Bis(tributyltin) Sulfide: An Effective and General Sulfur-Transfer Reagent[1]

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Bis(tributyltin) sulfide acts efficiently to transfer the sulfur atom as S^{2-} to a variety of halide substrates to afford the corresponding symmetrical sulfides in good overall yield.

Many synthetic reagents, including sodium sulfide nonahydrate ($Na_2S \cdot 9\ H_2O$), are known to transfer S^{2-} for making organic sulfides.[2,3] Only a few of them, however, deliver the sulfur atom in a precise amount under anhydrous, neutral, and homogeneous conditions. The hygroscopicity of $Na_2S \cdot 9\,H_2O$ make it difficult to quantify the amount of sulfur used; many procedures use this salt even though it has limited solubility in organic solvents.

We wish to report that bis(tributyltin) sulfide [bis(tributylstannyl) sulfide, **1**] possesses all these characteristics and is commercially available[4] or easily made.[5] A general reaction scheme for making sulfides is presented below.

$$2\ R{-}X \;+\; \underset{\mathbf{1}}{(n\text{-}C_4H_9)_3Sn{-}S{-}Sn(n\text{-}C_4H_9)_3} \longrightarrow \underset{\mathbf{2}}{R{-}S{-}R} \;+\; 2\ (n\text{-}C_4H_9)_3Sn{-}X$$

The scope of this chemical process was investigated with numerous substrates and found to be quite general (see Table). Some success with reagent **1** has been previously reported using sodium iodide in boiling butanone, however only with reactive halides.[3] With our methodology, for many halides, the reaction usually takes place near room temperature within 24 hours, giving modest to excellent yields. For less reactive substrates, such as 1-iodopropane, a sealed tube containing chloroform is heated at 140 °C for 12 to 24 hours, providing almost quantitative yield of product.

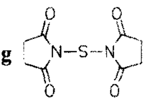
A solvent effect is noted for reactive substrates. Indeed, the rate of the reaction increases as the polarity and the ability to coordinate with tin increases,[6] suggesting an ionic mechanism.[7] The water sensitivity[8] and the thermal decomposition[9] of diacyl sulfides (thioanhydrides, RCO–S–COR; **2a**: $R = CH_3$, **2b**: $R = C_6H_5$) make them a difficult class of compounds to prepare. We report here that yields obtained are among the best in the literature to date.[10] Substrates halogenated in the α-position of a carbonyl group form sulfides that were used in the preparation of some heterocycles (thiophene, dihydrothiophene),[11] or as dienophilic thioaldehydes in the Diels-Alder reaction,[12] or in carbohydrate derivatives.[13] Thus, our method produces these useful sulfide intermediates under neutral and mild conditions.

Among the most interesting sulfides obtained are the carbonic acid derivatives **2c, d, e**. Although bis(alkoxycarbonyl) sulfide has received attention recently,[14] only one method giving high yield of products (> 90%) is known.[15] Surprisingly, little information is available in the literature on bis[(alkylthio)carbonyl] or bis(dialkylaminocarbonyl)sulfides. No general methods appear to be known for making these classes of compound in one step; thus, we present the first practical way to obtain them.[16] In addition to these sulfur derivatives, trisulfides (**2f**), sulfur-transfer reagents (**2g**), and other sulfides (thioethers **2h–n**) are readily available.

The major limitation of this method consists of the purification of sulfides unstable on silica gel. Despite this drawback, the methodology described here remains quite general as discussed above.

Reagent **1** is prepared by a modification of the method described in Ref.[5]

Table. Organic Sulfides **2** from Organic Halides and Reagent **1**

Halide	mol equiv of **1**	Solvent	Reaction Conditions (°C), (h)	Product[a]	Yield[b] (%)
CH_3COCl	1.00	$CHCl_3$	20, 5	**2a** $(CH_3CO)_2S$	(99)
	1.05	CH_2Cl_2	20, 24		86
C_6H_5COCl	1.00	$CHCl_3$	20, 5	**2b** $(C_6H_5CO)_2S$	(98)
C_2H_5OCOCl	1.00	$CHCl_3$	110, 12	**2c** $(C_2H_5OCO)_2S$	(94)
C_2H_5SCOCl	1.00	$CHCl_3$	110, 12	**2d** $(C_2H_5SCO)_2S$	(97)
$(CH_3)_2NCOCl$	1.00	$CHCl_3$	110, 12	**2e** $[(CH_3)_2NCO]_2S$	(92)
$C_6H_5CH_2SCl$	1.00	$CHCl_3$	0, 0.2	**2f** $(C_6H_5CH_2S)_2S$	~100
NCS[c]	1.00	$CHCl_3$	0, 0.5	**2g** 	~100
$C_6H_5CH_2Br$	1.00	$CHCl_3$	110, 12	**2h** $(C_6H_5CH_2)_2S$	(99)
	1.00	CH_2Cl_2	40, 28		25
	1.00	$CHCl_3$	61, 120		93
$n\text{-}C_3H_7I$	1.00	$CHCl_3$	140, 24[d]	**2i** $(n\text{-}C_3H_7)_2S$	(97)[d]
$H_2C{=}CHCH_2Br$	1.00	$CHCl_3$	110, 12	**2j** $(H_2C{=}CHCH_2)_2S$	(98)
$C_6H_5COCH_2Br$	1.00	$CHCl_3$	110, 12	**2k** $(C_6H_5COCH_2)_2S$	(98)
	1.20	CH_2Cl_2	20, 43		trace
	1.05	DMF/EtOAc (5 : 1)	20, 24		71
	1.20	DMF/EtOAc (5 : 1)	45, 3		94
$C_2H_5COCH_2Br$	1.10	DMF/EtOAc (5 : 1)	20, 22	**2l** $(C_2H_5COCH_2)_2S$	56
	1.10	DMF/EtOAc (5 : 1)	20, 60		69
	1.10	DMF/EtOAc (5 : 1)	55, 2		29
CH_3COCH_2Cl	1.10	DMF/EtOAc (5 : 1)	45, 3	**2m** $(CH_3COCH_2)_2S$	trace
$CH_3COCH(CH_3)Br$	1.05	$CHCl_3$	61, 78	(**2n**) –	nil

[a] The products were identified by comparison with authentic material and/or by GLC/MS, IR spectra, and ^{1}H-NMR spectra.

[b] Yield of isolated product (GLC yields in parentheses).

[c] *N*-Chlorosuccinimide.

[d] Sealed-tube method.

Bis(tributyltin) Sulfide [1, Bis(tributylstannyl) Sulfide]:
Sodium sulfide nonahydrate ($Na_2S \cdot 9\ H_2O$); 72.05 g, 0.200 mol) is dissolved in distilled H_2O (60 mL) at 35 °C and this solution is added to a stirred solution of tributyltin chloride (97.64 g, 0.300 mol) in THF (300 mL) in a 1000 mL flask. [The use of this solvent mixture appears to aid significantly in helping to obtain good yields]. Extra H_2O (30 mL) is used to aid in the complete transfer of the Na_2S. The mixture is heated at reflux (65 °C) for 4 h with vigorous stirring. After cooling, the phases are separated and the organic phase is evaporated. The residue (the crude reagent **1**) is extracted with dry Et_2O (4 × 50 mL) and the extract is dried ($MgSO_4$) with stirring (30 min). After filtration and solvent evaporation, the crude product is placed under vacuum to remove traces of solvent; yield: 88.18 g (96 %); pale yellow, viscous liquid. Further purification is achieved by distillation in vacuum; yield of pure **1**: 85.15 g (93 %); b.p. 225 °C/0.4 Torr; purity (GLC): ~ 99 %.

When the above procedure is carried out on a smaller scale (5 g of tributyltin chloride and 2 equiv of $Na_2S \cdot 9\ H_2O$) reagent **1** is produced in 97 % yield and 99 % purity. This product could be used directly without purification by distillation.

^{1}H-NMR ($CDCl_3/TMS_{int}$, 200 MHz): $\delta = 0.91$ (t, 18 H, 6 CH_3); 1.08 (t, 12 H, 6 CH_2Sn); 1.34 (sext, 12 H, 6 $CH_3\underline{H}_2CH_2CH_2$); 1.56 (m, 12 H, 6 $CH_3CH_2C\underline{H}_2CH_2$).

^{119}Sn-NMR ($CDCl_3/Me_4Sn_{ext}$, 200 MHz): $\delta = 82.69$.

Diphenacyl Sulfide (2k) from α-Bromoacetophenone; Typical Procedure:
A solution of α-bromoacetophenone (1.00 g, 5.02 mmol) and bis(tributyltin) sulfide (**1**; 1.85 g, 3.02 mmol) in DMF/EtOAc (5:1, 25 mL) is placed in a 50 mL flask. The mixture is kept under nitrogen and heated with an oil bath at 45° while stirring vigorously. The reaction is monitored by TLC (silica gel, acetone/hexane 5:95, UV visualization). Afeter 6 h, the solvent is removed under high vacuum: purification is carried out on silica gel using hexane as first eluent (to remove non-polar organotin) followed by gradually increasing the EtOAc content to 30 % of the solvent mixture. The eluate is evaporated and the residue is recrystallized from hexane to give product **2k** as a colorless solid; yield: 0.637 g (94 %); m.p. 75 °C (Lit.[17] m.p. 67–68 °C).

^{1}H-NMR: $\delta = 3.98$ (s, 4 H); 7.22–7.62 (m, 6 H); 7.68–8.05 (m, 4 H).

For non-moisture sensitive products, EtOAc is added and a solution of $Zn(OAc)_2$ in H_2O can be employed to destroy any excess tin sulfide.[18] A solution of KF in H_2O with a catalytic amount of tetrabutylammonium fluoride trihydrate suffices to remove most organotin by-products.[19] Filtration of the whole mixture followed by a second filtration on silica gel for the organic phase only affords a pure product. For volatile sulfides, a Kugelrohr distillation is carried out.

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