Synthesis and Lithiation of 2-Alkylthio- and 2-Arylthio-1,3-dithiolanes

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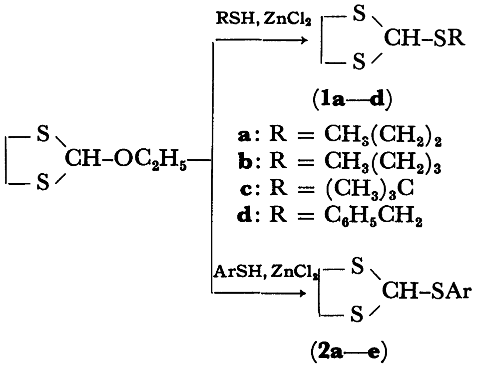
Synopsis. Several 2-alkylthio- and 2-arylthio-1,3-dithiolanes were synthesized by the reaction of 2-ethoxy-1,3-dithiolane with aliphatic and aromatic thiols in the presence of $ZnCl_2$. The lithiation of 2-alkylthio-1,3-dithiolanes with butyllithium in tetrahydrofuran followed by the addition of alkyl halides gave unsymmetrical dialkyl trithiocarbonates in moderately good yields.

Although the so-called six-membered cyclic trithioorthoformates (derivatives of 1,3-dithiane) have been studied[1] intensively, little is known about the five-membered analogues (derivatives of 1,3-dithiolane). To our knowledge, only a few compounds are reported in the literature. Nakayama[2] described the replacement of the butoxy-group of 2-(3-methylbutoxy)-1,3-benzodithiole by alkylthio- and arylthio-groups producing 2-alkylthio- and 2-arylthio-1,3-benzodithioles. The others are 2-phenylthio-1,3-dithiolane and 2,2′-[1,2-ethanediylbis(thio)]bis(1,3-dithilane); the former was synthesized in 1976 by Yoshida and his co-workers,[3] who obtained this compound by the thiolysis of the *N*-tosylsulfilimine derived from 1,3-dithiolane, and the latter is most easily available,[4] but it appears to be far from general. Recently, we described a process for the introduction of a formyl moiety to some phenols.[5] This procedure involved the reaction of the phenols with 2-ethoxy-1,3-dithiolane[4] in the presence of $BF_3 \cdot Et_2O$ and subsequent hydrolysis of the resulting 1,3-dithiolan-2-ylated phenols. We have now found that the reaction of aromatic thiols with 2-ethoxy-1,3-dithiolane proceeds smoothly by using $ZnCl_2$ as a catalyst to afford 2-arylthio-1,3-dithiolanes; in this case no nuclear substitution products are formed. This sulfur-for-oxygen interchange reaction proved to be quite general even when aliphatic thiols were used, although in the cases with low-boiling aliphatic thiols the reaction had to be performed with a large excess of the thiols. If the aliphatic thiols are not used in excess, the products are often isolated in an impure state. Thus an interchange reaction of 2-ethoxy-1,3-dithiolane with aliphatic and aromatic thiols was demonstrated; it was analogous to that observed previously in the case of 2-(3-methylbutoxy)-1,3-benzodithiole.[2] The results are summarized in Table 1.



(**1a**—**d**)

a: R = $CH_3(CH_2)_2$
b: R = $CH_3(CH_2)_3$
c: R = $(CH_3)_3C$
d: R = $C_6H_5CH_2$

(**2a**—**e**)

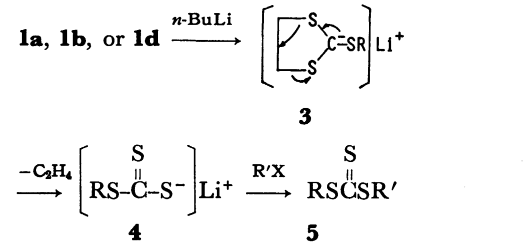
a: Ar = C_6H_5, **b**: Ar = *p*-ClC_6H_4, **c**: Ar = *p*-$CH_3C_6H_4$, **d**: Ar = *o*-$CH_3C_6H_4$, **e**: Ar = *m*-$CH_3C_6H_4$.

TABLE 1. REACTION OF 2-ETHOXY-1,3-DITHIOLANE WITH THIOLS

Run	RSH or ArSH	2-Alkylthio- or 2-arylthio-1,3-dithiolane			
		Abbr.	Yield[a)] %	Bp θ_b/°C(Torr)	^{1}H-NMR (δ, in $CDCl_3$)
1	$CH_3(CH_2)_2SH$	**1a**[b)]	75	153—158 (22.5)	5.60(s,1H),3.5—3.1(m,4H),2.66 (t,2H),1.9—1.3(m,2H),0.99(t,3H)
2	$CH_3(CH_2)_3SH$	**1b**[b)]	76	167—173 (22.5)	5.58(s,1H),3.5—3.2(m,4H),2.66 (t,2H),1.9—1.2(m,4H),0.93(t,3H)
3	$(CH_3)_3CSH$	**1c**[b)]	37	152—157 (22.5)	5.66(s,1H),3.5—3.1(m,4H),1.36 (s,9H)
4	$C_6H_5CH_2SH$	**1d**[c)]	54	174—180 (4.5)	7.4—7.1(m,5H),5.31(s,1H), 3.79(s,2H),3.4—3.1(m,4H)
5	C_6H_5SH	**2a**[c)]	72	156—159 (3.5) [lit,[3)]132—134(1)]	7.6—7.1(m,5H),5.73(s,1H), 3.4—3.1(m,4H)
6	*p*-ClC_6H_4SH	**2b**[c)]	53	181—186 (4.5)	7.6—7.1(m,4H),5.73(s,1H), 3.5—3.1(m,4H)
7	*p*-$CH_3C_6H_4SH$	**2c**[c)]	57	168—171 (5)	7.5—7.0(m,4H),5.71(s,1H), 3.4—3.1(m,4H),2.30(s,3H)
8	*o*-$CH_3C_6H_4SH$	**2d**[c)]	63	162—166 (3.5)	7.6—7.0(m,4H),5.75(s,1H), 3.4—3.1(m,4H),2.43(s,3H)
9	*m*-$CH_3C_6H_4SH$	**2e**[c)]	41	169—174 (4)	7.4—7.0(m,4H),5.77(s,1H), 3.4—3.1(m,4H),2.30(s,3H)

a) Yield of isolated product based on 2-ethoxy-1,3-dithiolane. b) Isolated by distillation under reduced pressure. c) Isolated by column chromatography on silica gel.

The removement of the trithioorthoformate proton of 2-alkylthio- and 2-arylthio-1,3-dithiolanes could be achieved by observing at −5—−10 °C and by the addition of an easily available metalating agent such as butyllithium. In reaction with 2-alkylthio-1,3-dithiolanes, the initially formed anion is assumed to be **3**, which decomposes to ethylene and alkyl trithiocarbonate anion (**4**), and the latter is subsequently alkylated by alkyl halides to afford the unsymmetrical dialkyl trithiocarbonates (**5**).[6—8]



R = $CH_3(CH_2)_2, CH_3(CH_2)_3, C_6H_5CH_2$
R′X = $CH_3I, C_2H_5I, CH_3(CH_2)_2I,$
$CH_3(CH_2)_3I, C_6H_5CH_2Br$

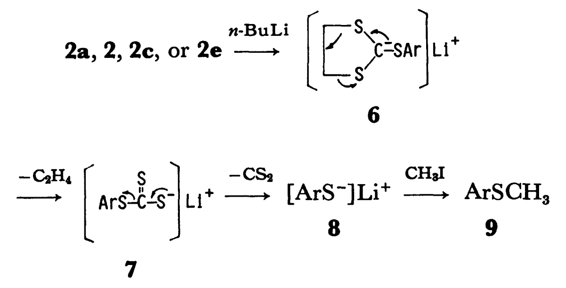
In cases where the experiments using 2-arylthio-1,3-dithiolanes were performed in the same way as that applied to 2-alkylthio-1,3-dithiolanes, the similarly formed aryl trithiocarbonate anion (**7**) undergoes further fragmentation to afford carbon disulfide and arenethiolate anion (**8**), presumably due to the electron-withdrawing effect of the benzene ring. The anion (**8**) would be then trapped by methyl iodide. In three cases where Ar=C_6H_5, *p*-$CH_3C_6H_4$, *m*-$CH_3C_6H_4$ in 2-arylthio-1,3-dithiolanes, none of the corresponding aryl methyl trithiocarbonates were recognized, but **9a**, **9c**, and **9e** were obtained in 75, 97 and 84% yield, respectively. It is also confirmed that **7** is unstable and decomposes similarly even at −78 °C. Thus an obvious difference in behavior between 2-alkylthio- and 2-arylthio-1,3-

Table 2. lithiation of 2-alkylthio-1,3-dithiolanes

Run	2-Alkylthio-1,3-dithiolane	R′X	Unsymmetrical dialkyl trithiocarbonate (5)			
			R in **5**	Yield[a)] %	Bp θ_b/°C(Torr)	^{1}H-NMR (δ, in $CDCl_3$)
1[b)]	**1a**	CH_3I	$CH_3(CH_2)_2$	99	66—71 (2) [lit,[7)] 129—130 (21)]	3.34(t,2H),2.72(s,3H), 2.0—1.3(m,2H),1.00(t,3H)
2	**1a**	C_2H_5I	$CH_3(CH_2)_2$	94	89—94 (2.5)	3.34(q,2H),3.32(t,2H), 2.0—1.3(m,2H),1.32(t,3H), 1.01(t,3H)
3	**1a**	$C_6H_5CH_2Br$	$CH_3(CH_2)_2$	71	162—167 (3)	7.4—7.1(m,5H),4.54(s,2H), 3.28(t,2H),2.0—1.3(m,2H), 0.94(t,3H)
4	**1b**	CH_3I	$CH_3(CH_2)_3$	88	92—93 (3)	3.36(t,2H),2.72(s,3H), 1.9—1.1(m,4H),0.93(t,3H)
5	**1b**	C_2H_5I	$CH_3(CH_2)_3$	88	99—104 (2.5) [lit,[6)] 80—82 (0.1)]	3.33(q,2H),3.32(t,2H), 1.8—1.1(m,4H),1.32(t,3H), 0.92(t,3H)
6	**1b**	$C_6H_5CH_2Br$	$CH_3(CH_2)_3$	87	167—170 (3)	7.4—7.2(m,5H),4.55(s,2H), 3.32(t,2H),1.8—1.1(m,4H), 0.91(t,3H)
7	**1d**	CH_3I	$C_6H_5CH_2$	78	140—144 (2.5) [lit,[7)] 134—136 (1)]	7.4—7.1(m,5H),4.52(s,2H), 2.63(s,3H)
8	**1d**	$CH_3(CH_2)_2I$	$C_6H_5CH_2$	77	154—156 (2.2)	——[c)]
9	**1d**	$CH_3(CH_2)_3I$	$C_6H_5CH_2$	81	165—167 (2.5)	——[d)]

a) Yield of isolated product based on 2-alkylthio-1,3-dithiolane. b) The product in this case was isolated by column chromatography on silica gel, using 10% ether–hexane as the eluent. c) The product is identical with that obtained in the case of Run 3. d) The product is identical with that obtained in the case of Run 6.

dithiolanes has been noted.



a: Ar = C_6H_5, **c**: Ar = p-$CH_3C_6H_4$, **e**: Ar = m-$CH_3C_6H_4$

Experimental

Reaction of 2-Ethoxy-1,3-dithiolane with a Thiol. The reaction was carried out by stirring a mixture of 2-ethoxy-1,3-dithiolane (5.0 g, 33.3 mmol), a thiol (33.6 mmol) (100 mmol was used in the cases of low-boiling aliphatic thiols, *i.e.*, in Runs 1, 2, and 3 in Table 1) and $ZnCl_2$ (4.6 g, 33.8 mmol) at room temperature for 24 h. The mixture was poured into a large quantity of dilute aqueous NaOH and extracted with several portions of ether. The combined ethereal extracts were washed repeatedly with dilute aqueous NaOH, dried, filtered, and concentrated *in vacuo* to give a residue. The product was isolated by distillation under reduced pressure or by column chromatography on silica gel, using 10% ether–hexane as the eluent.

Conversion of a 2-Alkylthio-1,3-dithiolane to an Unsymmetrical Dialkyl Trithiocarbonate (5). To a stirred solution of a 2-alkylthio-1,3-dithiolane (5.0 mmol) dissolved in tetrahydrofuran (20 ml), under nitrogen at −5—−10 °C, was added a 1.56 molar solution (3.8 ml, 5.9 mmol) of butyllthium in hexane; the stirring was continued for 20—30 min at that temperature. A solution of an alkyl halide (10 mmol) (6—7 mmol was used in the case of benzyl bromide) in tetrahydrofuran (2—3 ml) was added, and the mixture was stirred at −5—−10 °C for 1 h and further at room temperature for 4 h. Water (30 ml) and a saturated aqueous solution (30 ml) of ammonium chloride were added, and the mixture was extracted with several portions of ether. The combined ethereal extracts were dried, filtered, and concentrated *in vacuo* to give a residue, which was distilled under reduced pressure to afford an unsymmetrical dialkyl trithiocarbonate. Only in the case of Run 1 (Table 2) was the product isolated by column chromatography.

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