from its β isomer by filtration chromatography.[9] Compound **5** was obtained from **2** in 85% overall yield. We next faced regiospecific ring opening of the epoxide residue in **5** which was accomplished by reaction of the epoxide with 2 equiv of sodium phenyl selenide in ethanol at 80 °C for 3 h—a process affording **6** in 82% yield from **5**.[10] Sodium bicarbonate buffered 95% *m*-CPBA oxidation of **6** in dilute methylene chloride solution at −78 °C followed by warming to 22 °C gave a 95% yield of the corresponding diene **7**. Submission of this material to further oxidation with 95% *m*-CPBA in methylene chloride at −40 °C selectively gave the epoxide **8** in 77% yield. Esterification of the primary alcohol present in **8** was accomplished with benzoyl chloride in methylene chloride at −40 °C in the presence of triethylamine to give an 85% yield of **9**. This substance was desilylated at 0 °C in methanol with 5% HCl, and the resulting diol **10** then reacted with acetic anhydride in pyridine to give after chromatography pure senepoxide (**1**), mp 97–98 °C in 83% yield from **9**. Senepoxide prepared in this manner agreed in all respects to both spectra and a sample of racemic **1** kindly provided by Professor B. Ganem.[11]

To complete a formal total synthesis of crotepoxide, we treated compound **5** as its lithium alkoxide salt with benzyl bromide and HMPA at −78 °C to obtain in 67% yield compound **11**. Treatment of **11** with 2 equiv of sodium phenyl selenide gave the ring-opened substance **12** (80% yield) which on oxidative-elimination with 95% *m*-CPBA afforded the diene **13** in 87% yield. Desilylation of **13** in methanol with 5% HCl gave the diene-diol **14** in essentially quantitative yield. This material proved identical in all respects with both a sample and spectra of this compound kindly provided by Professor J. D. White, who has reported the conversion of **14** into crotepoxide.[12]

Lastly, we carried out a formal synthesis of pipoxide by reacting compound **6** with benzoyl chloride in methylene chloride containing triethylamine at 22 °C to obtain **15** in 95% yield. Treatment of **15** with 95% *m*-CPBA resulted in the formation of the corresponding diene which was then desilylated in methanol with 5% HCl to give **16** in 78% yield from **15**. Compound **16** proved identical with both sample and spectra kindly provided by Professor B. Ganem, who has converted **16** into pipoxide.[11]

(9) All new compounds gave satisfactory spectral and physical data.
(10) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697.
(11) We thank Professor B. Ganem for a sample of senepoxide as well as spectra of it. We also thank Professor Ganem for a sample and spectra of compound **16**.
(12) We thank Professor J. D. White for a sample and spectra of compound **14**.

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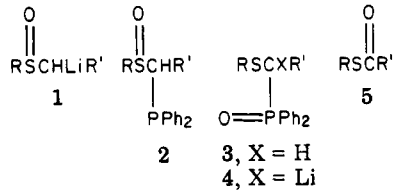
## Thiol Esters from Sulfoxides via Rearrangement of Sulfoxide Phosphines to Sulfide Phosphine Oxides

*Summary:* Treatment of α-lithio sulfoxides with (1) $ClP(C_6H_5)_2$ and (2) $I_2$ (isolate sulfide phosphine oxide **3**) followed by (3) $C_4H_9Li$ and (4) $O_2$ affords thiol esters.

*Sir:* The Pummerer oxidation converts sulfoxide α-carbon into the aldehyde or ketone oxidation state. However, there is no generally applicable method known for further oxidation to give carboxylic acid derivatives.[1] We report a method for conversion of sulfoxides into thiol esters that are versatile carboxylic acid equivalents. This technique depends on the observation that sulfoxide phosphines **2** rearrange readily to the isomeric sulfide phosphine oxides **3**. The latter can be oxygenated via the α-lithio derivatives **4** to give the thiol esters **5**.




Thiol esters have not previously been made by Horner–Bestmann oxygenation[2] of anions similar to **4** although other carbonyl compounds have been prepared from diphenylphosphine oxide or phosphonate anions.[3] Best results are obtained by bubbling oxygen into a THF solution of cold anion at individually optimized temperatures until the yellow-orange anion color fades. The readily available **4**[4] with R = $CH_3$ and R′ = $CH_2CH_2C_6H_5$ affords the thiol ester in 79% yield (93% based on recovered **3**) when oxygenation is performed at −100 °C.[5,6] This optimized procedure is generally effective when R = alkyl, but aryl sulfoxide anions (**4**, R = $C_6H_5$, R′ = alkyl) are less reactive and oxygenation at −44 °C is usually required.

The desired overall conversion of sulfoxides to thiol esters can now be achieved by combining the oxygenation process with a unique and effective method for introducing phosphorus at the correct oxidation state, **1** → **3**. Typical α-lithio sulfoxides react rapidly with $ClP(C_6H_5)_2$ to give sensitive sulfoxide phosphines **2** at −78 °C. The latter are reasonably stable when pure,[7] but rearrangement to **3** occurs slowly in the crude product at 20 °C (variable yield) or, more efficiently, in the presence of iodine at 0–20 °C.[8]

(1) Pummerer oxidation to orthoformic acid derivatives is a special case which succeeds because elimination pathways are not available to the Pummerer intermediate; Dinizo, S. E.; Watt, D. S. *Synthesis* **1977**, 181.
(2) Horner, L.; Hoffmann, H.; Klahre, G.; Toscano, V. G.; Ertel, H. *Chem. Ber.* **1961**, *94*, 1987. Bestmann, H. J. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 830.
(3) Davidson, A. H.; Warren, S. *J. Chem. Soc., Chem. Commun.* **1975**, 148. Zimmer, H.; Koenigkramer, R. E.; Cepulis, R. L.; Nene, D. M. *J. Org. Chem.* **1980**, *45*, 2019.
(4) Preparation: $Ph_2PLi + Br(CH_2)_3Ph \rightarrow Ph_2P(CH_2)_3Ph$; $H_2O_2 \rightarrow Ph_2PO(CH_2)_3Ph$; $LDA/CH_3SSCH_3 \rightarrow$ **4**; mp 139–142 °C.
(5) The intermediate oxygenation product fragments very rapidly to thiol ester at −78 °C according to quenching experiments. No peroxidic products have been detected.
(6) *CAUTION*: Oxygenation of THF solutions is inherently dangerous; the exit gases should be diluted with $N_2$ to minimize risks, and a good safety shield should be used.
(7) Isolation of sulfoxide phosphines **2** is possible by rapid chromatography or by crystallization but is not recommended due to losses induced by decomposition. The isomers **2** and **3** are most easily distinguished by systematic differences in the HCP coupling constant. Coupling is small in **2** (<4 Hz) and large in **3** (>7 Hz). Typical examples: **2** (R = *t*-$C_4H_9$, R′ = *i*-$C_3H_7$), mp 95–97 °C dec; δ(PCH) 2.88 (br s, $J_{PH}$ < 2 Hz); **3** (R = *t*-$C_4H_9$, R′ = *i*-$C_3H_7$), sublimes without melting, 130 °C, δ(POCH) 3.04 (dd, $J_{PH}$ = 13.6 Hz, $J_{HH}$ = 2.6 Hz); **2** (R = *t*-$C_4H_9$, R′ = *n*-$C_3H_7$), mp 113–115 °C dec, δ(PCH) 3.0 (dt, $J_{PH}$ = 4 Hz, $J_{HH}$ = 7 Hz); **3** (R = *t*-$C_4H_9$, R′ = *n*-$C_3H_7$) mp 151–152.5 °C, δ(POCH) 3.02 (ddd, $J_{PH}$ = 15.1 Hz, $J_{HH}$ = 8.8, 4.0 Hz); **2** (R = $C_6H_5$, R′ = $CH_3$), oil after chromatography, TLC $R_f$ 0.5 on silica gel (ether), δ(PCH) 2.88 (dq, $J_{PH}$ = 1.5 Hz, $J_{HH}$ = 7.0 Hz, q); **3** (R = $C_6H_5$, R′ = $CH_3$), mp 153–156 °C (lit.[8] mp 154–156 °C), δ(POCH) 2.79 (dq, $J_{PH}$ = 9.2 Hz, $J_{HH}$ = 7.4 Hz) (NMR spectra in $CDCl_3$; satisfactory elemental composition for all compounds).
(8) Representative procedure for conversion of sulfoxides into **3**: A solution of sulfoxide (5 mmol) in dry THF (10 mL or more if needed to dissolve anion) was cooled to −78 °C and alkyllithium (5.5 mmol) was added dropwise. After 30 min, the solution was added by cannula over 1–2 min to $ClP(C_6H_5)_2$ (5.5 mmol) in THF (5 mL) at −78 °C, with a $N_2$ atmosphere throughout. After 5 min, the mixture was warmed to 0 °C

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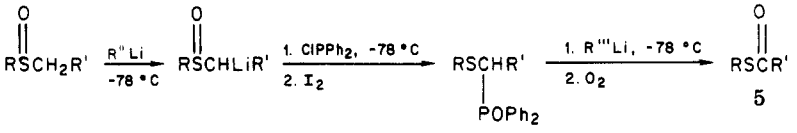
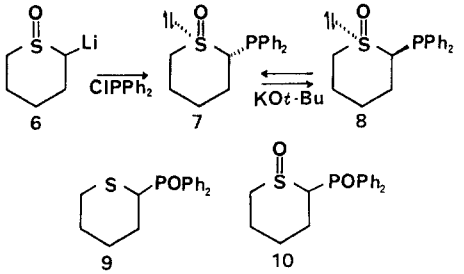
Table I




| entry | R | R' | R'' | R''' | % yield of 3[a] | oxygenation temp,[c] °C (time) | % yield of 5[d] |
|---|---|---|---|---|---|---|---|
| 1 | $C_6H_5$ | $CH_2CH_2C_6H_5$ | $CH_3$ | $CH_3$ | 81 | −78 (15 min), −44 (20 min) | 67 |
| 2 | $CH_3$ | $CH_2CH_2C_6H_5$ | *b* | n-$C_4H_9$ | *b* | −100 | 79 |
| 3 | $C_6H_5$ | n-$C_{11}H_{23}$ | $CH_3$ | $CH_3$ | 81 | −78 (15 min), −44 (20 min) | 76 |
| 4 | t-$C_4H_9$ | $CH(CH_3)_2$ | n-$C_4H_9$ | $(i\text{-Pr})_2N$ | 86 | −100 | 80 |
| | t-$C_4H_9$ | $CH(CH_3)_2$ | n-$C_4H_9$ | n-$C_4H_9$ | 86 | −78 | 84 |
| 5 | $C_6H_5$ | c-$C_6H_{11}$ | $CH_3$ | $CH_3$ | 78 | −44 | 87 |
| 6 | $C_6H_5CH_2$ | $C_6H_5$ | $(i\text{-Pr})_2N$ | $CH_3$ | 63 | −44 | 63 |
| 7 | $C_6H_5$ | $CH_3$ | $(i\text{-Pr})_2N$ | $CH_3$ | 63 | −78 (15 min), −44 (20 min) | 60 |
| 8 | t-$C_4H_9$ | n-$C_4H_9$ | n-$C_4H_9$ | n-$C_4H_9$ | 85 | −78 (30 min), −24 (30 min) | 63 |
| 9 | R = R' = $(CH_2)_4$ | | n-$C_4H_9$ | n-$C_4H_9$ | *e* | −78[f] | 57 |

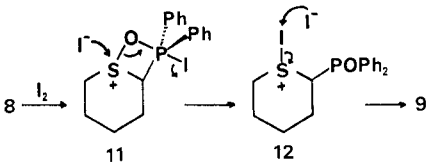
[a] Iodine (1 equiv) was added to sulfoxide phosphine at 0 °C (ref 8). [b] Alternate preparation of 3 was used (ref 4). [c] < 0.5 h sufficient to discharge anion color. [d] Isolated yields; recovery of 3 is typically ≤ 15%. [e] Diastereomer 7 is isolated, 71% without $I_2$ treatment; see text for oxygen transfer discussion. [f] Inverse addition (anion to $O_2$-saturated THF) was used; $O_2$ addition to anion gave 33% thiolactone, 40% recovered 9.

Treatment of α-lithiothiane *S*-oxide **6** with $ClP(C_6H_5)_2$ affords an unusually stable phosphine sulfoxide **7**,[9] single diastereomer. The trans stereochemistry is assigned by




analogy to previous reactions of **6** or related thiane *S*-oxide anions with electrophiles[10] and is tentative. In the presence of KO-*t*-Bu in THF, **7** equilibrates with a new isomer **8**[9] (ca. 1:1). Under representative conditions for oxygen transfer, 0.2 equiv of iodine/THF/0 °C, **8** is converted into **9**[9] (99% isolated) within 1–2 min. In contrast, **7** requires 5 h for complete conversion, and the complex product mixture includes **9** (35%) and the sulfoxide phosphine oxide **10**[9] (16%). The possibility of partial conversion of **7** to **8** under these conditions can not be ruled out.

These experiments show that intermolecular oxygen transfer occurs to some extent with **7** (as evidenced by formation of **10**) and suggest that an intramolecular mechanism is responsible for oxygen transfer with **8** and conformationally unrestricted acyclic analogues. The reactivity difference between **7** and **8** is consistent with the stereochemical assignment if the internal oxygen transfer mechanism resembles the general scheme proposed for the intermolecular deoxygenation of sulfoxides by $Ph_3P/I_2$/NaI.[11] A reasonable rationale involves **11** and **12** as key intermediates in the rearrangement.




Various sulfoxides have been converted into thiol esters by using this two-step sequence (Table I),[12] as have more complex functionalized sulfoxides to be described elsewhere. Isolated yields of thiol esters are in the 60–85% range, and the only other significant product in typical oxygenation mixtures is unreacted **3**.

**Acknowledgment.** This work was supported by a grant from National Science Foundation.

and iodine (5 mmol) was added. After 5 min, sufficient aqueous 10% sodium thiosulfate was added to decolorize the iodine. Products were isolated by extraction ($CH_2Cl_2$) and standard purification methods.

(9) **7**: mp 110–111 °C; δ(PC*H*) 3.67 ppm (br s). **8**: mp 144–146 °C; δ(PC*H*) ~3.18 (br d, $J_{HH}$ = 12.1 Hz, $J_{PH}$ = 2.5 Hz) or 3.09 (br d, $J_{HH}$ = 11.8 Hz, $J_{PH}$ = 2.5 Hz), no assignment possible of CHP vs. $CH_2SO$ positions. **9**: mp 159–162 °C; δ(POCH) 2.98 (ddd, $J_{PH}$ = 9 Hz, $J_{HH}$ = 9, 3 Hz). **10**: mp 179–181 °C; δ(POCH) 3.48–3.66 (overlapping signals with $CH_2SO$).

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*Received September 9, 1981*