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Novel reaction of bis(trifluoromethyl)disulfide with organolithium reagents

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Abstract

The reaction of bis(trifluoromethyl) disulfide with organolithium reagents at −78 °C results in simultaneous scission of both the C−S and S−S bonds. Under similar conditions, the alkyl and aryl disulfides undergo only S−S bond cleavage. This unusual behavior of bis(trifluoromethyl) disulfide is due to the presence of the trifluoromethyl function. The product distribution, the mechanism of bond fission and the mass spectral data of compounds thus formed are presented in this paper.

Introduction

Sulfur exhibits unusual susceptibility to 'thiaphilic attack' in its reactions with organolithium reagents [1a, b]. The attack by nucleophiles is said to take place more often at sulfur than at carbon [1c]. Butyllithium has been reported to cleave the S−S bond of disulfides in less than 1 min [2]. Nucleophilic attack on the S−S bond of dimethyl and diphenyl disulfides by pentafluorophenyllithium (**1**) has been stated to furnish the corresponding methyl and phenyl pentafluorophenyl sulfides, respectively [3]. It has been claimed that **1** causes the displacement of CF_3 from bis(trifluoromethyl)-disulfide (**2**) to give bis(pentafluorophenyl)sulfide, undoubtedly resulting from both C−S bond and S−S bond scission [3]. In addition to the above, there have been only two or three reports of C−S bond scission by organolithium reagents [4]. However, these are special cases; in one case the C−S bond belonged to sp-hybridized carbon [4a] and in the second case four sulfur atoms were directly attached to the same carbon atom to hasten its reaction [4b]. The case of a perfluoride undergoing a structure-dependent C−S scission is another novel example [4c]. Homolytic displacement at the α-carbon center of an alkyllithium by the thiyl radical, derived from the disulfide, has been observed [5].

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Recently, the simultaneous scission of the C—S and S—S bonds of bis(trifluoromethyl)trisulfide by Grignard reagents has been reported [5b]. The reaction of organolithium reagents with **2** at −78 °C has now been investigated and this communication discusses the mechanism of scission of the C—S and S—S bonds and the mass spectral data of the reaction products.

Results and discussion

The reaction of organolithium reagents (RLi) with **2** at −78 °C gave R_fSSR, R_fSR and R—R, where $R_f = CF_3$ and $R = t\text{-}C_4H_9$, $n\text{-}C_4H_9$ and C_6H_5 (Table 1). In the reaction with $t\text{-}C_4H_9Li$, 13.1% $t\text{-}C_4H_9SC_5H_{11}$ (**3**) was detected. This was evidently formed from pentane, the solvent used in the preparation of $t\text{-}C_4H_9Li$. The unsymmetrical di- and mono-sulfides, namely R_fSSR and R_fSR, where $R_f = CF_3$ and $R = t\text{-}C_4H_9$, are formed in almost equal amounts. The formation of these compounds can be rationalized on the basis of simultaneous cleavage of the C—S and S—S bonds of **2** (Scheme 1). Tatlow and coworkers were among the first to observe an unusual C—S bond cleavage of a perfluoride [4c]. It is interesting to note that the pentyl radical ($^{\cdot}C_5H_{11}$), formed from hydrogen abstraction from pentane by free radicals, was also able to cause the fission of the C—S bond of **2** to furnish the disulfide $CF_3SSC_5H_{11}$ (19%). The pentenyl derivative, $CF_3SSC_5H_9$, must have been formed from its saturated analog via hydrogen abstraction. There are precedents for hydrogen abstraction [6a, b]. What is even more interesting is the formation of $t\text{-}C_4H_9SC_5H_{11}$ (13%). This must have resulted from the attack by $^{\cdot}C_5H_{11}$ (derived from

TABLE 1

Compounds characterized from the reaction of bis(trifluoromethyl)disulfide with organolithium reagents

$CF_3SSCF_3 + RLi \longrightarrow$ Products

R	Product yield (%)					
	CF_3SSR	CF_3SR	$CF_3SSC_5H_{11}$	$CF_3SSC_5H_9$	RSC_5H_{11}	R—R
$t\text{-}C_4H_9$	32.6	35.0	19.4[a]	–	13.1	–
$n\text{-}C_4H_9$	1.0	84.8	–	0.6[b]	–	13.6
C_6H_5[c]	1.3	71.6	–	–	–	13.6

[a] The pentyl and pentenyl moieties arise from pentane, the solvent used to prepare $t\text{-}C_4H_9Li$. The pentenyl derivative is evidently formed from hydrogen abstraction, followed by the loss of hydrogen. There are precedents for hydrogen abstraction processes [15].

[b] This may originate from the impurity present in the alkyllithium reagent and/or from disproportionation reaction(s).

[c] In addition, $C_6H_5SC_6H_5$ (2.8%), $C_6H_5SC_2H_5$ (1.6%), $C_6H_5C_2H_5$ (7.4%) and $C_6H_5C_4H_9$ (1.6%) were also detected and characterized from their GC–MS data.

$$CF_3SSCF_3 + \overset{-}{R}\overset{+}{Li} \longrightarrow [(CF_3SSCF_3)^{\overline{\bullet}} + \overset{\bullet}{R}\overset{+}{Li}] \tag{1}$$

$$(CF_3SSCF_3)^{\overline{\bullet}} \longrightarrow CF_3S\overset{\bullet}{S} + \overset{-}{C}F_3 \tag{2}$$

$$CF_3S\overset{\bullet}{S} + \overset{\bullet}{R} \longrightarrow CF_3SSR \tag{3}$$

$$(CF_3SSR) + R\overset{+}{Li} \longrightarrow [(CF_3SSR)^{\overline{\bullet}} + \overset{\bullet}{R}\overset{+}{Li}] \tag{4}$$

$$(CF_3SSR)^{\overline{\bullet}} \longrightarrow CF_3\overset{\bullet}{S} + R\overset{-}{S} \tag{5}$$

$$CF_3\overset{\bullet}{S} + \overset{\bullet}{R} \longrightarrow CF_3SR \tag{6}$$

$$CF_3SSR + R\overset{-}{S} \longrightarrow (CF_3SSR)^{\overline{\bullet}} + R\overset{\bullet}{S} \tag{7}$$

$$\overset{\bullet}{R} + R\overset{\bullet}{S} \longrightarrow RSR \tag{8}$$

$$2\overset{\bullet}{R} \longrightarrow R{-}R \tag{9}$$

$$\overset{+}{Li} + \overset{-}{C}F_3 \longrightarrow [LiCF_3] \tag{10}$$

Scheme 1. Reaction of organolithium reagents with bis(trifluoromethyl)disulfide.

pentane) on the S−S bond of $CF_3SSC_4H_9$-t. There are precedents for the participation of the solvents in chemical reactions [7]. The mixed monosulfides are generally observed in the reaction of alkyl or aryl disulfides with organolithiums and Grignard reagents [3, 8]. In view of the observation that methyl radicals failed to react with dimethyl disulfide in the gas phase [9], the above results are indeed interesting.

The formation of biphenyl and octane is obviously the result of the dimerization of phenyl and butyl radicals, respectively. In the reaction of phenyllithium with **2**, diphenyl sulfide (**4**), ethyl phenyl sulfide (**5**), ethylbenzene (**6**) and butylbenzene (**7**) were identified along with the compounds listed in Table 1. The origin of **4** is similar to the reaction of pentafluorophenyllithium (**1**) with **2** [3]; it is formed by the attack of the phenyl radicals on the S−S bonds of trifluoromethyl phenyl disulfide, initially formed from the scission of the C−S bond. However, **6** and **7** are the results of the participation of diethyl ether, the solvent used in the preparation of phenyllithium. There are also precedents for such a solvent-involved reaction [7]. Butylbenzene is formed from the reaction of **6** with $^{\bullet}C_2H_5$. The formation of **5** can similarly be rationalized.

Under similar experimental conditions, both alkyl and aryl disulfides primarily furnished unsymmetrical sulfides (Table 2) when treated with

TABLE 2

Reaction of organolithium reagents with alkyl and aryl disulfides at −78 °C

$RSSR + R'Li \longrightarrow$ Products

R ; R′	Product yield (%)		
	RSSR	RSR	R′R′
C_2H_5 ; C_6H_5[a]	1.8	89.1	6.5
C_2H_5 ; t-C_4H_9[b]	1.0	97.5	–
s-C_4H_9 ; t-C_4H_9[c]	99.6	0.3	–
s-C_4H_9 ; C_6H_6[d]	26.0	65.3	7.2

[a] In addition, $C_6H_5C_2H_5$ (1.8%), $C_6H_5C_4H_9$ (0.5%) and $C_6H_5C_2H_4SC_2H_5$ (0.2%) were also identified.
[b] Two other isomeric compounds, $C_2H_5SC_4H_9$-i (1.0%) and $C_2H_5SC_4H_9$-s (0.5%), were detected.
[c] Trace amounts of s-$C_4H_9SSC_5H_{11}$ were also observed.
[d] Two other compounds, $C_6H_5C_2H_5$ (1.1%) and $C_6H_5C_4H_9$ (0.4%), were characterized.

organolithium reagents at −78 °C [8]. The unsymmetrical disulfides were not detected in the reaction of methyl radicals with disulfides [9]. What is significant in these reactions is the characterization of biphenyl (6.5%) and octane (7.2%). They are evidently the products of the dimerization of their respective free-radical precursors, namely $^{\bullet}C_6H_5$ and $^{\bullet}C_4H_9$.

In contrast to the disulfides, the sulfides exhibit a greater propensity to undergo rearrangements [10]. The mass spectra of the alkyl sulfides [10a], aryl sulfides [10b], alkyl aryl sulfides [10c, d] and alkyl disulfides [10e] have been discussed. The mass spectral data are listed in Table 3. The ions corresponding to the molecular weights of all compounds described in Table 1 were observed. The characteristic feature of the mixed disulfides R_fSSR and sulfides R_fSR containing the SCF_3 group is the loss of SCF_3 ($m/e = 101$), CSF_2 ($m/e = 82$) and CF_3 ($m/e = 69$) (Table 3). In many cases the ion corresponding to $m/e = 45$ (CSH) was observed as well. The mass spectra of the alkyl sulfides (Table 2) are similar to those described by others [10a–e, 11]. The mass spectral fragmentation of octane has been described [12]. The structure assigned to the compounds described in Tables 1 and 2 are consistent with their mass spectral fragmentation behavior.

With regards to the possible mechanism of the reaction of RLi with organic substrates, the single-electron-transfer (SET) process has been proposed to account for the products formed and characterized [13]. Compelling evidence has also been furnished to indicate the involvement of free radicals in the reaction of organolithium reagents with organic substrates [14]. Ashby and coworkers have convincingly demonstrated the wide applicability of the SET process to organic reactions [14d, e]. Using the SET mechanism, the formation of the compounds listed in Table 1 can be rationalized (Scheme 1). Since the reaction between organolithium reagents and **2** is exothermic and occurs under extremely mild conditions and without any external assistance

TABLE 3

Mass spectral fragments of sulfides and disulfides formed during the reaction of bis(trifluoromethyl)disulfide with organolithium reagents

$C_6H_5SC_2H_5$	$M^+ = 138$ (100%); 123 ($M-CH_3$); 110 (C_6H_5SH); 77 (C_6H_5); 65 (C_5H_5); and 45 (CSH).
$C_6H_5CH(CH_3)(SC_2H_5)$	$M^+ = 166$; 104 ($M-C_2H_5SH$); 91 ($C_6H_5CH_2$); 77 (C_6H_5); 75 (100%; SC_3H_7); and 47 (CH_3S).
$C_6H_5CH_2CH_3$	$M^+ = 106$.
$C_6H_5C_4H_9$	$M^+ = 134$; 105 ($M-C_2H_5$); 91 (C_7H_7); and 77 (C_6H_5).
s-$C_4H_9SSC_5H_{11}$	$M^+ = 192$; 136 ($HS_2C_5H_{11}$); 122 ($HS_2C_4H_9$); 71 (C_5H_{11}); 64 (SS); 57 (100%; C_4H_7); and 45 (CSH).
$CF_3SC_4H_9$-t	$M^+ = 158$; 143 ($M-CH_3$); 115 (CF_3SCH_2); 101 (SCF_3); 82 (CSF_2); 69 (CF_3); 63 (CSF); 59 (SC_2H_3); 57 (100%; C_4H_9); 50 (CF_2); 45 (CSH); and 41 (C_3H_5).
$CF_3SSC_4H_9$-t	$M^+ = 190$; 171 ($M-F$); 101 (SCF_3); 69 (CF_3); 64 (SS); 57 (100%; C_4H_9); 45 (CSH); and 41 (C_3H_5).
$CF_3SSC_5H_{11}$	$M^+ = 204$; 115 (CF_3SCH_2); 57 (100%; C_4H_9); 45 (CSH); and 41 (C_3H_5).
$C_5H_{11}SC_4H_9$-t	$M^+ = 160$; 145 ($M-CH_3$); 89 (SC_4H_9); 71 (C_5H_{11}); 57 (100%; C_4H_9); and 41 (C_3H_5).
n-$C_4H_9SCF_3$	$M^+ = 158$; 139 ($M-F$); 129 ($M-C_2H_5$); 115 ($129-CH_2$); 89 ($M-CF_3$); 82 (CSF_2); 69 (CF_3); 63 (CSF); 56 (100%; C_4H_8); and 47 (SCH_3).
n-$C_4H_9SSCF_3$	$M^+ = 190$; 147 (CF_3SSCH_2); 133 ($SSCF_3$); 82 (CSF_2); 78 (C_2H_3SF); 69 (CF_3); 64 (SS); 57 (C_4H_9); and 45 (CSH).
$CF_3SSC_5H_9$	$M^+ = 202$; 183 ($M-F$); 160 ($CF_3SSC_2H_3$); 145 ($160-CH_3$); 133 (CF_3SS or SSC_5H_9); 115 (CF_3SCH_2); 101 (SCF_3); 91 (SSC_2H_3); 75 (SC_3H_7); 71 (100%; SC_3H_3); 58 (C_4H_{10}); and 45 (CSH).
$CF_3SSC_6H_5$	$M^+ = 210$; 141 (100%; $M-CF_3$); 109 (98%, $M-SCF_3$); 82 (CSF_2); 77 (C_6H_5); and 69 (CF_3).
$CF_3SC_6H_5$	$M^+ = 178$; 159 ($M-F$); 109 (100%; $M-CF_3$); 82 (CSF_2); 77 (C_6H_5); and 45 (CSH).
C_8H_{18}	$M^+ = 114$; 85 (100%; $M-C_2H_5$); 71 (C_5H_{11}); and 57 (C_4H_9).
$C_6H_5C_6H_5$	$M^+ = 154$ (100%); and 77 (C_6H_5).

such as photo-initiation, the SET process is expected to facilitate this reaction [15].

The reaction is initiated by the transfer of an electron from the organolithium reagent to the substrate to give a radical–cation/radical–anion pair (step 1), which subsequently dissociates to yield the perthiyl radical ($R_fSS^•$; step 2). Step 3 then furnishes R_fSSR. Steps 4–6 lead to mixed sulfides (R_fSR), while steps 7 and 8 explain the formation of alkyl/aryl sulfides. Of course, step 9 reflects the dimerization reaction. The 'unstable' trifluoromethyllithium (step 10) has been reported to form a polymeric material [3].

In the past, trifluoromethylated compounds have been synthesized by electrofluorination of organic compounds [16a] and anodic oxidation [16b, c]. The reaction of bis(trifluoromethyl)di- and tri-sulfides with Grignard reagents [16d] and organolithium reagents [16e] provides a convenient alternative for the preparation of biologically interesting fluorine-containing compounds. Thus, phenyl trifluoromethyl sulfide, which was first prepared in four steps [16f, g], can now be synthesized via a one-step process using either the trifluoromethylthiocopper [15h] or by reacting **2** with phenyllithium as described in this communication.

Experimental

Warning! Because of the high toxicity associated with 2 via inhalation, efficient hoods and extreme care should be used in working with this compound. Mass spectra were obtained on a Finnigan model 5100 GC–MS instrument equipped with a silica 25 m×0.3 mm (i.d.) SE-54 capillary column (J & W Scientific, Rancho Cordova, CA). Routine GC separations were carried out on a Hewlett Packard 5890A gas chromatograph equipped with a 30×0.53 mm (i.d.) DB-5 column (J & W Scientific, Folsom, CA). The solvents used were dry and freshly distilled. The reactions were carried out in a flame-dried, argon-gas purged 10 ml or 25 ml three-necked flash equipped with a magnetic stirrer, a gas inlet, a pressure equalizing dropping funnel and a reflux condenser carrying a Dry Ice/acetone-cooled trap. The temperature of the coolant passing through the condenser was maintained at −20 °C. All reactions were carried out by adding the cold organolithium reagent (0.01 mol) to the disulfide (0.01 mol) cooled to −78 °C. After the addition was over, the mixtures were stirred at −78 °C for 45–60 min. The reactions were terminated by the addition of moist ether and a saturated solution of ammonium chloride, followed by extraction with ether, drying the solution over anhydrous sodium sulfate and processing in the usual manner. The results described in Table 1 are based on GC–MS data.

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