

Carbophilic versus thiophilic attack in the reaction of metallated aromates and heteroaromates with carbon disulfide

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(Received March 11th, 1987)

Abstract

Copper(I) halides catalyse the formation of carbodithioates RCSSLi in the reaction of aryl- or heteroaryl-lithium reagents with carbon disulfide. Subsequent addition of methyl iodide gives the dithioesters RCSSCH_3 in high yields. Appreciable amounts of the methyl sulfides RSCH_3 and tars are obtained when the reaction with CS_2 is carried out in the absence of copper(I) salts, especially in the case of more basic organoalkali compounds.

Introduction

In 1973 [1] we described an improved procedure for the synthesis of dithioesters RCSSR' from Grignard compounds RMgX in tetrahydrofuran (THF), carbon disulfide, and alkyl halides $\text{R}'\text{Hal}$. Methyl, aryl and heteroaryl Grignard compounds reacted sluggishly, while *t*-butyl- and cyclohexyl-magnesium halides mainly gave other products, such as trithiocarbonates $(\text{R}'\text{S})_2\text{C}=\text{S}$. Vermeer et al. [2] later showed that use of catalytic amounts of copper(I) halide considerably enhance the rate of the reaction of RMgX with CS_2 and which also provides a route to the dithioesters $\text{t-C}_4\text{H}_9\text{CSSR}'$ and $\text{c-C}_6\text{H}_{11}\text{CSSR}'$.

Since in many cases aryl- and heteroaryl-lithium compounds are more easily prepared than the Grignard reagents, we decided to study the possibility of synthesizing dithioesters RCSSCH_3 from the lithium compounds, CS_2 , and methyl iodide.

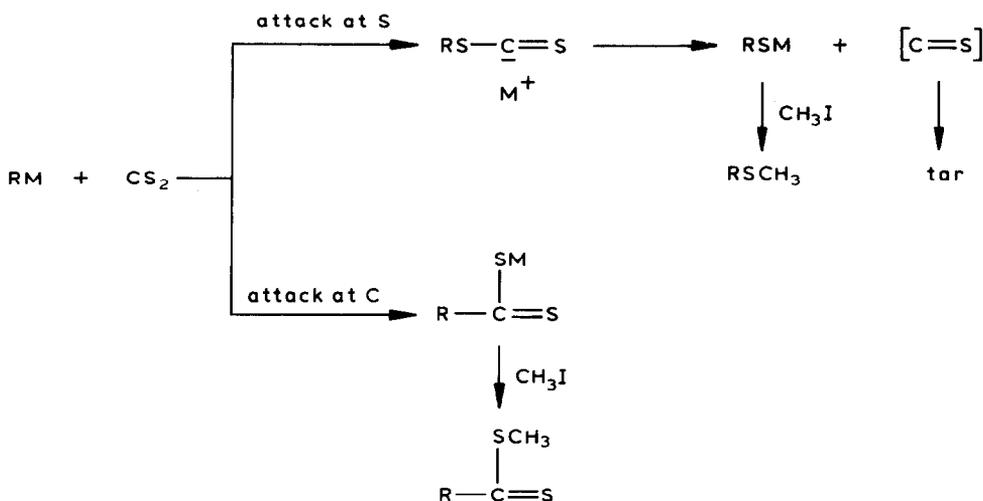
Results and discussion

Addition of carbon disulfide at about -50°C to a solution of phenyllithium in THF and hexane containing ~ 30 mol% of copper(I) bromide resulted in a smooth reaction. Subsequent addition of methyl iodide afforded the dithioester PhCSSCH_3 .

in good yield. As shown previously [2], use of phenylmagnesium bromide in combination with copper(I) bromide gives a similar result. In the absence of copper(I) bromide, CS_2 also reacted smoothly with phenyllithium in THF, but subsequent quenching with methyl iodide gave PhSCH_3 in moderate yield as the only isolated product, along with much tar. Experiments with *o*-methoxyphenyllithium and *p*-fluorophenyllithium showed also this marked effect, but with 2-furyllithium and 2-thienyllithium it was much less evident, the corresponding dithioesters RCSSCH_3 also being formed in appreciable amounts even when no CuBr was present, though with yields somewhat lower than those obtained in the presence of copper(I) halides.

In the case of metallated thiophene the influence of the alkali metal counter ion was investigated. One equivalent of *t*-BuOK in THF and followed by one of CS_2 , were added to a solution of 2-thienyllithium in THF and hexane and the dark reaction mixture was quenched with methyl iodide. Work-up gave 2-thienyl methyl sulfide in ca. 25% yield, together with intractable brown viscous products. We assume that the reactive intermediate in the conversion with CS_2 is 2-thienylpotassium (compare ref. 3). This result sharply contrasts with that obtained from the reaction of 2-thienyllithium with CS_2 , which gave a reasonable yield (~ 50%) of 2-thienyl CSSCH_3 , a small amount of 2-thienyl SCH_3 and some tar. It is known that treatment of furan or thiophene in liquid ammonia with lithium amide does not give a significant amount of any 2-lithio-furan or -thiophene, whereas 5-lithio-2-methylthio-thiazole is formed from 2- CH_3 Sthiazole under these conditions [8], which means that lithio-thiazole is a weaker base than 2-lithiofuran and 2-lithiothiophene. In THF, lithio-thiazole reacts smoothly with CS_2 even in the absence of copper(I) salts to give the corresponding carbodithioate. Methylation with methyl iodide affords the dithioester in an excellent yield. Okazaki et al. [4] recently reported the first example of attack at a sulphur atom of CS_2 . Previously Schönberg [5], Beak [6] and Paquer [7] had described thiophilic reactions on the sulphur centres of other thiocarbonyl compounds.

Our results show that CS_2 can undergo two modes of attack by aromatic and heteroaromatic metal compounds:



Our results show that the course of the reaction is strongly influenced by the nature of the counter ion and also suggest that basicity is an important factor. On going from aryllithium to the less strongly basic 2-thienyllithium and 2-furyllithium (in the absence of copper salts) the proportion of attack at sulphur markedly decreases. The catalytic role of copper(I) halides is accounted for by assuming that the arylcopper- or heteroaryl-copper intermediates react faster with CS_2 than do the lithium compounds and the copper is subsequently transferred from the copper dithiolates to the organolithium compounds.

Although we can not provide a full explanation of the observations, the variations in reactivities and products result in satisfactory procedures for the preparation of aromatic and heteroaromatic dithioesters.

Experimental

All reactions were carried out under nitrogen.

Preparation of methyl dithioesters from o-bromomethoxybenzene, p-bromofluorobenzene, o-bromofluorobenzene, and 3-bromothiophene

A solution of 0.105 mol of butyllithium in 73 ml of hexane was added to 80 ml of THF kept below -20°C . The halogen compound (0.10 mol) was then added during 10 min with the solution kept between -70 and -90°C . After an additional 10 min a solution of 0.02 mol of copper(I) bromide and 0.04 mol of anhydrous lithium bromide in 30 ml of THF was added below -60°C , and the mixture was stirred for 15 min at about -50°C (in the case of *o*-bromofluorobenzene -65°C). Carbon disulfide (0.12 mol) was then added dropwise during 20 min with the temperature of the dark-brown solution normally being kept between -35 and -50°C (at higher temperatures the butyl bromide present in the solution may react with the aryllithium compounds); in the case of the reaction with *o*-lithiofluorobenzene, however, the temperature was maintained between -55 and -65°C . After an additional period of 30 min (at -45°C except that in the case of 3-lithiothiophene, the temperature was allowed to rise to -10°C), 0.15 mol (excess) of methyl iodide was added during a few min at -45°C . The temperature of the mixture was allowed to rise during 30 min to $+15^\circ\text{C}$, then a solution of 5 g of potassium cyanide in 100 ml of water was added with vigorous stirring. After separation of the layers, extraction with ether, and drying over MgSO_4 , the brown to red solutions were concentrated in vacuo. For yields, boiling points, and refractive indices see Table 1.

Preparation of methyl dithioesters from thiophene, furan, 1-methylimidazole, 1,3-thiazole, and 2-methylthio-thiazole

A solution of 0.105 mol of butyllithium in ~ 75 ml of hexane and 80 ml of THF was prepared as described above. The heterocyclic compound (0.11 mol) was then added during 10 min; with thiophene and furan at 0°C , with thiazole between -80 and -90°C (occasional cooling in a bath with liquid nitrogen), and with 1-methylimidazole and 2-methylthio-thiazole below -40°C . After an additional 10 min (at the temperatures mentioned) a solution of 0.02 mol of copper(I) bromide and 0.04 mol of anhydrous lithium bromide in 30 ml of THF was added dropwise during 10 min, and then 0.11 mol of carbon disulfide during 5 min at the same temperature. Methyl iodide (usually 0.15 mol but in the case of the thiazoles and 1-methylim-

Table 1
Yields, boiling points and refractive indices for the compounds

Compound ^a	B.p. or m.p. (°C/mmHg)	n_D^{20}	Yield (%)
<i>o</i> -CH ₃ OC ₆ H ₄ CSSCH ₃	~ 125/0.6	1.662	80
<i>o</i> -FC ₆ H ₄ CSSCH ₃	135–138/14	1.6344	65
<i>p</i> -FC ₆ H ₄ CSSCH ₃	~ 90/0.6	1.652	75
2-thienylCSSCH ₃	~ 100/0.5	– ^b	90
3-thienylCSSCH ₃	157–159/12	– ^b	64
2-furylCSSCH ₃	120/15	– ^b	85
1-CH ₃ -2-pyrrolylCSSCH ₃	109–112/0.3	– ^b	72
1-CH ₃ -2-imidazolylCSSCH ₃	132–138/0.3	1.5688	74
2-thiazolylCSSCH ₃	55.5–56.5 m.p.	–	68
2-CH ₃ S-2-thiazolylCSSCH ₃	52–54 m.p.	–	88

^a Purities were at least 95%. ^b The red colour prevented accurate determination of the refractive index.

idazole 0.12 mol) was then added in one portion. The temperature was then allowed to rise to +15°C, and the mixture was then worked up as described above. For yields and physical properties see Table 1.

Conversion of 1-methylpyrrole into the methyl dithioester

Since metallation of 1-methylpyrrole with BuLi in THF and hexane proceeded sluggishly and incompletely (because of competitive attack of THF by BuLi), this substrate (0.13 mol) was first added at room temperature to a mixture of BuLi (0.105 mol) and *N,N,N',N'*-tetramethylethanediamine (0.11 mol) in hexane (~ 75 ml). The mixture was kept for 15 min at 40–45°C and then cooled to –20°C and THF (80 ml) was added. The further reactions with CS₂ and methyl iodide were then carried out as described above.

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