 2 H, 2 × Ph). ^{13}C NMR: δ 68.8, 127.4, 128.1, 128.4, 129.6, 129.7, 130.6, 133.3, 134.7, 165.8. MS: 244 (9, *M*), 214 (11), 123 (3), 110 (3), 109 (4), 105 (100), 77 (36).

1-(Phenylthio)ethyl acetate[2] (**3d**). Acetyl chloride (95 µl, 1.34 mmol) was added to a solution of 1-phenylsulfinylethyl(tributyl)stannane (381 mg, 0.86 mmol) at 0 °C. The mixture was stirred under N_2 for 20 min and worked up as described for **3a**. Ethyl acetate–hexane (1:9) was used for chromatography. Yield 78 mg (46%). ^{1}H NMR: δ 1.53 (d, *J* 6.5 Hz, CH_3CH), 2.03 (s, CH_3CO), 6.22 (q, *J* 6.5 Hz, CH), 7.25–7.55 (m, Ph). ^{13}C NMR: δ 21.0, 21.1, 76.5, 128.3, 128.9, 131.4, 133.8, 169.8.

1-(Phenylthio)ethyl propionate (**3e**). Propionyl chloride (136 µl, 1.56 mmol) was added to a solution of 1-phenylsulfinylethyl(tributyl)stannane (533 mg, 1.20 mmol) in dichloromethane (5 ml) at 0 °C. The mixture was stirred under N_2 for 20 min and worked up as described for **3a**. Ethyl acetate–hexane (1:9) was used for chromatography. Yield 154 (61%), liquid. ^{1}H NMR: δ 1.09 (t, *J* 7.6 Hz, CH_3CH_2), 1.53 (d, *J* 6.5 Hz, CH_3CH), 2.30 (q, *J* 7.6 Hz, CH_2), 6.24 (q, *J* 6.5 Hz, CH), 7.25–7.55 (m, Ph). ^{13}C NMR: δ 9.7, 21.7, 28.3, 76.3, 127.6, 128.2, 130.9, 133.1, 172.0. MS: 210 (5, *M*), 166 (32), 137 (13), 136 (17), 135 (20), 110 (28), 109 (15), 77 (6), 57 (100).

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