IR (KBr) ν 1787, 1765, 1758, 1731, 1718 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ 6.92–7.93 (m, 8 H, Ar), 5.61 (d, 1 H, J = Hz, H-3), 4.79–4.96 (m, 1 H, H-4), 3.82 (s, 3 H, p-CH_3OPh), 3.62 (s, 3 H, COCH$_2$COOCH_3), 3.35 (s, 2 H, COCH_2COOCH$_3$), 3.07 (dd, 1 H, J = 8.7 Hz, J' = 17.4 Hz, CH_AH$_B$CO), 2.66 (dd, 1 H, J = 5.1 Hz, J' = 17.4 Hz, CH$_A$$H_B$CO). Anal. Calcd for $C_{23}H_{20}N_2O_7$: C, 63.29; H, 4.63; N, 6.42. Found: C, 63.58; H, 4.75; N, 6.73.

***trans*-3-Acetyl-1,4-phenylazetidin-2-one (30a).** Following the general procedure starting from **25a** (1.76 g, 6 mmol), the title compound was obtained: yield 1.18 g (78%); mp 90–93 °C (CHCl$_3$/hexane); IR (KBr) ν 1740, 1708 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.40–7.06 (m, 10 H, Ar), 5.48 (d, 1 H, CH, J = 2.55 Hz), 4.14 (d, 1 H, CH, J = 2.55 Hz), 2.39 (s, 3 H, CH$_3$). Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.95; H, 5.70; N, 5.28. Found: C, 76.90; H, 5.69; N, 5.00.

***trans*-3-Acetyl-4-(2,5-dimethylphenyl)-1-phenylazetidin-2-one (30b).** Following the general procedure starting from **25b** (1.86 g, 6 mmol), the title compound was obtained: yield 1.32 g (75%); mp 86–87 °C (CHCl$_3$/hexane); IR (KBr) ν 1764, 1701 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.27–7.00 (m, 8 H, Ar), 5.66 (d, 1 H, CH, J = 2.63 Hz), 4.07 (d, 1 H, CH, J = 2.63 Hz), 2.39 (s, 6 H, CH$_3$, CH$_3$NO$_2$), 2.21 (s, 3 H, CH$_3$). Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.54; H, 6.59; N, 4.67.

***trans*-3-Acetyl-4-(α-methylstyryl)-1-(4-methoxyphenyl)-azetidin-2-one (30c).** To a solution of *anti*-**29c** (1 mmol, 0.36 g) in methylene chloride (3 mL) and *N*,*O*-bis(trimethylsilyl)-acetamide (BSA) (1.5 mmol, 0.37 mL) cooled to 0 °C was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (1 drop). After 15 min of stirring at the same temperature, the resulting solution was added to a cooled (0 °C) solution of MCPBA (1.2 mmol, 0.26 g) in methylene chloride (3 mL) and stirred at room temperature for 1 h. The mixture was then washed with 1 N Na$_2$SO$_3$, 1 N HCl, and aqueous NaHCO$_3$ (saturated solution). The organic layer was separated and dried (MgSO$_4$) and evaporation of solvent gave a mixture of *cis,syn*-**29c** and *trans*-**30c** in a ratio of 30:70. Compound **30c** was isolated by column chromatography as an oil[25]: yield 50%; IR (CHCl$_3$) ν 1749, 17151 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.38–7.25 (m, 7 H, Ar), 6.85 (d, 2 H, Ar, J = 9 Hz), 6.74 (s, 1 H, =CH), 5.01 (d, 1 H, H-4, J = 2.4 Hz), 4.13 (d, 1 H, H-3, J = 2.4 Hz), 3.77 (s, 3 H, OCH$_3$), 2.33 (s, 3 H, CH$_3$), 1.86 (d, 3 H, CH$_3$, J = 1.5 Hz).

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New Methodologies: Fluorodemetalation of Organogermanium, -tin, and -lead Compounds. Applications with Organometallic Sulfides To Produce Highly Active Anions and Spectroscopic Evidence for Pentavalent Intermediates in Substitution at Tin

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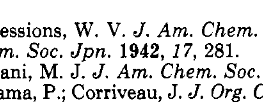
The general concept of fluorodemetalation is illustrated with three novel methodologies. Fluoride ion smoothly demetalates organogermanium, -tin, and -lead sulfides under mild and neutral conditions to liberate active nucleophilic sulfur species. Eight different sulfur transfer agents derived from group IV are used to demonstrate fluorodemetalation. The reactions of fluorodeplumbylation and fluorodegermanylation are presented for the first time along with a discussion of their potential uses in chemistry. The study of fluoride sources as demetalating agents, solvents, substituents and substrates variation is reported. Mechanistic and kinetic aspects of fluorodemetalation are also discussed. We propose that a metal proximate to an anion will increase the nucleophilicity of the latter. In addition, we present spectroscopic evidence for a pentacoordinated intermediate involved in the mechanism of substitution at tin by the use of low-temperature ^{19}F and ^{119}Sn NMR spectroscopy.

Introduction

While organotins are widely used for industrial applications,[1] in organic synthesis organotin sulfides have not been significantly explored.[2-5] Recently, we reported that bis(trialkyltin) sulfide (2) is useful as a general sulfur transfer agent for the high-yield synthesis of thioethers and related derivatives, albeit under forcing conditions.[6] Further, we communicated that fluoride and cyanide ions attack organotin sulfides and smoothly liberate the corresponding sulfur ligand.[7] While several methods are known for making sulfides, fluorodestannylation[8-10] represents a real improvement in methodology because of the neutrality of the medium, the mildness of the conditions, and the high reactivity of the sulfide ion released. This intriguing reactivity has been exploited by two groups using this methodology since classic procedures had failed.[11] The fast rate of these reactions favors the formation of macrocyclic sulfides, and the mild and neutral conditions could open new synthetic routes to other interesting structures.[12-14]

Scheme I. Fluorodemetalation



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[1] Among the uses: agrochemicals, disinfectants, wood preservatives, and biocides in marine paints; Davies, A. G.; Smith, P. J. *Comprehensive Organometallic Chemistry*; Pergamon Press: Toronto, 1982; Vol. 2, pp 608–616.

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Table I. Fluoride Effect

	without fluoride		with fluoride		
substrates	time, h	yield,[c] %	time, h	yield,[c] %	fluoride
		$(Bu_3Sn)_2S$[a]			
$PhCOCH_2Br$	24	71	<0.3	100	$TBAF{\cdot}3H_2O$
$PhCOCH_2Br$	–	–	1.0	98	CsF
$PhCH_2Br$[d]	22	17	0.8	85	$TBAF{\cdot}3H_2O$
$CH_3COCH(Br)CH_3$	78	0[d]	24	75	$TBAF{\cdot}3H_2O$
		$(Ph_3Pb)_2S$[e]			
$PhCH_2Br$	96	5	9.5	67	CsF
		$(Ph_3Ge)_2S$[f]			
$CH_3(CH_2)_4CH_2Br$	24	>1	10.0	60[f]	CsF

[a] Reaction conditions: 20 °C, DMF/EtOAc (5:1), halide (2.00 mmol), bis(tributyltin) sulfide (**2**, 1.10 mmol), fluoride: CsF (excess) or $TBAF{\cdot}3H_2O$ (2.10 mmol), same concentration of each reagent for all different reactions. [b] Z = Br or F depending on reagents used. [c] Isolated yields. [d] Not usual reactions conditions: $CHCl_3$ reflux (61 °C). [e] Reaction conditions: 20 °C, DMF, halide (2.00 mmol), bis(triphenyllead) sulfide (1.05 mmol), cesium fluoride (4.80 mmol), and 18C6 (catalytic). [f] Reaction conditions: 55 °C, DMF/THF (1:4) bis(triphenygermanium) sulfide (**4**, 1.00 mmol), 1-bromohexane (2.00 mmol, 18C6 nat.), CsF (5.8 mmol).

$Me_3Sn\text{-}S\text{-}SnMe_3$ **1** $Bu_3Sn\text{-}S\text{-}SnBu_3$ **2** $Me_3Si\text{-}S\text{-}SiMe_3$ **3**

$Ph_3Ge\text{-}S\text{-}GePh_3$ **4** $Ph_3Pb\text{-}S\text{-}PbPh_3$ **5** $Ph_3Sn\text{-}S\text{-}SnPh_3$ **7**

$(Bu_2SnS)_3$ **8**

Figure 1. List of sulfur transfer agents.

We already demonstrated the general aspect of this new technique for liberating naked anions from organotin oxides, organotin selenides, and tetraorganotins.[15] Organotins thus act as "group 16 (VIB) transfer agents" in the presence of fluoride ions,[15] and we wish to generalize the methodology of fluorodemetalation while reporting the first use of fluorodegermanylation and fluorodeplumbylation (Scheme I).

In organic synthesis, organogermanium reagents are practically nonexistent,[16,17] and their use is relatively rare in industry as well.[18] In organolead chemistry there are a variety of important reagents.[19-23] We prepared some organometallic sulfides of group IV as reagents for our study (Figure 1). Most of them are often solid or liquid with high boiling points and are easily made or commercially available (vide infra).[24] Further advantages are their solubility in many organic solvents, in contrast to the insoluble and less reactive $Na_2S{\cdot}9H_2O$, and their easy handling since they are not hygroscopic or odorous (except **1**).

Results and Discussion

Synthesis of Organotin, Organogermanium, and Organolead Sulfides. There are numerous, well-established procedures for the preparation of organotin sulfides.[25,26] Organotin sulfides are prepared from the appropriate organotin chloride (all commercially available) and sodium sulfide (eq 1). The simple and practical

$$2R_3MX + Na_2S{\cdot}9H_2O \rightarrow R_3M\text{-}S\text{-}MR_3 + 2NaX \quad (1)$$

$$M = Ge, Sn, Pb \qquad X = Cl \text{ (or OAc with } M = Pb)$$

procedure was also reasonably successful with organogermanium chloride (53% yield) and organolead acetate (80–90% yield). Tributyltin benzyl sulfide (**9**) was prepared using Wilkinson's catalyst in the presence of tributyltin hydride and benzyl mercaptan with excellent yield and purity.[27]

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(8) Other types of fluorodestannylation reactions include: Pearlman, B. A.; Putt, S. R.; Fleming, J. A. *J. Org. Chem.* **1985**, *50*, 3622 as well as those in ref 9 and 10.

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(23) Kauffmann, T. *Topics in Current Chemistry*; Springer-Verlag, New York, 1980; pp 132–144.

(24) Bis(tributyltin) sulfide (**2**) can be obtained from Pfaltz and Bauer USA; other tin sulfides are sold by the Strem Chemical Co. Some triaralkyltin mercaptides are currently sold by the Aldrich Chemical Co.

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Fluoride Effects. As can be seen in Table I, the fluoride effect in fluorodestannylation provides a general decrease in reaction time and an increase in yields of sulfide compared to the same reaction without fluoride ion[6] when reacting organic halides with some sulfur transfer agents (Figure 1). This strong effect was also observed for organolead sulfides. As an example, bis(triphenyllead) sulfide (**5**) is relatively inert toward benzyl bromide after 4 days at 20 °C in DMF (see Table I). However, a drastic change resulted when cesium fluoride was added: after only 5 h, it was possible to isolate the corresponding sulfide in 67% yield. Bis(triphenylgermanium) sulfide (**4**) showed a similar fluoride effect. In the case of 1-bromohexane and fluoride ion, the symmetrical sulfide was isolated in 80% yield in 10 h.

In the organosilicon case, it has already been shown by Abel and co-workers[28] that strong heating at 160 °C for 100 h was required to react 1-bromooctane with bis(trimethylsilyl) sulfide (**3**) for the formation of di-*n*-octyl sulfide (72% yield). In our methodology, the reaction took place at 20 °C within a few minutes with cesium fluoride.

We found that hexamethyldisilthiane (**3**) formed a 2.3:1 mixture of monosulfide and disulfide when treated with fluoride in the presence of halide (eq 2) whereas the tin analogue gave a quantitative yield of monosulfide under the same conditions (eq 3). Fluorodegermanylation gives exclusively monosulfide when the reaction parameters are controlled properly (eq 4). Fluorodeplumbylation gave an isolable intermediate triphenyllead hexyl sulfide (**6**) that is slowly transformed into di-*n*-hexyl sulfide (eq 5). New ways for generating nucleophiles could be envisaged because of the high affinity of fluoride for these metals.[29]

$$2CH_3(CH_2)_5Br + \underset{\mathbf{3}}{Me_3Si\text{-}S\text{-}SiMe_3} \xrightarrow{F^-} \underset{(2.3:1)}{C_6H_{13}\text{-}S\text{-}C_6H_{13} + C_6H_{13}\text{-}S\text{-}S\text{-}C_6H_{13}} \quad (2)$$

$$2CH_3(CH_2)_5Br + \underset{\mathbf{2}}{Bu_3Sn\text{-}S\text{-}SnPh_3} \xrightarrow{F^-} \underset{(99\%)}{C_6H_{13}\text{-}S\text{-}C_6H_{13}} \quad (3)$$

$$2CH_3(CH_2)_5Br + \underset{\mathbf{4}}{Ph_3Ge\text{-}S\text{-}GePh_3} \xrightarrow{F^-} \underset{(80\%)}{C_6H_{13}\text{-}S\text{-}C_6H_{13}} \quad (4)$$

$$2CH_3(CH_2)_5Br + \underset{\mathbf{5}}{Ph_3Pb\text{-}S\text{-}PbPh_3} \xrightarrow{F^-} Ph_3Pb\text{-}S\text{-}(CH_2)_5CH_3 + \underset{\mathbf{6}}{C_6H_{13}\text{-}S\text{-}C_6H_{13}} \quad (5)$$

ratio:5.7:1

Cyanide ion also decreases the reaction time for the formation of sulfides from organotin sulfides, but the magnitude of this effect is less pronounced than for fluoride (see entry 3 in Table III). Because the best results were obtained with fluoride in the tin case, we did not study cyanodemetalation with germanium and lead.

Solvent Effects. The second most important parameter with fluorodestannylation (and fluorodemetalation) appears to be the solvent used. Without fluoride ion, the rate of formation of sulfide using bis(tributyltin) sulfide (**2**) while varying the solvents follows this order: DMF/EtOAc (5:1) > CH_3CN > CH_2Cl_2 (cat. DMF) > EtOAc = CH_2Cl_2 = $CHCl_3$. Essentially the same order is followed when fluoride is employed.

Table II. Effects of Substituents on Tin vs the Rate of Sulfide Formation Using Organotin Sulfides[a]

$$Br(CH_2)_5Br + (R_3Sn)_2S \xrightarrow{F^-} \text{thiane} + 2R_3SnF$$

R	yield,[b] %	*T*, °C	time, min	solvent
Bu	100	42	1200	DMF/EtOAc (5:1)
Ph	100	42	720	DMF/EtOAc (5:1)
Bu	96	60	30	DMF/EtOAc (5:1)
Ph	88	60	30	DMF/EtOAc (5:1)
Bu	97	60	60	DMF/EtOAc (5:1)
Ph	94	60	60	DMF/EtOAc (5:1)
Me	75	20	<20	CH_3CN
Bu	100	20	45	CH_3CN
Me	90	50	45	CH_3CN
Bu_2SnS	100	50	45	CH_3CN

[a] $Br(CH_2)_5Br$ (1.00 mol), $(R_3Sn)_2S$ (1.00 mol), fluoride, TBAF·$3H_2O$ (1.00 mol). [b] GC yield.

Although DMF and acetonitrile have roughly the same dielectric constant (DMF, 37 D, CH_3CN, 39 D, at 25 °C),[30] we observed different rates with various organotins. This can be rationalized if we assume that solvent coordination on tin is important; this was demonstrated by a ^{119}Sn NMR study. When bis(tributyltin) sulfide (**2**) (in $CHCl_3$, 20 °C) is used as a standard reference, we obtained a slightly different shift of the ^{119}Sn signal in DMF and in CH_3CN for an identical number of millimoles added to the reference system; DMF complexes bis(tributyltin) sulfide (**2**) more strongly than CH_3CN at the same concentration. A broad ^{119}Sn NMR signal resulted when adding DMF to the reference sample, suggesting a labile DMF–Sn complex formation.

The complexation effect with solvents is consistent with the observed reaction rates using fluoride or cyanide ions in acetonitrile or DMF. It should be noted that the solvent effect on the rate of sulfide formation with and without fluoride favors DMF over CH_3CN. The solvent is still very important even in the presence of a potential complexing agent such as fluoride ion.

For organogermanium and organolead sulfides, we briefly investigated the role of solvent and found that DMF has a strong effect on the reaction rate even if used as a minor cosolvent with THF. Because of the insolubility of triphenyllead or triphenylgermanium groups in some solvents (such as acetonitrile, hexane, acetone), coupled with difficult workup associated with DMF, we used tetrahydrofuran as the main solvent.

Substituent Effects. Several organotin sulfides having the general structure $R_3SnSSnR_3$ were investigated (where R represents a phenyl, butyl, or methyl substituent). Table II demonstrates that for identical reaction conditions the substituent effects can be considered to be negligible compared to the solvent and the fluoride effects.[31]

Fluoride and Cyanide Study. Several sources of fluoride ion are known; however, only a few of them are strictly anhydrous because of the strong hydrogen bonding

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[29] The average bond energies of Si–F and Ge–F derived from SiF_4 and GeF_4 are 139 kcal/mol (582 kJ/mol) and 111 kcal/mol (465 kJ/mol) in: Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 4th ed.; John Wiley & Sons: Toronto, 1980; p 375. We approximated the Sn–F bond energy to 100 kcal/mol in our previous work (see ref 15. The Sn–F bond energy in SnF_4 was evaluated as 107.4 kcal/mol: Sanderson, R. T. *Polar Covalence*; Academic Press: New York, 1983; p 74) but the Pb–F bond energy seems to be unavailable. These bond energies are as high or higher than a sp^3 C–C bond (~85 kcal/mol) or a sp^3 C–H bond (~99 kcal/mol).

[30] Nilles, G. P.; Schuetz, R. D. *J. Chem. Educ.* **1973**, *50*, 267.

[31] The observation of a slight substituent effect is described qualitatively as: $(Bu_2SnS)_3 \geq (Me_3Sn)_2S = (Bu_3Sn)_2S > (Ph_3Sn)_2S$. This effect can be caused by the lack of solubility of some organotin sulfides, e.g. bis(triphenyltin) sulfide (**7**) in DMF. Most are somewhat soluble in acetonitrile and DMF, but ethyl acetate was added for better homogeneity. For organolead or -germanium sulfides ($R_3M\text{-}S\text{-}MR_3$), R = phenyl, the compounds were thermally stable, crystalline solids.

Table III. Fluoride Study in the Formation of Sulfides Using Organotin Sulfides

entry	halide[a]	organotin	solvent[i]	T, °C	time, h	F^- or CN^- (mol)	sulfide	yield,[f] %
1	$PhCOCH_2Br$	$(Bu_3Sn)_2S$[c]	B	20	1.0	CsF·18C6 (xs)	$(PhCOCH_2)_2S$	98
2	$PhCOCH_2Br$	$(Bu_3Sn)_2S$[c]	B	20	<0.3	$TBAF \cdot 3H_2O$ (2.2)	$(PhCOCH_2)_2S$	100
3	$PhCH_2Br$	$(Bu_3Sn)_2S$[c]	A	20	0.8	TBACN (2.1)	$(PhCH_2)_2S$	41
4	$PhCH_2Br$	$(Bu_3Sn)_2S$[c]	A	20	1.0	$TBAF \cdot 3H_2O$ (2.1)	$(PhCH_2)_2S$	86
5	$Br(CH_2)_5Br$	$(Bu_3Sn)_2S$[d]	A	40	0.5	TBAF (anh., 2.2)	thiane	26[g]
6	$Br(CH_2)_5Br$	$(Bu_3Sn)_2$[d]	A	40	<0.5	$TBAF \cdot 3H_2O$ (2.0)	thiane	100[g]
7	$Br(CH_2)_5Br$	$(Bu_3Sn)_2S$[d]	A	20	0.5	TBAF (anh., 2.0)	thiane	25[g]
8	$Br(CH_2)_5Br$	$(Bu_3Sn)_2S$[d]	A	20	0.8	$TBAF \cdot 3H_2O$ (2.0)	thiane	100[g]
9	$CH_3(CH_2)_5Br$	$(Me_3Sn)_2S$[c]	A	20	1.0	KF·18C6 (xs)	$(CH_3(CH_2)_5)_2S$	0[g]
10	$CH_3(CH_2)_5Br$	$(Me_3Sn)_2S$[b]	A	75	1.0	CsF·18C6 (xs)	$(CH_3(CH_2)_5)_2S$	99
11	$CH_3(CH_2)_5Br$	$(Me_3Sn)_2S$[b]	A	50	5.5	$TBAF \cdot 3H_2O$ (2.0) on SiO_2	$(CH_3(CH_2)_5)_2S$	2–5[g]
12	$CH_3(CH_2)_5Br$	$(Ph_3Sn)_2S$[d]	A	50	21	Me_3PyrHF/Na_2CO_3	$(CH_3(CH_2)_5)_2S$	0[g]
13	$CH_3(CH_2)_5Br$	$(Ph_3Sn)_2S$[e]	A	50	5.0	TBAI/CsF (3.0)		
14	$CH_3(CH_2)_5Br$	$(Me_3Sn)_2S$[c]	A	20	5.5	$TEAF \cdot 3H_2O$ (2.0), sieves 3Å	$(CH_3(CH_2)_5)_2S$	56
15	$CH_3(CH_2)_5Br$	$(Bu_3Sn)_2S$[c]	A	20	2.5	TBAF (anh., 2.0)	$(CH_3(CH_2)_5)_2S$	13[g]
16	$CH_3(CH_2)_5Br$	$(Me_3Sn)_2S$[b]	A	20	1.0	DAST (2.0)	$(CH_3(CH_2)_5)_2S$	0[g]
17	$CH_3(CH_2)_5Br$	$(Me_3Sn)_2S$[c]	A	20	24	BTAF (anh., 2.0) TBAI	$(CH_3(CH_2)_5)_2S$	70[g]
18	$CH_3(CH_2)_5Br$	$(Me_3Sn)_2S$[c]	A	20	12	TASF (2.1)	$(CH_3(CH_2)_5)_2S$	40[g]

[a] 1.00 mol. [b] 1.00 mol. [c] 1.05 mol. [d] 2.00 mol. [e] 4.00 mol. [f] Isolated yields except if noted GC yield; identified by NMR, IR, MS and compared to authentic material. [g] GC yield. [h] TBAF, tetrabutylammonium fluoride; BTAF, benzyltributylammonium fluoride; TBACN, tetrabutylammonium cyanide; TBAI, tetrabutylammonium iodide; TEAF, tetraethylammonium fluoride; DAST, (diethylamino)sulfur trifluoride; TASF, tris(dimethylamino)sulfur (trimethylsilyl)difluoride. [i] A = acetonitrile; B = DMF/EtOAc (5:1).

Table IV. Formation of Symmetrical Sulfides Using Organotin Sulfides and Alkyl Halides

entry	halide	organotin	solvent[i]	T, °C	time, h	F^- or CN^- (mol)	sulfide	yield,[a] %
1	CH_3COCH_2Cl	$(Bu_3Sn)_2S$[f]	A	20	0.8	$TBAF \cdot 3H_2O$ (1.0)	$(CH_3COCH_2)_2S$	83[e]
2	$PhCOCH_2Br$	$(Bu_3Sn)_2S$[f]	B	20	1.0	CsF (xs)	$(PhCOCH_2)_2S$	98
3	$PhCOCH_2Br$	$(Bu_3Sn)_2S$[f]	B	20	0.3	$TBAF \cdot 3H_2O$ (2.2)	$(PhCOCH_2)_2S$	99
4	$PhCH_2Br$	$(Bu_3Sn)_2S$[f]	B	20	0.8	$TBAF \cdot 3H_2O$ (4.6)	$(PhCH_2)_2S$	85[e]
5	$PhCH_2Br$	$(Bu_3Sn)_2S$[g]	A	20	0.3	$TBAF \cdot 3H_2O$ (4.0)	$(PhCH_2)_2S$	99[b]
6	$PhCH_2Br$	$(Bu_3Sn)_2S$[h]	A	20	1.0	$TBAF \cdot 3H_2O$ (2.1)	$(PhCH_2)_2S$	86[e]
7	MeCOCH(Me)Br	$(Bu_3Sn)_2S$[h]	B	20	24	$TBAF \cdot 3H_2O$ (1.0)	$(MeCOCH(Me))_2S$	75[e]
8	MeCOCH(Me)Br	$(Bu_3Sn)_2S$[h]	B	20	7	$TBAF \cdot 3H_2O$ (2.0)	$(MeCOCH(Me))_2S$	57[e]
9	$EtCH(Me)CH_2Br$	$(Me_3Sn)_2S$[h]	A	80	2.5	CsF·18C6 (xs)	$(EtCH(Me)CH_2)_2S$	63[e]
10	$CH_3(CH_2)_5Br$	$(Me_3Sn)_2$[h]	A	75	1.0	CsF·18C6 (xs)	$(CH_3(CH_2)_5)_2S$	99
11	$Br(CH_2)_5Br$	$(Bu_3Sn)_2S$	A	20	0.8	$TBAF \cdot 3H_2O$ (2.1)	thiane	99[c]
12	$Br(CH_2)_5Br$	$(Bu_3Sn)_2S$	A	20	0.5	$TBAF \cdot 3H_2O$ (2.1)[f]	thiane	99[c]
13	$(ClCH_2)_2CO$	$(Bu_3Sn)_2S$	A	20	0.5	$TBAF \cdot 3H_2O$ (2.2)	$cyclo(SCH_2COCH_2)_2$	16

[a] Isolated yields except if noted NMR or GC yield; identified by NMR, IR, MS and compared to authentic material. [b] ^1H NMR yield. [c] GC yield without internal standard. [d] Cyclic trimer. [e] Not optimized. [f] 1.1 mol. [g] 2.0 mol. [h] 1.05 mol. [i] A = acetonitrile; B = DMF/EtOAc (5:1). [j] 2.0 mol of tetrapropylammonium iodide added.

of fluoride with water.[32,33] In some of our reactions with nonactivated halides such as 1-bromohexane, we had to use an anhydrous source fluoride to avoid competing thiol formation.[34] As a consequence, we developed new anhydrous fluorinating systems[35] involving 18-crown-6[36] or dibenzo-24-crown-8 with dried cesium fluoride.

Table III lists the fluoride and cyanide sources that were examined: tetrabutylammonium fluoride (trihydrate or anhydrous[37]), the same compound adsorbed on silica gel,[38] benzyltrimethylammonium fluoride,[39] benzyltrimethylammonium fluoride combined with tetrabutylammonium iodide, tetraethylammonium fluoride trihydrate combined with molecular sieves, 3 Å, 2,4,6-trimethylpyridinium hydrogen fluoride,[40] cesium fluoride complexed with 18-crown-6,[36] cesium fluoride alone, cesium fluoride combined with tetrabutylammonium iodide, potassium fluoride complexes with 18-crown-6,[41] diethylaminosulfur trifluoride (DAST)[42] and tris(dimethylamino)sulfur (trimethylsilyl)difluoride (TASF).[43]

The qualitative effectiveness of the fluoride sources in the fluorodestannylation procedure of organotin sulfide follows the trend: $TBAF \cdot 3H_2O$ > CsF·18C6 > CsF > BTAF > $TEAF \cdot 3H_2O$/sieves > TASF > TBAF anh. > KF·18C6. As a general rule, we found that tetrabutylammonium fluoride trihydrate is the most reactive fluoride, but its water content limits its use only with an activated electrophile such as α-bromo ketones. Benzyl bromide appears to be the limiting case where this fluoride can be used without too much formation of thiol as a side product.[35] The reagent is decomposed to H_2S and the yield of sulfide is diminished with $TBAF \cdot 3H_2O$. With nonactivated alkyl halides such as 1-bromohexane, the anhydrous fluorinating system cesium fluoride complexed with a catalytic amount of 18-crown-6[36] is preferred. The latter system was found to be general and also very effective with activated alkyl halides. Surprisingly, tetrabutylammonium fluoride dried accordingly to Cox, Terpinski, and Lawry-

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(33) Kuwajima, I.; Nakamura, E. *Acc. Chem. Res.* **1985**, *18*, 181.

(34) Gingras, M.; Harpp, D. N., unpublished results.

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(36) Dried according to Gokel, G. W.; Cram, D. J.; Liotta, C. L.; Harris, H. P.; Cook, F. L. *J. Org. Chem.* **1974**, *39*, 2445.

(37) Dried accordingly to Cox, D. P.; Terpinski, J.; Lawrynowicz, W. *J. Org. Chem.* **1984**, *49*, 3216. Instability of TBAF anhydrous: Sharma, R. K.; Fry, J. L. *J. Org. Chem.* **1983**, *48*, 2112.

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Table V. Comparison of Sulfur Anion Reactivities

reagents	solvent	*T*, °C	time, h	base	yield,[a] %	ref
		Aqueous Medium				
$Na_2S\cdot 9H_2O$	EtOH	20	20	neutral	89	48[a]
$Na_2S\cdot 9H_2O$[b]	H_2O	70	0.3	neutral	91	48[b]
RSH/RBr[c]	H_2O/org. solv.	20	20	NaOH	>70	48[c]
$CH_3C{=}SR(NH_2)^{+}$[d]	$CHCl_3$	20	7–10	KOH(s)	<70	48[d]
RSH/RBr[e]	DMF	45–50	12–15	$CsCO_3$	>90	50
		Anhydrous Medium				
S_8	THF	20	5.0	$LiEt_3BH$	71	64
$(Me_3Si)_2S$	THF	65	8.0	MeLi	>95	4
$ROH/RSH/Ph_3PN(CH_3)Ph^{+}I^{-}$	DMF	20	>8.0	NaH	52–90	48[e]
$R_3SnSSnR_3/F^{-}$	CH_3CN, DMF	20–65	<1.0	neutral	>95–100	this work
$Ph_3GeSGePh_3/F^{-}$	DMF/THF	60	8.0	neutral	80	this work

[a] Average yields of aliphatic sulfides. [b] Catalytic addition of hexadecyl tributyl phosphonium bromide. [c] Catalytic amount of various phase-transfer catalysts. [d] Catalytic amount of tribenzylmethylammonium chloride. [e] Taken from a macrocyclic cyclization reaction where the reagents were added slowly.

Table VI. Formation of Unsymmetrical Sulfides from Organotin Sulfides and Alkyl Halides

entry	halide	organotin[e]	solvent[d]	*T*, °C	time, h	F^- or CN^- (mol)	sulfide	yield,[a] %
1	$CH_3(CH_2)_5Br$	$PhCH_2SSnBu_3$	A	24	2	CsF·18C6 (xs)	$PhCH_2S(CH_2)_5CH_3$	82[b]
2	$CH_3(CH_2)_5Br$	$PhCH_2SSnBu_3$	A	24	2	CsF·18C6 (xs)	$PhCH_2S(CH_2)_5CH_3$	76
3	$CH_3(CH_2)_5Br$	$PhCH_2SSnBu_3$	A	24	12	CsF (xs)	$PhCH_2S(CH_2)_5CH_3$	55
4	$CH_3(CH_2)_5Br$	$PhCH_2SSnBu_3$	A	20	2.0	TBACN (2.2)	$PhCH_2S(CH_2)_5CH_3$	84[c]

[a] Isolated yields except if noted as NMR or GC yield. Identified by NMR, IR, MS and compared to authentic material. [b] ^1H NMR yield. [c] GC yield without internal standard. [d] A = acetonitrile. [e] 1.05 mol.

Table VII. Formation of Sulfides Using Organolead or Organogermanium Sulfide

entry	halide	organolead	solvent[a]	*T*, °C	time, h	fluoride (mol)	sulfide	yield,[b] %
1	$PhCH_2Br$	$(Ph_3Pb)_2S$[c]	D	20	9.5	CsF (4.6)	$(PhCH_2)_2S$	67
2	$PhCH_2Br$	$(Ph_3Pb)_2S$	D	65	5.0	CsF (5.2)	$(PhCH_2)_2S$	81
3	$PhCOCH_2Br$	$(Ph_3Pb)_2S$	D	20	3.0	CsF (6.5)	$(PhCOCH_2)_2S$	95
4	$CH_3(CH_2)_5Br$	$(Ph_3Pb)_2S$	D	65	8.0	CsF (7.5)	$(CH_3(CH_2)_5)_2S$	11
5	$CH_3(CH_2)_5Br$	$(Ph_3Ge)_2S$	D	60	10.0	CsF (5.8)	$(CH_3(CH_2)_5)_2S$	80

[a] D = DMF/THF 1:4 v/v. [b] Isolated yield. [c] 1.05 molar equiv used.

nowicz[38] was not very reactive in the fluorodestannylation procedure. It should also be noted that a "slightly wet" fluoride ion has been demonstrated to have a higher nucleophilicity in some special cases.[44] Tetrabutylammonium cyanide (TBACN) was investigated mostly with activated organic halides such as benzyl bromide, but its reactivity did not permit us to use it with nonactivated electrophiles for making symmetrical sulfides (see entry 3 in Table III). However, TBACN is useful in the reaction of tributyltin benzyl sulfide with 1-bromohexane for making an unsymmetrical sulfide (see entry 4 in Table VI).

Applications of Fluorodemetalation. Organotin Sulfides. Cyano- and fluorodestannylation concepts provide new and useful methods for releasing anions under *mild and neutral conditions*. The methodology can be considered as a general one and no disulfide is formed (see Table IV). The yield is usually higher than 90% when the reaction parameters are optimized. The temperature required is relatively low, and the reaction time is about 1 h for nonactivated halides such as 1-bromohexane.

A rough comparison of the methods available for achieving symmetrical sulfide formation can be divided in two general groups: one that operates under anhydrous conditions and the other in nonanhydrous conditions (Table V). Our method belongs to the first category; a comparison in this group shows that our method is the fastest way to obtain sulfide under anhydrous conditions because of the high reactivity of the sulfur released. A general overview of both groups indicates that only the method involving hexadecyltributylphosphonium bromide as phase-transfer catalyst, competes effectively.[45] Other methods[46,47] can be compared.

The commercial availability of several organotin sulfides[24] plus the special reactivity of the nucleophilic sulfur ions released make this fluorodestannylation one of the most powerful methodologies available.[48] Gleiter and Rittinger[11a] succeeded in the thiacyclization of a 10-membered cyclodiyne by using our procedure. The use of ammonium sulfide $(NH_4)_2S$ did not give satisfactory results.[49] Recently, our method has also been found successful for closing a 13-membered ring,[11b] whereas the classic procedures failed. These macrocyclizations are usually helped by the "cesium effect" (a kinetic effect from "loose" ions pairing of the anionic nucleophile with the cation), as reported by Kellogg.[50] Our procedure is also compatible with hydroxy,[51] nitrile, amide, and α-ketone groups.

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(44) Some fluorides required moisture (exposure to humidity) to achieve the maximum of effectiveness. The explanation is not entirely clear. Clark, J. H. *J. Chem. Soc., Chem. Commun.* **1980**, *80*, 429. Tordeux, M.; Wakselman, C. *Synth. Commun.* **1982**, *12*, 513.

(45) Landini, D.; Rolla, F. *Synthesis* **1974**, 565.

(46) See ref 4; hexamethyldisilthiane (**3**) is unstable and very reactive in the atmosphere, releasing H_2S.

(47) This method uses $Na_2S\cdot 9H_2O$ under basic conditions: Klieser, B.; Rossa, F.; Vogtle, F. *Kontakte (Merck)* **1984**, 3.

(48) A comparison of different methods is given in Table V: (a) Vogel, A. *Textbook of Practical Organic Chemistry*, 4th ed.; Longmans: New York, 1981, p 584. (b) Landini, D.; Rollas, F. *Synthesis* **1984**, 565. (c) Herriott, A. W.; Picker, D. *J. Am. Chem. Soc.* **1975**, *97*, 2345. (d) Singh, P.; Batra, M. S.; Singh, H. *Ind. J. Chem.* **1984**, *24B*, 131. (e) Tanigawa, Y.; Kanamura, H.; Murahashi, S.-I. *Tetrahedron. Lett.* **1975**, 4655.

(49) Eglinton, R.; Lardy, I. A.; Raphael, G. A.; Sim *J. Chem. Soc.* **1964**, 1154. See also Gleitner in ref 8.

(50) Dijkstra, G.; Kruizinga, W. H.; Kellogg, R. M. *J. Org. Chem.* **1987**, *52*, 4230 and references therein. Buter, J.; Kellogg, R. M. *J. Org. Chem.* **1981**, *46*, 4481.

(51) Gingras, M.; Chan, T. H.; Harpp, D. N., unpublished results.

Unsymmetrical sulfide formation can also be grouped into two divisions: the anhydrous and the aqueous. Our method gives yields comparable to the classic way of deprotonation and alkylation of thiols in a basic aqueous mixture or the modern method involving cesium carbonate in a polar aprotic solvent with DMF.[50] The thioiminium[52] and aminophosphonium salts[53] as well as the amide acetal procedures[54] are less versatile, and the yield usually varies with the substrate used (see Table V). A strong feature of our fluorodestannylation procedure favors the neutrality of the conditions, both in the coupling step and in the preparation of the triorganotin mercaptide (see Table VI); only a few reagents have been developed for transferring mercaptides in a neutral medium.[55,56]

As shown in Table VII, an investigation with bis(triphenyllead) sulfide (**5**) in the presence of cesium fluoride and activated organic halides gave excellent yields of thioethers. For instance, benzyl bromide or α-bromoacetophenone (entries 2, 3) afforded 81 and 95% yields, respectively. However, unactivated organic halides such as 1-bromohexane produced low yield of thioethers and gave mainly triphenyllead alkyl sulfides (entry 4). No organic disulfide was detected in any cases. The first fluorodeplumbylation reactions are thus reported here. Bis(triphenylgermanium) sulfide (**4**) was almost as successful as the tin derivative for making thioethers (Table VII).

Comparison of the Reactivities of Organic Silicon, Germanium, Tin, and Lead Sulfides in Fluorodemetalation. Hexamethyldisilthiane or bis(trimethylsilyl) sulfide (**3**) is the only sulfur transfer reagent that gives disulfide as a side product. Germanium and tin analogues react similarly with organic halides to afford thioethers in excellent yield. The reactivity of the Ge–S bond is similar to the Sn–S bond in fluorodemetalation. Germanium resembles tin rather than silicon in its behavior. Organolead (**5**) mainly gives a triorganolead alkyl sulfide intermediate with unactivated halides but generates thioethers with the activated ones; the Pb–S bond is less reactive in the fluorodemetalation process.

Based on product formation, it appears that the Si–S bond is very labile under these conditions. For achieving the formation of organic disulfides, stable transient species such as **10** appear to be generated in some way. The question of the existence of free sulfide ion S^{2-} derived from **3** in the mixture, being responsible for this reaction, has not been ruled out (eq 6). Also, S_N2 displacement with trimethylsilylthiolate ion (Me_3SiS^-) on the sulfur atom of the starting material could be possible (eq 7).

$$S^{2-} + \underset{\mathbf{3}}{Me_3Si\text{–}S\text{–}SiMe_3} \rightarrow Me_3Si\text{–}S\text{–}S^- + \text{“}Me_3Si^-\text{”} \quad (6)$$

$$Me_3Si\text{–}S^- + Me_3Si\text{–}S\text{–}SiMe_3 \rightarrow Me_3Si\text{–}S\text{–}S\text{–}SiMe_3 + \text{“}Me_3Si^-\text{”} \quad (7)$$

$$\underset{\mathbf{10}}{Me_3Si\text{–}S\text{–}S^-}$$

The other sulfur metal bonds do not show this lability. Hexamethyldisilthiane (**3**) decomposes rapidly in air, liberating H_2S. Other organometallics do not show this tendency. However, the lead reagent **6** changes color slowly from pale yellow to dark orange. The most important thermodynamic driving force of these fluorodemetalations is certainly the formation of the metal fluoride bond.[29]

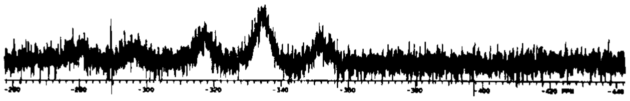

Figure 2. ^{119}Sn NMR spectra (200 MHz) of $(Ph_3Sn)_2S$ + TBAF “anhydrous” in a 1:4 ratio at 20 °C in CD_2Cl_2 showing the triphenyltin difluoride anion along with the proposed complexes **19** or **20** having a sulfur ligand.

$$R_3M\text{–}S\text{–}MR_3 + 2CsF\cdot18C6 \rightarrow \text{“}Cs_2S\text{”}\cdot18C6 + 2R_3MF \quad (8)$$

$$R_3M\text{–}S\text{–}MR_3 + 2n\text{-}Bu_4NF \rightarrow \text{“}(n\text{-}Bu_4N)_2S\text{”} + 2R_3MF \quad (9)$$

$$M = Si, Ge, Sn, Pb$$

The different complexing ability of the metal centers with the free sulfur anion released is probably responsible for the different metal reactivities (eq 10).

$$R_3M\text{–}S\text{–}MR_3 + CsF \rightarrow \text{“}Cs_2S\text{”}\cdot R_3MF \quad (M = Si, Ge, Sn, Pb) \quad (10)$$

Spectroscopic Evidence for Pentavalent Intermediates in Reactions of Substitution at Tin. For all bis(triorganotin) sulfides listed in Figure 1, we observed that a labile pentacoordinated complex was formed at 20 °C with TBAF·$3H_2O$ or TBAF “anhydrous” in CD_2Cl_2. A rapid fluorine nucleus exchange, relative to the NMR time scale, provoked a large broadening of the original signals and an upfield shift of a few ppm in the ^{119}Sn NMR spectra. Tetrabutylammonium cyanide produced the same effect on **2**, but the complexation seemed to be weaker based on the signal broadening and the change in the chemical shift. A strong evolution of H_2S took place in most cases when using TBAF·$3H_2O$, and pentacoordinated anionic tin complexes were formed.[57]

The most interesting results came from a scanning of the ^{119}Sn spectral window from 400 ppm to –550 ppm at low temperature (from 20 °C to –68 °C). It demonstrated a clear triplet at –339 ppm ($^1J[^{119}Sn\text{–}^{19}F]$ = 1958 Hz) and a doublet at –288 ppm (see Figure 2) when using a ratio of 4:1 “dried” TBAF[37]/organotin (mol/mol) at 20 °C in CD_2Cl_2. We never observed hexacoordination at higher field in the ^{119}Sn NMR spectra. The first triplet signal corresponds to difluorotriphenylstannate anion (**11**). This was also confirmed independently with the synthesis of the same anion (**11**) from triphenyltin fluoride with TBAF·$3H_2O$ in a 1:1 ratio.[57]

The second doublet signal has the chemical shift in the range of pentavalent tin species from the ^{119}Sn NMR. We assigned these data to complexes **12a** and **12b**. We ruled out doubly charged complexes because they should have their ^{119}Sn resonance frequencies at much higher field due to a large increase and spread of electron density through the whole molecule and especially on the ^{119}Sn nucleus. Furthermore, we are unaware of reports of doubly charged pentavalent triorganotin complexes. The coupling constant $^1J[^{119}Sn\text{–}^{19}F]$ is 1730 Hz. This value is in the range of our observed $^1J[^{119}Sn\text{–}^{19}F]$ couplings (1958 Hz) for the difluorotriarylstannate anion[57] (**11**); the lower value is clearly indicative of a different species. From an initial observation (^{119}Sn NMR alone) structure **13** appears valid;

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(52) Singh, P.; Batra, M. S.; Singh, H. *Ind. J. Chem.* **1983**, *22B*, 484; **1985**, *24B*, 131.

(53) Tanigawa, Y.; Kanamaru, H.; Murahashi, S.-I. *Tetrahedron Lett.* **1975**, 4655.

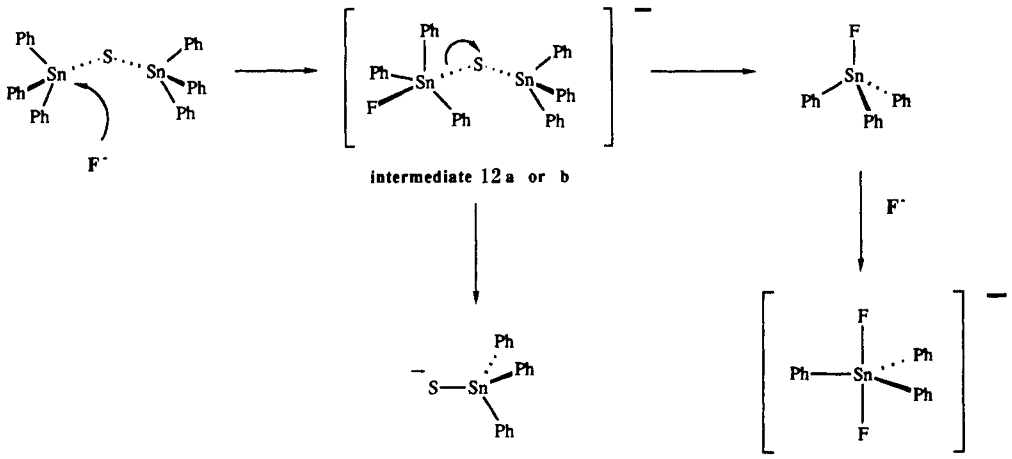
(54) Holy, A. *Tetrahedron Lett.* **1972**, 585.

(55) Harpp, D. N.; Kobayashi, M. *Tetrahedron Lett.* **1986**, *27*, 3975.

(56) Guggenheim, T. L. *Tetrahedron Lett.* **1987**, *28*, 6139.

(57) This is in analogy to the triphenyldifluorotriphenylstannate anion prepared under similar conditions: Sau, A. C.; Carpino, L. A.; Holmes, R. R. *J. Organomet. Chem.* **1980**, *197*, 181. A detailed dynamic multinuclear NMR study will be published elsewhere for such complexes.

Scheme II



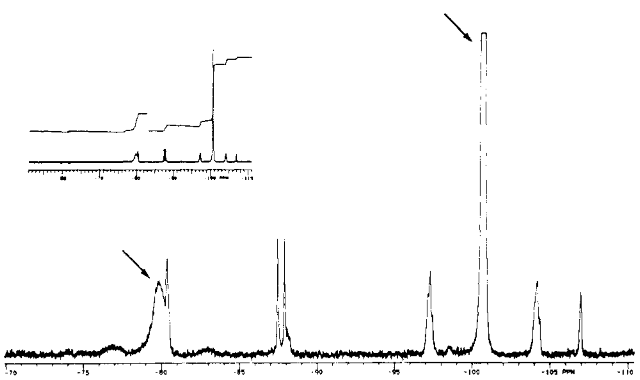
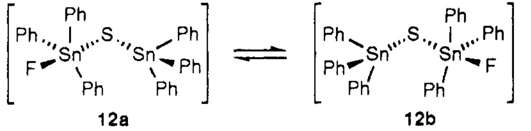
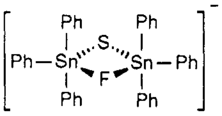


Figure 3. ^{19}F NMR spectra (300 MHz) of $(Ph_3Sn)_2S$ + TBAF "anhydrous" in 1.3/1.0 ratio at -80 °C in CD_2Cl_2 showing the triphenyltin difluoride anion (right arrow) and the proposed complexes **19** or **20** with its tin satellites (left arrow). Other signals not mentioned in the text are impurities.

however, it is inconsistent with the ^{19}F NMR of Figure 3 (vide infra).



12a **12b**



13

A ^{19}F NMR study at -80 °C in CD_2Cl_2 also confirmed the presence of the difluorotriphenylstannate anion (**11**) plus the presence of complexes (**12a** or **12b**). As shown in Figure 3, the signal at -100.7 ppm corresponds to difluorotriphenylstannate anion (**11**) with its ^{119}Sn and ^{117}Sn satellites at -97.2 and -104.1 ppm. The broad signal at -79.9 ppm indicated an organotin-fluoride complex as judged from the broad ^{119}Sn and ^{117}Sn satellites centered at -77.01 and -83.00 ppm.

Assuming a doublet signal coming from **12a** or **12b** and centered at -79.9 ppm from both tin satellites, a rough evaluation of $^1J[^{119}Sn-^{19}F]$ and $^1J[^{117}Sn-^{19}F]$ gives a value of 1680 Hz (from the peak center of both signals). A previous evaluation of $^1J[^{119}Sn-^{19}F]$ established a slightly higher coupling constant than $^1J[^{117}Sn-^{19}F]$ (~87 Hz).[57] Adding a correction of ~44 Hz (87 Hz/2) to the centered ^1J[Sn-F] found, gives $^1J[^{119}Sn-^{19}F]$ = 1722 Hz. This value is close to 1730 Hz found with ^{119}Sn NMR. We can conclude that we observed the same species as with ^{119}Sn NMR (see Figure 2). A symmetrically bridged structure (**13**), would be expected to give a triplet signal and a ^1J-[Sn-F] coupling constant much different than a normal value of ~1958 Hz for $^1J[^{119}Sn-^{19}F]$, but no data are available for such exotic coupling constants. Finally, as the signal is broad even at -80 °C, we concluded that a slow exchange between **12a** and **12b** took place at this temperature.

In summary, the combined results of tin and fluorine NMR studies indicate that there is a species in addition to $Ph_3SnF_2^-$ showing coupling between one fluorine and one tin atom with a coupling constant of about 1730 Hz. An equilibrium between structures **12a** and **12b** would appear to best satisfy the above data. From the publication of Holmes, Sau, and Carpino, it is well described that the triphenyltin moiety gives stable and isolable crystalline pentacoordinated tin complexes at 20 °C.[57]

From this spectroscopic evidence we conclude that substitution at tin proceeds through a pentacoordinated tin species best represented in Scheme II. A sulfur ligand on tin is replaced by a fluorine ligand through a pentacoordinated intermediate. This latter strongly activates the release of the highly nucleophilic sulfur anion in our fluorodestannylation. These results confirmed the model of substitution at tin.[58] To date, this model was fully described in some racemization processes at tin where kinetic evidence stated or assumed the existence of a pentavalent species as intermediate; however, to the best of our knowledge, only one spectroscopic evidence was reported.[58] Some intramolecular complexations on tin with a bidentate ligand were also used to model substitution derived from an external nucleophile.[59] As an extension

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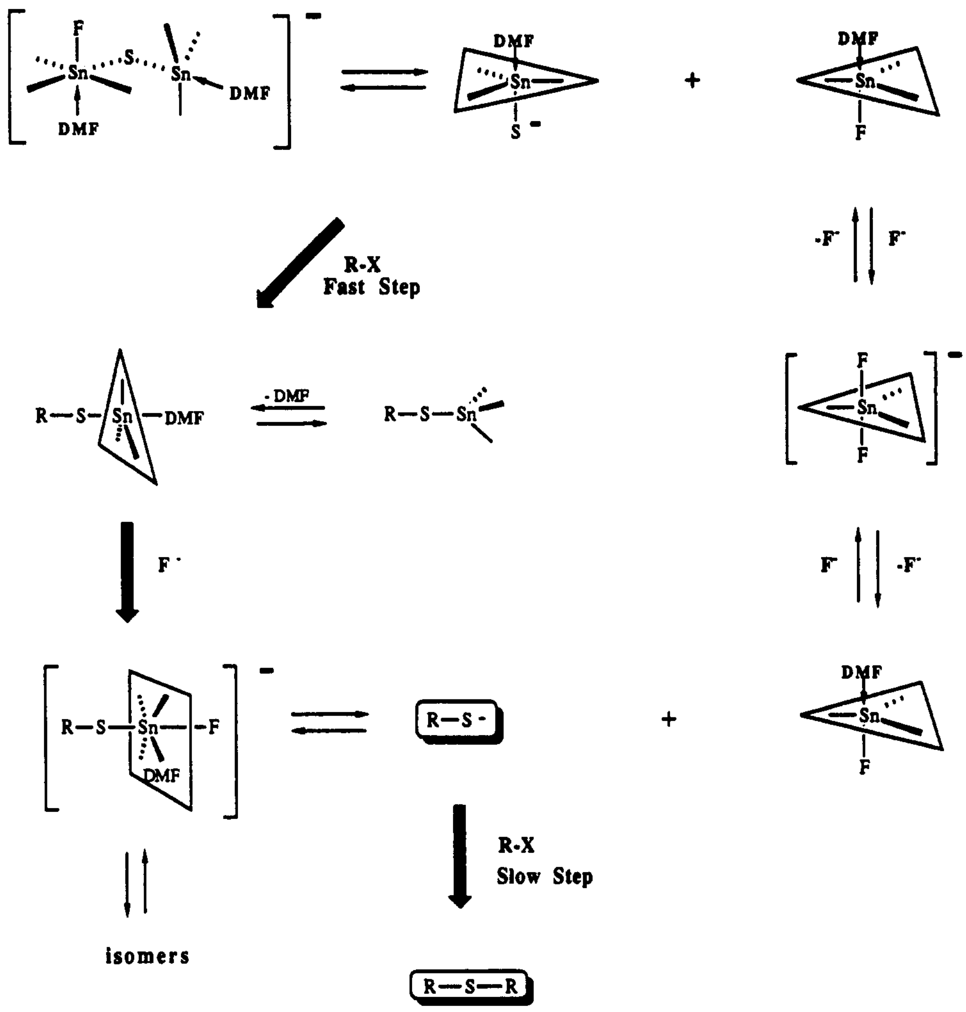
Scheme III



of our work, it might also reinforce the model for the substitution at silicon where the racemization process has been well studied.[60]

Toward the Mechanism of Fluorodemetalation. The work of Ohya and Kozuka in 1978[61] on organotin sulfides proposed a sulfonium salt intermediate to explain the formation of several sulfides in nonpolar and noncoordinating solvents. We determined that the most important parameter in this kind of reaction in the absence of fluoride or cyanide ion is the solvent effect;[6] this seems to be in agreement with the sulfonium salt mechanism proposed.

However, the fluoride and cyanide effects became crucial when these ions were incorporated in the mixture, followed by the usual solvent effect. We determined by ^{119}Sn and ^{19}F NMR that bis(triphenyltin) sulfide (**7**) reacted with TBAF (anh.) to form a pentacoordinated tin complex corresponding to difluorotriphenylstannate anion $[Ph_3SnF_2^-]$ (**11**) in CD_2Cl_2 plus some nucleophilic sulfur species (**12a** or **12b**). In an anhydrous medium, the liberation of hydrogen sulfide should be minimized, and we feel that a slightly different complexation should take place in polar coordinating solvents. To explain the strong solvent effects in these reactions (with DMF, CH_3CN), we propose the formation of hexacoordinated complexes in low concentration having as ligands a solvent molecule (DMF, CH_3CN), a fluorine, and a sulfur atom. We think that other substituents on tin (like butyl and methyl) should act in a similar way.

A likely mechanism derived from our complexation study (CD_2Cl_2) with fluorine ion is shown in Scheme III. We describe most of the pentavalent triorganotin complexes having trans ligands. Although some cis complexes could be present in solution, it is well known that trans triorganotin complexes are more stable, and this stereochemistry usually predominates for triaralkyltin complexes.[62] For hexacoordination, the stereochemistry is difficult to predict. Such penta- or hexacoordination with fluoride in order to enhance the nucleophilicity of a ligand has precedents in the silicon literature: for an example among many others, a kinetic study with trimethylsilane and TBAF supported the existence of a hexacoordinated silicon atom in a reaction where a hydride was transferred to a carbonylated compound.[63]

We observed the formation of an intermediate triorganotin alkyl sulfide on TLC using 1-bromohexane and bis(tributyltin) sulfide (**2**). With the same organic halide, we were able to trap this intermediate by adding a small

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[60] Corriu, R. J. P.; Guérin, C.; Moreau, J. J. E. *Topics in Stereochemistry*; Eliel, E. L., Wilen, S. H., Allinger, N. L., Eds.; John Wiley & Sons: New York, 1984; Vol. 15, pp 167–174. See also: Deiters, J. A.; Holmes, R. R. *J. Am. Chem. Soc.* **1987**, *109*, 1686.

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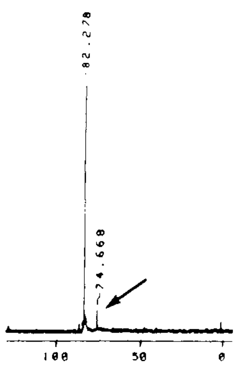

Figure 4. ^{119}Sn NMR spectra (200 MHz) of possible intermediate $PhCH_2SSnBu_3$.

amount of water to the mixture, obtaining the corresponding 1-hexanethiol in 59% yield along with some thioether.[35] We also followed the reaction of bis(tributyltin) sulfide (**2**) (1.1 mol equiv) with benzyl bromide (2.0 mol equiv) and $TBAF{\cdot}3H_2O$ (1.4 mol equiv) at −20 °C by ^{1}H NMR spectroscopy with slow increase of the temperature to 20 °C (CD_3CN as solvent). The CH_2 signal of benzyl bromide at 4.63 ppm gradually decreased as a new signal at 3.63 ppm corresponding to the CH_2 of dibenzyl sulfide increased. We noted a small peak at 3.75 ppm remaining during the whole reaction which corresponded exactly to tributyltin benzyl sulfide (**9**) prepared independently.[27] Similarly, a ^{119}Sn NMR study also confirmed the formation of this product (see Figure 4). It should be noted that this reaction was carried out under such conditions to favor a high concentration of the possible intermediate; i.e. $TBAF{\cdot}3H_2O$ was used in 1.4 mol equiv instead of 2.0 mol equiv. With benzyl bromide, the second nucleophilic substitution seemed to be the slowest step because of this observed tin intermediate.

Considering these intermediates, it is obvious that the sulfur atom is not liberated in the form of a sulfide "S^{2-}" ion which is characteristic of the methods developed by Steliou (hexamethyldisilthiane (**3**) and methyllithium)[4] and Gladysz[64] ($LiBHEt_3$ and elemental sulfur) in anhydrous media. There remains a tin substituent bound to the sulfur atom until the last step of the reaction in this stepwise transformation.

To explain the relative rates of the two nucleophilic substitutions, we thought that the rate of the first alkylation with the sulfur anion should be favored by the proximity of the tin atom. It should increase the electron density on sulfur, hence facilitate the S_N2-reaction (while lowering the energy of the transition state with a polarizability and delocalization of the electronic cloud through the tin atom). To our knowledge, the metal proximity effect of anions in S_N2 reactions has not been clearly delineated in the literature. The second step is likely slower because of the lack of this metal proximity effect.

Explanations for different reactivities observed with different fluoride sources come from the cations associated with the fluoride ions. These cations become the counterions of sulfur anions in some step in the mechanism. It is well known that these ion pairs directly affect the alkylation rate. For example, tetrabutylammonium cation makes the sulfur anion more "loose" or free than the cesium cation. As proof of this hypothesis, the effect of the complexation of 18-crown-6 with cesium fluoride provoked an initial rate enhancement of five for the formation of benzyl *n*-hexyl sulfide while reacting tributyltin benzyl sulfide (**9**), 1-bromohexane, cesium fluoride, and 18-crown-6 in CD_3CN.[36]

As an extension of the proposals above, bis(triphenylgermanium) sulfide (**4**) reacted in a stepwise manner as with organotin sulfides. While reacting 1-bromohexane with this reagent and cesium fluoride, we followed the reaction by TLC using 5% EtOAc/95% *n*-hexane as eluent. Bis(triphenylgermanium) sulfide (**4**) ($R_f = 0.40$) disappeared slowly in favor of a new spot slightly less polar ($R_f = 0.65$). This spot also disappeared and a new, even less polar spot ($R_f = 0.80$) was formed, corresponding to di-*n*-hexyl sulfide. We believe that the intermediate spot corresponds to triphenylgermanium *n*-hexyl sulfide but we were unable to characterize it.[65]

The rate of the first S_N2 attack as proposed in the mechanism seems to be fast for silicon and tin but slightly slower with germanium and lead. However, the second alkylation offered several differences between the rates: for silicon and tin, it is fast; slower for germanium, and very slow for lead. The tendency of lead to easily complex the free thiolate ligands prevents them from further alkylation. As triorganogermanium fluorides do not generally form polymeric pentacoordinated chains like triorganotin fluorides, it is a better Lewis acid for the thiolate anions released; this might explain the slower rates of alkylation in the last step in the fluorodegermanylation. From our results, we can make a generalization; we always observed a fast nucleophilic substitution in the first step of the fluorodemetalation reactions but a slower substitution in the second one.

We propose that a metal or a metalloid atom of group IV directly attached to an anion (i.e. having structure R_3MNu^-) will increase the nucleophilicity of the latter if the organic groups R on the metal do not sterically inhibit the reactivity of this anion (M = Si, Ge, Sn, Pb and R = aralkyl group). Work on the trimethylsilanolate anion Me_3SiO^- is also in agreement with this statement.[66]

Conclusions

We reported three novel, general methodologies: fluorodestannylation and for the first time, fluorodegermanylation, and fluorodeplumbylation. From the results with sulfur, it appears to us that the fluorodemetalation reactions of germanium and lead could open wide fields of totally new synthetic procedures involving Ge–O, Ge–Se, Ge–Te, Ge–C, Pb–O, Pb–Se, Pb–Te, and Pb–C bond cleavage reactions under mild and neutral conditions, in the presence of fluoride ion. Some sulfur transfer agents (listed in Figure 1) released one of the most active sulfur anions known to date.

We have given spectroscopic evidence for a pentacoordinated intermediate involved in the substitution at tin from low-temperature ^{19}F and ^{119}Sn NMR spectroscopy. A mechanistic proposal has been demonstrated for such fluorodemetalations based on results from organotin chemistry. We propose that the metal-proximity effect on a charged anion will increase the nucleophilicity of the latter in the absence of major steric hindrance coming from the organic ligands on the metal.

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(65) With bis(triphenyllead) sulfide (**5**), we essentially obtained the same chromatographic results as with bis(triphenylgermanium) sulfide (**4**). The intermediate spot corresponding to triphenyllead *n*-hexyl sulfide (**6**) has been isolated and characterized by ^{1}H NMR; it decomposed slowly at room temperature. The fluorodeplumbylation also proceeded in a stepwise manner as evidence by TLC.

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Experimental Section

Chemicals. Bis(tributyltin) sulfide (2) was purchased from Pfaltz and Bauer or prepared as previously described.[26] All organotin chlorides, triphenylgermanium chloride, trimethylgermanium bromide, tributyltin hydride, tetrabutylammonium cyanide, tetrabutylammonium fluoride trihydrate, 18-crown-6, DAST, TASF, and sodium sulfide nonahydrate were purchased from Aldrich Chemical Co. and used without further purification. Triphenyllead acetate, dibutyltin sulfide (7), and tetramethylgermanium were bought from Morton Thiokol (Alfa Products). Bis(trimethylsilyl) sulfide (3) was purchased from Petrarch Systems. Most organic halides or thiols were used as received from Aldrich excepted benzyl bromide, which was distilled prior to use. Cesium fluoride was dried (110 °C) in a pistol dryer for 2 days at 5 mmHg. Acetonitrile (reagent grade) was refluxed for several days over calcium hydride and distilled prior to use. Dimethylformamide (reagent grade) was distilled over calcium hydride and kept over molecular sieves 3Å (dried in an oven at 180 °C for several weeks) under a nitrogen atmosphere. When some water was involved in the medium, spectroscopic grade DMF and CH_3CN were used without purification. Finally, bis(triaralkyltin) sulfides react with an aqueous solution of zinc acetate ($Zn(OAc)_2$) to give a precipitate of zinc sulfide (ZnS) at room temperature.[67] A large excess of zinc acetate ($Zn(OAc)_2$) should be used because the residual fluoride ions also react with this reagent for giving zinc difluoride (ZnF_2).

Instrumentation. ^{119}Sn, ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded on a Varian XL-200 (4.75 T) or XL-300 (7.05 T) spectrometer. The NMR shifts are reported in ppm in reference to tetramethyltin, tetramethylsilane, benzotrifluoride, and $CDCl_3$ or CD_2Cl, respectively. The uncorrected melting points were recorded in capillary tubes on a Gallenkamp apparatus. Infrared spectra were recorded on an Analect AQS-20 FTIR spectrometer using neat liquid between two blank sodium chloride cells or in solution with 0.1 mm sodium chloride cells with chloroform as solvent. Low-resolution electron impact mass spectra were taken on a DuPont 21-492B mass spectrometer with a direct insertion probe (70 eV at 250 °C). Chemically induced mass spectra were recorded with a source of 70 eV at 210 °C (isobutane) on a Hewlett-Packard 5980A mass spectrometer. GC–MS was recorded on Finnigan Mat 800 linked to GC Varian Model 3500 using a capillary column as described below. An ionization source of 70 eV was used.

Gas chromatography was performed on a Hewlett-Packard Model 5890 combined with a Hewlett-Packard integrator Model 3390A or a Varian GC Model No. 3700. A capillary column with methylsilicone as adsorbent on the Hewlett-Packard GC was used to monitor some of the reactions, especially the conversion of 1,5-dibromopentane to pentamethylene sulfide. The progress of the reactions and the purity of final products were monitored by TLC on aluminum sheets precoated with 0.2 mm silica gel 60 F254 (E Merck 5554). Most of the thin-layer chromatograms were visualized using iodine absorbed on silica gel, with a molybdic acid solution, using a UV lamp or an acidic solution of *p*-anisaldehyde. The purity of all title compounds was judged to be >95% by GC and/or ^{13}C and ^{1}H NMR determinations. Flash chromatography was carried out using silica gel from E. Merck: Kieselgel 60 no. 9385; particles size, 0.040–0.063 mm.

Bis(triphenyltin) Sulfide (7). A 50-mL flask was charged with triphenyltin chloride (10.53 g, 2.73 mmol) and reagent grade tetrahydrofuran (27 mL). A solution of sodium sulfide nonahydrate (6.56 g, 2.73 mmol) in 8 mL of water was added to this in one portion. The mixture was stirred vigorously while refluxing for 2 h at 65 °C (ratio THF/H_2O, 3.3/1). The reaction was followed by TLC (UV detector). When completed, THF was evaporated and 150 mL of ethyl acetate was added, and the mixture was stirred for a few minutes to completely dissolve the bis(triphenyltin) sulfide. The organic phase was separated, washed with 2 × 30 mL of water, and dried over sodium sulfate. The mixture was filtered, and the solvent was evaporated. Crude bis(triphenyltin) sulfide (10.05 g, 99.8%; mp 139–140 °C, lit.[68] mp 141.5–143 °C) is obtained as colorless crystals. The solid was recrystallized from hexane: mp 144–145 °C; ^{1}H NMR (200 MHz) 7.15–7.40 (m); ^{119}Sn NMR (200 MHz) −54.70 (s).

Bis(trimethyltin) Sulfide (1). A 250-mL flask was charged with trimethyltin chloride (30.0 g, 0.150 mol), sodium sulfide nonahydrate (36 g, 0.150 mol), and absolute ethanol (100 mL). The mixture was heated at reflux (77–80 °C) for 5 h and monitored by GC. The solvent was evaporated, and *n*-hexane (~150 mL) was added and washed with water (~75 mL). The aqueous phase was kept and extracted more with diethyl ether (3 × 50 mL). The *n*-hexane and ether phases were dried separately over sodium sulfate; the last traces of solvent were removed with a vacuum pump. The *n*-hexane phase afforded 14.72 g of bis(trimethyltin) sulfide (1), and the ethereal phase gave 6.36 g (21.08, 78%) of pure liquid (99% by GC): ^{1}H NMR 0.45 (s); ^{119}Sn NMR 91.54 (s). The use of THF/H_2O (3.3/1) as solvent gave 70% yield. **Caution**! Trimethyltin compounds are highly toxic.

Tributyltin Benzyl Sulfide (9). This compound was made in a similar way as reported by Talley and Colley.[25a]

Bis(triphenylgermanium) Sulfide (4). In a 50-mL flask was placed triphenylgermanium chloride (2.00 g, 5.89 mmol) and sodium sulfide nonahydrate (0.780 g, 3.25 mmol) partly sponged with a paper for removing water and then crushed. Finally, absolute ethanol was added (25 mL), and the mixture was refluxed for 2.5 h. The completion of the reaction was indicated by the disappearance of triphenylgermanium chloride on TLC using 20% EtOAc/80% *n*-hexane as eluent. Ethanol was evaporated, and the residual yellowish solid was taken up in chloroform (30 mL). A filtration on porous glass for removal of sodium chloride and evaporation of the liquid afforded a stable, odorless, pale-yellowish solid corresponding to bis(triphenylgermanium) sulfide (4, 1.740 g, 46%), mp 118–119 °C. The solid was redissolved in dichloromethane and filtered through a short column of silica gel (dichloromethane as eluent), and the solvent was partly evaporated. The product was recrystallized with the addition of *n*-hexane; mp 126–127 °C (804 mg). A trituration of the solid in 25 mL of *n*-hexane (repeated twice) followed by a filtration afforded a pure product, mp 129–130 °C (lit.[69] 138 °C). A flash chromatography using 30% toluene/70% *n*-hexane or 10% EtOAc/90% *n*-hexane failed due to the insolubility of bis(triphenylgermanium) sulfide (4); ^{13}C NMR (300 MHz) 136.74, 134.63, 129.27, 128.02; MS (EI) (*m*/*z*, rel intensity) 643 (0.35), 642 (0.68), 641 (0.72), 640 (0.61), 638 (0.78), 637 (0.22), 636 (0.34) [M^+], 549 (47.4), 548 (31.2), 547 (61.2), 545 (56.1) [$M^+ - H_2S$ and $Ph^\bullet$], 471 (10.7), 469 (12.9), 467 (12.5) [$M^+ - H_2S$ and 2 $Ph^\bullet$], 379 (4.1), 377 (4.3), 375 (5.8) [$M^+ - H_2S$ and 3 $Ph^\bullet$], 307 (22.4), 305 (100), 304 (35.7), 303 (72.9), 301 (55.3) [Ph_3Ge^+], 227 (15.2), 225 (11.8), 151 (38.3), 149 (28.4), 147 (22.4) [$PhGe^+$].

Bis(triphenyllead) Sulfide (5). A 250-mL flask was charged with triphenyllead acetate (10.00 g, 20.10 mmol), sodium sulfide nonahydrate sponged with paper for removing excess water (2.53 g, 10.53 mmol), and 50 mL of absolute ethanol. The reaction was stirred for 2 days at room temperature. As the ethanol was added, a dark brownish color took place. Ethanol was evaporated, and chloroform (100 mL) was poured in the flask. The solution was stirred for a few minutes and then filtered on a pad of Celite. The solvent was evaporated, and to the oily residue was added a few milliliters of *n*-hexane in order to induce the crystallization of the solid. All of the solvent was then evaporated under reduced pressure. Bis(triphenyllead) sulfide (5) was obtained as an odorless, pale-yellowish solid (8.94 g, 94% yield), mp 133–134 °C (lit.[70] mp 137–139 °C). This solid was pure as shown by TLC and was used without further purification (TLC, 10% EtOAc/90% *n*-hexane; I_2 or UV). An attempt to recrystallize the solid in hot ethanol failed and decomposed it, giving some dark insoluble impurities. Dissolution of the solid in chloroform followed by a filtration through a short column of silica gel using chloroform as eluent and the trituration with *n*-hexane afforded a better purity: mp 136–137 °C; ^{13}C NMR (CD_2Cl_2, 200 MHz) 137.02, 129.96, 129.24, 129.03; MS (EI) (*m*/*z*, rel intensity) 833 (0.3), 832 (0.3), 831 (0.25) [$M^+ - Ph^\bullet$], 440 (17.5), 439 (9.1), 438 (42.3), 437

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(40.1) [Ph_3Pb^+], 285 (68.6), 284 (29.6), 283 (32.3) [$PhPb^+$], 208 (100), 207 (42.5), 206 (50.5) [Pb^+].

***n*-Hexyl Triphenyllead Sulfide (6).** Into a 25-mL flask was placed 1-bromohexane (0.363 g, 2.20 mmol), bis(triphenyllead) sulfide (**5**, 1.00 g, 1.10 mmol), an excess of dried cesium fluoride (1.10 g, 7.24 mmol), and 18-crown-6 (0.195 g, 0.74 mmol), and 10 mL of THF and 2.5 mL of DMF. The reaction was stirred at room temperature for 2.0 h and then heated at 60 C for 23 h. The completion of the reaction was indicated by the disappearance of bis(triphenyllead) sulfide on TLC (10% EtOAc/90% *n*-hexane; R_f = 0.33) and the formation of a less polar spot (R_f = 0.52); ^{1}H NMR (200 MHz) 7.67 (H ortho, 6 H, d, d, J[H ortho–H meta] = 8 Hz, J[H ortho–H para] = 1.5 Hz, J[^{207}Pb–H ortho] = 44 Hz), 7.44 (H meta + H para, m, 9 H), 2.78 (CH_2S, 2 H, t), ^{207}Pb satellite: 2.78 (d, t, J[CH_2–^{207}Pb] = 30 Hz, J[CH_2–CH_2–S] = 7.6 Hz), 1.50 (CH_2CH_2S, 2 H, q, J = 6.8 Hz), 1.18 (m, 6 H), 0.81 (CH_3, 3 H, t, J = 6.6 Hz).

Benzyl Triphenyllead Sulfide. This compound was isolated as an intermediate from the reaction of benzyl bromide and bis(triphenyllead) sulfide at room temperature. Flash chromatography using 5% EtOAc/95% *n*-hexane as eluent afforded a pale yellowish solid: 25 mg (0.024 mmol, 1% yield); ^{1}H NMR (200 MHz) 7.58 (H ortho, 6 H, d, d, J[H ortho–H meta] = 8 Hz, J[H ortho–H para] = 1.5 Hz [^{207}Pb satellites = 7.58 (d, d, d, J[Pb–H ortho] = 44 Hz, J[H ortho–H meta] = 8 Hz, J[H ortho–H para] = 1.5 Hz)], 7.40 (H meta + H para, 9 H, m), 7.14 (Ph of benzyl, 5 H), 3.98 (CH_2, 2 H, s) [satellites = 3.98 (d, J [^{207}Pb–CH_2] = 28 Hz)].

Formation of Sulfides with Organotin Sulfides. Without Fluoride or Cyanide Ion. Diphenacyl Sulfide. α-Bromoacetophenone (0.78 g, 3.92 mmol) was dissolved in 10 mL of DMF (spectrograde). To this solution was added another solution consisting of bis(tributyltin) sulfide (**1**, 1.20 g, 1.96 mmol) in 10 mL of DMF and 3 mL of ethyl acetate (spectrograde, to solubilize completely). The mixture was stirred at room temperature for 24 h; a yellow color usually appears. The ethyl acetate was evaporated, and *n*-hexane was injected slowly; the product precipitated, and a simple filtration gave 309 mg of diphenacyl sulfide (1.14 mmol, 58% yield) as a pure product, mp 74–75 °C. Another recrystallization in *n*-hexane gave a sulfide with a sharp mp of 75–75.5 °C. A second crop of sulfide from the initial reaction mixture afforded a further 71 mg, total mass 380 mg, 71% yield.

Dibenzyl Sulfide. In a 50-mL flask was placed 1.00 g of bis(tributyltin) sulfide (**2**, 1.63 mmol), 15 mL of DMF (spectrograde), 5 mL of ethyl acetate (spectrograde), and then freshly distilled benzyl bromide (560 mg, 3.27 mmol). The mixture was stirred for 22 h at 45 °C and taken up in 100 mL of ethyl acetate. The organic phase was washed with 5 × 60 mL with water to remove DMF. A solution of potassium fluoride was added and stirred vigorously for a few minutes. The precipitate was collected, and the organic phase was washed with water and then dried over sodium sulfate. The evaporation of the solvent gave a residue that was purified by a flash chromatography on silica gel using a mixture of cyclohexane/hexane (1:1) and afforded 60 mg of benzyl sulfide (17% yield).

General Procedure for the Formation of Symmetrical Sulfides Using Tetrabutylammonium Fluoride Trihydrate. The halide (2.00 mmol) and the bis(triaralkyltin) sulfide (1.05 mmol) are placed in the same flask, and a volume of acetonitrile or DMF/EtOAc (5:1 v/v) (spectrograde) was added to obtain a concentration of ca. 0.15–0.20 M based on the halide. Then tetrabutylammonium ammonium fluoride trihydrate (2.10–2.20 mmol) was added, and the mixture was stirred vigorously at room temperature for the appropriate time (very often a yellow to orange color appeared). For acetonitrile, the workup consisted of evaporating the solvent, adding ethyl acetate, and finally washing the organic phase with water (triaralkytin fluoride often precipitates). The mixture was filtered (Celite), and the organic phase was dried over sodium sulfate and filtered. The entire solution of ethyl acetate was passed through a short column of silica gel using only ethyl acetate. With DMF, some ethyl acetate was added and the organic phase was washed with water to get rid of the DMF before continuing the treatment in the same way as described with acetonitrile. For a better purification, flash chromatography was carried out only for some sulfides. The yield obtained was excellent in most cases. Only pure ethyl acetate should be used in the purification to get rid completely of residual tin derivatives. In some cases, the filtration through a short column of silica gel was not necessary and a usual flash chromatography was sufficient. However, for a safer purification, the short column method with ethyl acetate is strongly suggested (especially with nonpolar products). For hydrophilic sulfides such as diacetonyl sulfide we avoided the use of water in the workup. After acetonitrile was evaporated, the mixture was filtered through a short column of silica gel and continued as above. This general method was applied to all of the sulfides reported in Table III or IV where TBAF was used.

4-Thia-3,5-dimethyl-2,6-heptanedione [$(CH_3COCH(CH_3))_2S$]: one spot on TLC (EtOAc/hexane, 2:8); ^{1}H NMR (60 MHz) 3.43 (q, 2 H), 2.25 (s, 6 H), 1.40 (d, 6 H); MS 174 (M^+, 21), 131 (29), 114 (26), 113 (25), 87 (34), 72 (47), 71 (34), 69 (27), 60 (25), 59 (38), 57 (41), 55 (37), 45 (31), 43 (100), 41 (32), 29 (26), 28 (89), 27 (25).

3,7-Dithiacyclooctane-1,5-dione: white solid; IR (max, $CHCl_3$) 2945, 2920, 2865, 2850, 1700, 1395, 1260, 1175 (large band); ^{1}H NMR (60 MHz) 3.58 (s); MS 176 (M^+, 23), 133 (22), 103 (32), 101 (21), 98 (26), 92 (33), 91 (28), 74 (31), 71 (29), 61 (39), 60 (62), 59 (31), 58 (33), 57 (29), 56 (28), 55 (33), 49 (21), 47 (23), 46 (62), 45 (65), 43 (100), 42 (38), 41 (27), 39 (44), 29 (41), 28 (55), 27 (45), 26 (31).

General Procedure for the Formation of Symmetrical Sulfides Using Cesium Fluoride with 18-Crown-6. The halide (2.00 mmol), the bis(triaralkyltin) sulfide (1.05 mmol), and a catalytic amount of 18-crown-6 (~0.2 mmol) were added together, and a volume of dried acetonitrile was injected using a syringe to give a concentration of about 0.20–0.25 M based on the halide. An excess of dried cesium fluoride (~4 mmol) was added. The mixture was heated (if needed) and then cooled to room temperature, and the solvent was evaporated and taken up with ethyl acetate. Water was added, and organotin fluoride precipitated. The mixture was filtered through a pad of Celite and passed through a short column of silica gel. Only ethyl acetate must be used here; if needed a flash chromatography can be carried out.

Typical Procedure: Preparation of Di-*n*-hexyl Sulfide. To a 50-mL flask was added 1-bromohexane (409 mg, 2.48 mmol), bis(trimethyltin) sulfide (**1**, 445 mg, 1.24 mmol), and a catalytic amount of 18-crown-6 (132 mg, 0.50 mmol) under a nitrogen atmosphere. Ten milliliters of acetonitrile (dried over calcium hydride and P_2O_5) was added with a syringe. Cesium fluoride (800 mg, 5.27 mmol, dried at 110 °C for 2 days at 5 mmHg) was added in one portion. The mixture was stirred vigorously under nitrogen and heated at 75 °C for 75 min in an oil bath. After cooling, the solvent was removed and 50 mL of ethyl acetate was added. After stirring 5 min, the mixture was filtered over Celite and then passed through a short column of silica gel using only ethyl acetate as eluent. Di-*n*-hexyl sulfide (250 mg, quantitative yield) was obtained as a colorless liquid in a pure state, as confirmed by GC and ^{1}H NMR (200 MHz) analyses.

5-Thia-3,7-dimethylnonane: ^{1}H NMR (200 MHz) 2.50 (d, d, ^1J = 20 Hz, ^2J = 5.6 Hz, 2 H), 2.33 (d, d, ^1J = 20 Hz, ^2J = 7.0 Hz, 2 H), 1.52 (m, 4 H), 1.22 (m, 2 H), 0.97 (d, 6 H), 0.89 (t, 6 H).

Formation of Symmetrical Sulfides with Tetrabutylammonium Cyanide (TBACN). Dibenzyl Sulfide. In a 25-mL flask was placed freshly distilled benzyl bromide (428 mg, 2.50 mmol), bis(tributyltin) sulfide (**2**, 803 mg, 1.31 mmol), dried acetonitrile (12 mL), and TBACN (706 mg, 2.63 mmol). The reaction mixture was kept under nitrogen and stirred for 50 min at room temperature. The acetonitrile was evaporated and replaced with ethyl acetate (25 mL); a solution saturated with zinc acetate was then added to destroy any excess of organotin sulfide, and stirring was continued for 15–30 min. The white precipitate that formed (ZnS) was collected, and the organic phase was washed with water (~20 mL). A saturated solution of potassium fluoride and TBAF·$3H_2O$ (~200 mg) was added, and stirring was continued for 15–30 min. The phases were separated or filtered (if a precipitate was formed). The organic phase was washed with water (20 mL) and dried over sodium sulfate. A flash chromatography on silica gel (hexane as eluent) afforded 109 mg of a semisolid with a low melting point corresponding to dibenzyl sulfide (41%).

Other Fluorides Used in This Study. Anhydrous tetrabutylammonium fluoride (TBAF) was prepared as usual.[37]

TBAF·3H_2O adsorbed on silica gel was made by following the procedure of Clark[71] except that silica gel having particles size of 0.040–0.063 mm was used.

TEAF·3H_2O with 3-Å Sieves. TEAF·3H_2O (555 mg, 3.72 mmol), 7.0 mL of dried THF, and 1–1.5 g of molecular sieves (3-Å) were placed in a flask under a nitrogen atmosphere. The mixture was stirred overnight, and then the solvent was evaporated to dryness with a strong flow of nitrogen while warming the flask slightly over a hot water bath. 1-Bromohexane (585 mg, 3.54 mmol), bis(trimethyltin) sulfide (**1**, 667 mg, 1.86 mmol), and acetonitrile (10 mL) were added to the flask, and stirring at room temperature was continued for 5.5 h. The solvent was evaporated and ethyl acetate was added, followed by a filtration through a short column of silica gel using ethyl acetate as eluent. The crude product showed good purity by ^{1}H NMR (202 mg, 56% yield): ^{1}H NMR (200 MHz) 2.51 (t, 4 H), 1.58 (quintuplet, 4 H), 1.48–1.20 (m, 12 H), 0.90 (t, 6 H).

Anhydrous Benzyltrimethylammonium Fluoride (BTAF). BTAF·H_2O (2.49 g), dried THF, and spherical molecular sieves, 3-Å (12.8 g), were placed in a flask and stirred gently for 10 h under nitrogen. The whole mixture was filtered through a strainer under a stream of nitrogen, and the solvent was evaporated with the same technique as used for TEAF·3H_2O. 1-Bromohexane (409 mg, 2.48 mmol), bis(trimethyltin) sulfide (**1**, 467 mg, 1.30 mmol), BTAF dried as above (419 mg, 2.48 mmol), and dried acetonitrile (10 mL) were placed in the same flask under nitrogen. Tetrabutylammonium iodide (350 mg) was added to ensure a better solubility of BTAF while increasing the ionic strength of the medium. The mixture was stirred at room temperature for 12 h; the yield of di-*n*-hexyl sulfide was determined to be 70% by GC.

Cesium Fluoride and Tetrabutylammonium Iodide. Bis(triphenyltin) sulfide (**7**, 362 mg, 0.494 mmol), 1-bromohexane (84 mg, 0.25 mmol), cesium fluoride (200 mg), and tetrabutylammonium iodide (100 mg) were placed in the same flask under nitrogen. Acetonitrile (5 mL) was added, and the reaction mixture was stirred for 5 h at 50–52 °C. GC showed incomplete conversion of the halide and an approximate yield of 70–80% of di-*n*-hexyl sulfide.

2,4,6-Trimethylpyridine Hydrofluoride. Bis(triphenyltin) sulfide (**6**, 2.50 g, 3.41 mmol), 1-bromohexane (563 mg, 3.41 mmol), 2,4,6-trimethylpyridine hydrofluoride (722 mg, 5.12 mmol), and acetonitrile were mixed together and heated at 50 °C for 21 h. Only some small traces of di-*n*-hexyl sulfide were detected by TLC.

Potassium Fluoride and 18-Crown-6. 1-Bromohexane (409 mg, 2.48 mmol), bis(trimethyltin) sulfide (**1**, 445 mg, 1.24 mmol), acetonitrile (10 mL), potassium fluoride (excess) and 18-crown-6 (catalytic amount) were placed in a flask and stirred at room temperature under nitrogen for 1 h. A sample was taken and analyzed by GC; no sulfide was detected.

Formation of Unsymmetrical Sulfides. Typical Procedure with Cesium Fluoride: Preparation of Benzyl *n*-Hexyl Sulfide. 1-Bromohexane (277 mg, 1.68 mmol), tributyltin benzyl sulfide (727 mg, 1.76 mmol), and dried acetonitrile (12 mL) were placed into a flask. Cesium fluoride (800 mg, 5.28 mmol) alone or complexed with 18-crown-6 (96 mg, 0.36 mmol) were added. The mixture was stirred vigorously at room temperature for 2 h under nitrogen with CsF/18C6 and for 12 h with CsF alone. The reaction was monitored by GC and ^{1}H NMR; the yields were recorded as described in Table VII. The purification involved evaporation of the acetonitrile, addition of ethyl acetate (30 mL), and addition of a saturated aqueous solution of potassium fluoride (~15 mL); the mixture was stirred for 30–45 min. A filtration was carried out if needed at this stage or later (to remove organotin fluoride), and the phases were separated. The organic phase was washed with water and dried over sodium sulfate. Flash chromatography using hexane as eluent was carried out if needed. Benzyl *n*-hexyl sulfide was obtained as a colorless liquid (260 mg, 76%). Some traces of unreacted starting material were observed by ^{1}H NMR prior to purification: ^{1}H NMR (60 MHz) 7.27 (s, 5 H), 3.70 (s, 2 H), 2.43 (t, 2 H), 1.7–1.03 (m, 8 H), 0.85 (t, 3 H); MS 208 (M^+, 14), 207 (22), 181 (19), 180 (10), 179 (11), 149 (12), 117 (14), 105 (12), 103 (12), 92 (19), 91 (100), 65 (15), 57 (12), 56 (13), 55 (13), 43 (13), 41 (22), 29 (16), 28 (21).

With TBACN. 1-Bromohexane (139 mg, 0.84 mmol), tributyltin benzyl sulfide (364 mg, 0.88 mmol), acetonitrile (5 mL), and TBACN (245 mg, 0.91 mmol) were mixed together and stirred at room temperature for 2.3 h under nitrogen to give benzyl *n*-hexyl sulfide in 84% yield by GC. The retention time was compared to the isolated and characterized product obtained before.

Formation of Sulfides with Bis(triphenylgermanium) Sulfide with Cesium Fluoride and 18-Crown-6. Typical Procedure: Preparation of Di-*n*-hexyl Sulfide. In a 25-mL flask were placed 1-bromohexane (165 mg, 1.00 mmol), bis(triphenylgermanium) sulfide (**4**, 320 mg, 0.50 mmol), and a catalytic amount of 18-crown-6 (26 mg, 0.10 mmol). THF (4.0 mL) and DMF (1.0 mL) were added. Flamed-dried cesium fluoride (440 mg, 2.90 mmol) was added to the main flask while stirring for 45 min at room temperature and then at 55 °C for 10 h. THF was evaporated, and to the remaining residue was poured ether (~25 mL) and water (~25 mL). The ethereal phase was further washed with water (3 × 20 mL) and then dried over Na_2SO_4/$MgSO_4$. A flash chromatography using 2% EtOAc/98% *n*-hexane as eluent afforded di-*n*-hexyl sulfide (80 mg, 80% yield) of a colorless liquid. The spectral data were as described before.

Formation of Sulfides with Bis(triphenyllead) Sulfide with Cesium Fluoride and 18-Crown-6. Typical Procedure: Preparation of Dibenzyl Sulfide. In a 50-mL flask was placed benzyl bromide (171 mg, 1.00 mmol) and bis(triphenyllead) sulfide (**5**, 478 mg, 0.53 mmol). THF (8.0 mL) and DMF (2.0 mL) were added (a black color appeared immediately) via a syringe, followed by cesium fluoride (416 mg; 2.77 mmol) and 18-crown-6 (66 mg; 0.25 mmol). The flask was heated at 65 °C for 5 h. The black color resulting from a complex formation between the organolead and DMF became pale gray after a few minutes in the presence of fluoride. After only 1.5 h, most of the starting material (R_f = 0.40) reacted as determined by TLC (10% EtOAc/90% *n*-hexane) and was transformed in a more polar product corresponding to benzyl triphenyllead sulfide (R_f = 0.50). After evaporation of the solvent and addition of diethyl ether (30 mL), the mixture was filtered through a pad of Celite, and the contents were poured in a separating funnel. Water (30 mL) was added and then discarded. The ether phase was washed further with 3 × 15 mL of water and dried on Na_2SO4/$MgSO_4$. Flash chromatography (using the same eluent as above) gave pure dibenzyl sulfide (69 mg, 0.32 mmol, 81% yield) with the same spectral data as before. The product was compared to authentic material; the purity was excellent as verified by ^{1}H NMR and TLC. For other sulfide formations involving bis(triphenyllead) sulfide, a similar procedure is followed but under the conditions specified in Table VII.

^{19}F and ^{119}Sn Complexation Study of Bis(triphenyltin) Sulfide with "Dried" TBAF. In a 5-mm NMR tube was placed bis(triphenyltin) sulfide (50 mg, 0.068 mmol) and CD_2Cl_2 (0.30 mL). A solution of "anhydrous" TBAF in CD_2Cl_2 was prepared according to Cox.[37] In a small flask, TBAF·3H_2O (539 mg, 1.708 mmol) was dried overnight under high vacuum while heating at 40–45 °C. Deuteriomethylene chloride (1.00 mL) was added, and the solution was kept under N_2; 0.160 mL was transferred to the NMR tube containing the organotin sulfide. A weak evolution of H_2S resulted along with a yellowish color. ^{19}F and ^{119}Sn NMR spectra were recorded immediately. All of the manipulations were executed under nitrogen. In the presence of water, complex **12a** or **12b** is not observed.

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Registry No. 1, 1070-91-3; **2**, 4808-30-4; **3**, 3385-94-2; **4**, 1802-77-3; **5**, 1802-88-6; **6**, 27345-01-3; **7**, 77-80-5; **8**, 16892-65-2; **9**, 23728-85-0; **11**, 75861-76-6; **12**, 125227-89-6; TBAF, 429-41-4; TBACN, 10442-39-4; Me_3PyrHF, 45725-47-1; TEAF, 665-46-3; DAST, 38078-09-0; TASF, 59218-87-0; BTAF, 60436-02-4; Ph_3SnCl, 639-58-7; Me_3SnCl, 1066-45-1; Bu_3SnH, 688-73-3;

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$PhCH_2SH$, 100-53-8; Ph_3GeCl, 1626-24-0; Ph_3PbOAc, 1162-06-7; CsF, 13400-13-0; $PhCH_2SSnPh_3$, 2034-10-8; $PhCOCH_2Br$, 70-11-1; $PhCH_2Br$, 100-39-0; $CH_3COCH(Br)CH_3$, 814-75-5; $CH_3(CH_2)_5Br$, 111-25-1; $(PhCOCH_2)_2S$, 2461-80-5; $(PhCH_2)_2S$, 538-74-9; $(CH_3COCH(CH_3))_2S$, 113334-17-1; $(C_6H_{13})_2S$, 6294-31-1; $Br(CH_2)_5Br$, 111-24-0; KF, 7789-23-3; CH_3COCH_2Cl, 78-95-5; $EtCH(Me)CH_2Br$, 10422-35-2; $(ClCH_2)_2CO$, 534-07-6; $(CH_3COCH_2)_2S$, 63578-76-7; $(EtCH(Me)CH_2)_2S$, 96034-00-3; cyclo-$(SCH_2COCH_2)_2$, 16631-05-3; $PhCH_2S(CH_2)_5CH_3$, 34005-03-3; $(C_6H_{13}S)_2$, 10496-15-8; thiane, 1613-51-0.

Effective Molarities and Ionic Chain Mechanism in the Reaction of a Bifunctional Nucleophile with Substituted Bicyclobutane[1]

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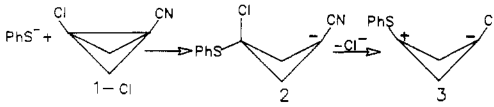
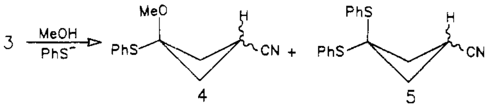
The reactions of ethylenethioglycolate with 3-chlorobicyclobutanecarbonitrile in MeOH and dimethoxyethane (DME) were studied. The reaction in MeOH involves nucleophilic attack followed by solvolysis of the α-chloro thioether moiety to give the ionic bicyclobutane. The latter undergoes mainly internal trapping of the carbenium ion to give the spiro derivative **8** along with addition products of MeOH (**9**) and a second nucleophile molecule (**10**). Addition of $HOCH_2CH_2SH$ to the reaction mixture inhibits the formation of the spiro derivative indicating that the reaction of O^- and not OH is involved in the cyclization process. The effective molarity of O^- in the cyclization reaction is estimated to be 66. In DME, the reactions were heterogenous. Substitution of Cl by $HOCH_2CH_2S$ in a nucleophilic addition–elimination mechanism gave the corresponding bicyclobutane derivative. This reacted further to give the spiro compound by an ionic chain mechanism.

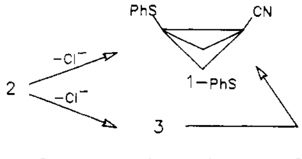
In the course of the reaction of the cyano-activated halobicyclobutane **1** with nucleophiles such as MeO^- and PhS^- in MeOH, the ionic bicyclobutane **3** was obtained as a short lived intermediate.[2,3] The reaction sequence (given for PhS^- in eq 1) involves a nucleophilic attack followed by solvolysis of the α-halo thioether moiety in **2**. Under the reaction conditions, **3** yields mainly addition products as shown in eq 2.[3] On the other hand, when the reaction is conducted in dimethoxyethane (DME) rather than in MeOH, the bicyclic product **1**-PhS is obtained as the major product. This can be derived from **2** by either of two ways: 1,3-elimination (eq 3a) or solvolysis to **3** followed by a collapse of the zwitterion to form the covalent bond (eq 3b).



(1)



(2)



(3a)

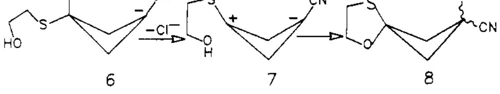
(3b)

In order to explore the possibility of the collapse pathway, an experiment in which increasing quantities of MeOH were added to the DME solution was performed.[3] Quantum mechanical and strain barriers reduce the collapse rate of the zwitterion to much below that of a molecular vibration.[2] The added MeOH, depending on its concentration, could therfore trap the carbenium ion, if formed, before the collapse would occur. This should give rise to the trapped product **4** at the expense of **1**-PhS. It was found[3] that in up to 2.5 M of MeOH, **4** is not formed at all, indicating that in DME **2** undergoes 1,3-elimination rather than solvolysis. At higher concentrations of MeOH, the medium polarity is sufficiently increased, inflicting a change in the reaction mechanism.

It is concluded therefore that the reaction pathway is medium dependent. At low medium polarity 1,3-elimination (eq 3a) should prevail whereas at high polarity the solvolytic path (eq 3b) should be favored. In order to further quantify the polarity effect on the two reaction channels we had to find a suitable probe for the detection of carbenium ions. Making use of MeOH as the probe, as we have done in DME,[3] suffers from two major deficiencies: (a) at low MeOH concentration the trapping of the carbenium ion is not very effective and (b) at high MeOH concentration, MeOH affects the medium polarity. The present study describes, therefore, an attempt to design an internal probe which is attached to the nucleophile. Since intramolecular cyclizations are in general relatively very fast, the use of such a probe is likely to eliminate the two aforementioned problems.

Results and Discussion

Ethylenethioglycolate (TEG^-) was chosen as the bifunctional nucleophile. The S^- will launch the first nucleophilic attack whereas the OH function will trap the carbenium ion, if formed. Thus, the solvolytic path will be evidenced by the formation of the spiro compound **8** (eq 4). All the reactions were performed at room temperature. The reaction were followed by gas chromatog-



(4)

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[1] This is part 16 in the series Cyclobutane–Bicyclobutane System.

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