Synthesis of Dithioesters from Organocopper(I) Compounds

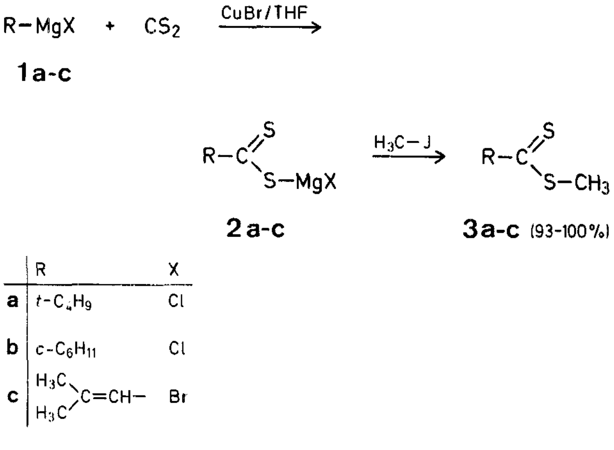
H. Westmijze, H. Kleijn, J. Meijer, P. Vermeer

Department for Organic Chemistry, State University, Croesestraat 79, Utrecht, The Netherlands

Some years ago[1] we reported a simple preparation of dithioesters by reacting alkyl- and arylmagnesium halides with carbon disulfide in tetrahydrofuran medium followed by adding an alkyl halide. Generally, the dithioesters were obtained in good yields but when *t*-alkyl- or cyclohexylmagnesium halides were used polymeric products were mainly formed.

As organocopper(I) reagents are useful for C—C bond forming reactions, we decided to investigate the use of organocopper(I) compounds instead of Grignard reagents under the conditions of Ref. [1]. Our first attempts were directed to develop a suitable synthesis for the methyl dithioates **3** in which R was *t*-butyl or cyclohexyl.

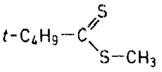
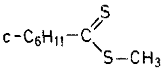
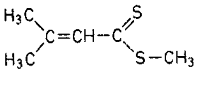
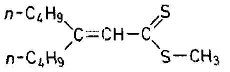
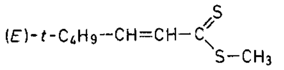
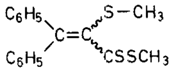
In this paper we wish to report that we have obtained both dithioesters in excellent yields by reacting the Grignard reagents **1** with carbon disulfide in the presence of catalytic amounts of copper(I) bromide (5–10 mol %) followed by alkylating the intermediary adduct **2** in tetrahydrofuran. Under the same conditions, we were also able to convert 2,2-dimethylvinylmagnesium bromide into the corresponding α-olefinic dithioester. An attempt to prepare **3** with the unsubstituted vinyl group (R = $H_2C=CH-$) failed, however.



Scheme A

Undoubtedly, organocopper(I) compounds are the reacting species in Scheme A. This assumption is supported by our observation that the same dithioesters **3** could be obtained in high yields by using the preformed cuprate species **4**, prepared from **1** and appropriate amounts of copper(I) bromide (Scheme **B**).

Table. Synthesis of Dithioesters **3** and **8** from Carbon Disulfide and the Organometallic Compounds **1**, **4**, and **7**

Substrate	Product[a]	Yield [%]	b.p./torr or m.p.	n_D^{20}	Molecular formula[b]	I.R. (film) $\nu_{C=C}$	¹H-N.M.R. (CCl_4)[c] δ [ppm]
1a **4a** **4b**		95 81 80	74–75°/20	1.5449	$C_6H_{12}S_2$ (148.4)		2.59 (H_3C—S); 1.45 (H_3C—C)
1b		100	128–130°/18	1.5751	$C_8H_{14}S_2$ (174.3)	—	2.57 (H_3C—S); 3.05 (>CH—C=S)
1c **4c**		93 95	46–48°/0.5	1.6255	$C_6H_{10}S_2$[d] (146.3)	1612	2.58 (H_3C—S); 6.62 (=CH—)
7a		80	94–96°/0.6	1.5536	$C_{12}H_{22}S_2$ (230.4)	1603	2.57 (H_3C—S); 6.53 (=CH—)[e]
7b		75[f]	119–120°/18	1.5810	$C_8H_{14}S_2$ (174.3)	1620	2.65(H_3C—S);6.60,6.95(2=CH—)[g]
7c		98	111.0–111.5°	—	$C_{17}H_{16}S_3$ (316.5)	1570	2.59 [>C(S)—SCH_3]; 2.17 (=C—SCH_3)[h]

[a] Purity: >98% as determined by ¹H-N.M.R. and G.L.C. (conditions: SE 33, 10% on Chromosorb W). All compounds showed the expected absorptions in the ¹³C-N.M.R. spectrum. A characteristic example is given under note[d].

[b] Microanalyses were not carried out.

[c] The ¹H-N.M.R. spectra were recorded on a Varian EM-390 spectrometer.

[d] ¹³C-N.M.R. values, Varian CFT-20 spectrometer, solution in $CDCl_3$, δ $(CH_3)_4Si = 0$ ppm; 224.31 ($\underline{C}=S$); 148.48 ($\underline{C}=C-C=S$); 131.83 ($=\underline{C}-C=S$); 28.38 ($-S-\underline{C}H_3$). This compound could also be prepared from the Grignard reagent, carbon disulfide and methyl iodide in the absence of copper(I) bromide but this reaction proceeded much slower than the copper(I) catalysed reaction and had to be carried out at +25°.

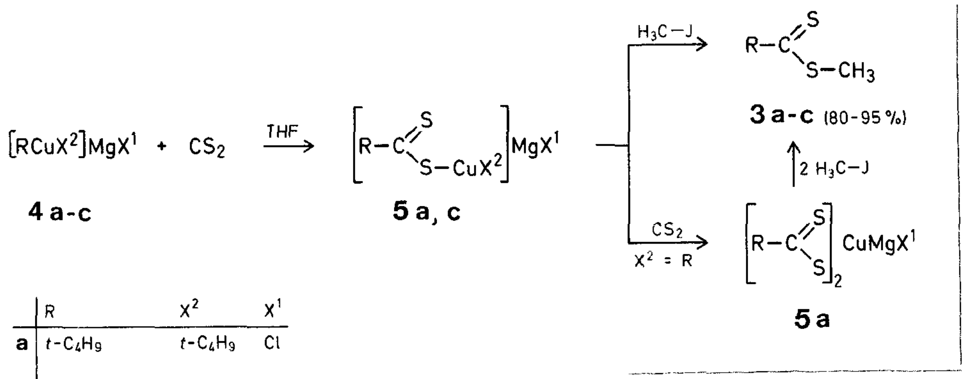
[e] Due to the structure of the cuprate, the crude dithioester was contaminated with an equimolar amount of n-C_4H_9—$CSSCH_3$ but it could easily be purified by distillation.

[f] (*E*/*Z*)-ratio ≥98/2.

[g] ${}^3J_{H-C=C-H} = 15.9$ Hz.

[h] Our compound was identical to the one reported in Ref. [11]. The authentic sample was kindly supplied by the authors of Ref. [11].

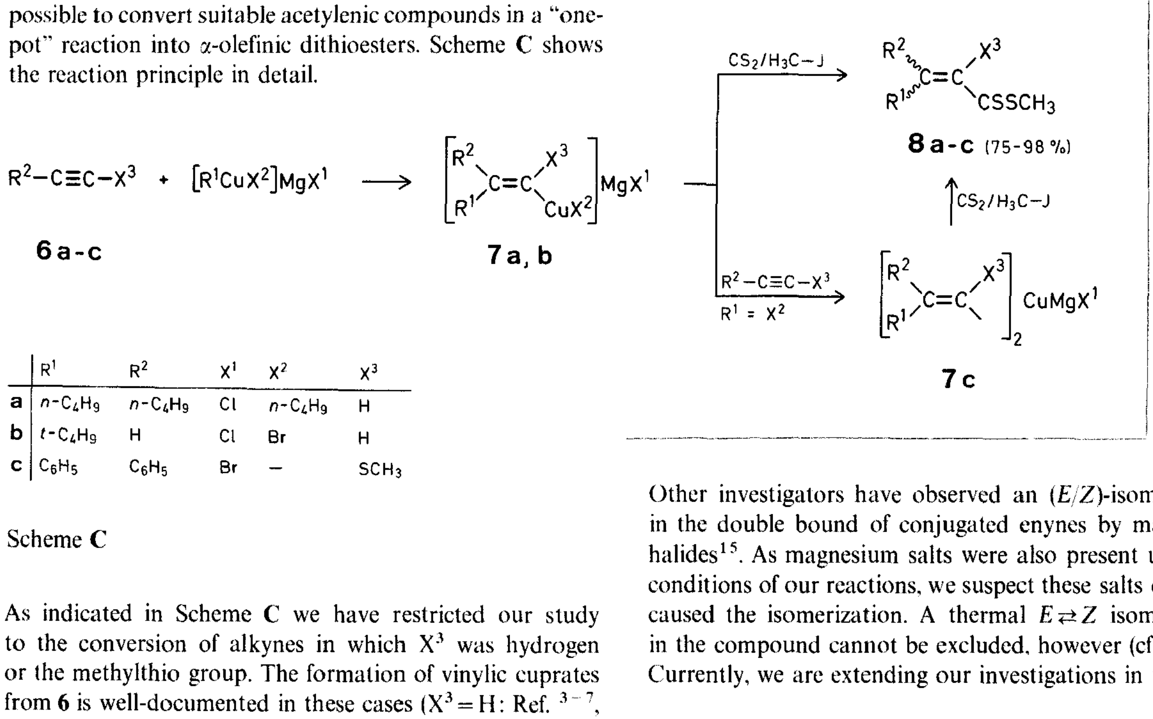
0039-7881/79/0632-0432 $ 03.00



	R	X²	X¹
a	t-C_4H_9	t-C_4H_9	Cl
b	t-C_4H_9	Br	Cl
c	$(H_3C)_2C{=}CH–$	Br	Br

Scheme B

The ability of organocuprates to react with carbon disulfide gives a new, simple synthesis of a wide range of dithioesters **3** with a vinylic R group, compounds which have scarcely appeared in the literature (cf. Ref. [2]). Many vinylic cuprates are easily accessible by reacting acetylenic compounds with alkyl- or arylcopper(I) compounds. So, it is in principle possible to convert suitable acetylenic compounds in a "one-pot" reaction into α-olefinic dithioesters. Scheme **C** shows the reaction principle in detail.



	R¹	R²	X¹	X²	X³
a	n-C_4H_9	n-C_4H_9	Cl	n-C_4H_9	H
b	t-C_4H_9	H	Cl	Br	H
c	C_6H_5	C_6H_5	Br	–	SCH_3

Scheme C

As indicated in Scheme **C** we have restricted our study to the conversion of alkynes in which X^3 was hydrogen or the methylthio group. The formation of vinylic cuprates from **6** is well-documented in these cases ($X^3 = H$: Ref. [3-7], $X^3 = CH_3S$: Ref. [8]), but other substituents X^3, for instance CN[9] and PR_2[10] can be expected to be suitable too.

Recently, dithioester **8c** was prepared photochemically from thiobenzophenone and bis[methylthio]acetylene in rather low yield[11]. The high yield synthesis of the same compound in our case nicely illustrates the usefulness of the procedure. Nevertheless, the formation of dithioesters of type **8** from acetylenic compounds **6** is also subjected to restrictions. The fact is that we were not able to prepare the dithioester n-C_4H_9–CH=CH–$CSSCH_3$ following Scheme **C**. The product in this case was probably a dimer resulting from a Diels-Alder reaction of the initially formed α-olefinic dithioester (cf. Ref. [2]).

In order to study the stereochemistry of the conversion of **6** into **8** we converted acetylene **6b** stereospecifically into the (*Z*)-cuprate **7b**[4] by reacting it with [t-C_4H_9CuBr]MgCl. After adding carbon disulfide and subsequent alkylation with methyl iodide we isolated the (*E*)-isomer of **8b** (see Table). Based on the (*Z*)-structure of **7b** and the fact that reactions of vinylcuprates with electrophiles generally proceed with retention of configuration[12,13,14], it is obvious that under the conditions of the reaction a rapid isomerization of the initially formed (*Z*)-isomer into the thermodynamically more stable (*E*)-isomer took place.

Other investigators have observed an (*E*/*Z*)-isomerization in the double bound of conjugated enynes by magnesium halides[15]. As magnesium salts were also present under the conditions of our reactions, we suspect these salts of having caused the isomerization. A thermal $E \rightleftarrows Z$ isomerization in the compound cannot be excluded, however (cf. Ref. [16]). Currently, we are extending our investigations in this field.

All reactions were carried out in an inert atmosphere of dry nitrogen.

Dithioesters 3 from Grignard Reagents 1 under Copper(I) Bromide Catalysis:

To a stirred solution of **1** (0.030 mol) in tetrahydrofuran (50 ml), a small amount of copper(I) bromide (5–10 mol %) is added at –50° and subsequently carbon disulfide (0.030 mol) at this temperature. After stirring of the resultant reaction mixture for 30 min at –50° methyl iodide (0.039 mol) is added. When the addition of the methyl iodide is completed, the reaction temperature is allowed to rise to 0° over a period of 30 min. Subsequently, the reaction mixture is poured into a saturated aqueous solution of ammonium chloride (200 ml). The dithioester is isolated by extracting the water layer with pentane (3 × 100 ml), washing the combined extracts with water (3 × 100 ml), drying the extract with magnesium sulfate, and removing the solvent by distillation. The crude product is distilled (see Table).

Dithioesters 3 from Cuprates 4:
To the cuprates **4** (0.015 mol: $X^2 = R$; 0.030 mol: $X^2 = Br$) in tetrahydrofuran (50 ml), carbon disulfide (0.030 mol) is added under efficient stirring at −50°. After 30 min methyl iodide (0.039 mol) is added, followed by raising the reaction temperature to 0° over a period of 30 min. The reaction mixture is poured into a saturated aqueous solution of ammonium chloride (200 ml) containing sodium cyanide (2 g). The dithioester is isolated as described above. The cuprates are prepared following the procedures in Refs. [4,5].

Dithioesters 8a and 8b from Alkynes 6a and 6b:
The 1-alkynes **6a** and **6b** are converted into the corresponding cuprates **7a** and **7b** following the procedures given in Refs. [4,5]. The conditions for the conversion of **7a** (0.030 mol) into **8a** and **7b** (0.030 mol) into **8b** by treating with carbon disulfide (0.060 mol in the case **7a**; 0.030 mol in the case **7b**) and subsequent alkylation with methyl iodide (0.080 mol in the case **7a**) and subsequent alkylation with methyl iodide (0.080 mol in the case **7a**; 0.039 mol in the case **7b**) are exactly the same as given above for the conversion **4**→**3**.

Methyl 3,3-Diphenyl-2-propenedithioate (8c) from 1-Methylthio-2-phenylethyne (6c):
To a stirred solution of $(C_6H_5)_2CuMgBr$ (0.015 mol) in tetrahydrofuran (50 ml) the 1-alkyne **6c** (0.030 mol) is added at +30°. Stirring is continued for 1 h at this temperature. To the cuprate **7c** thus obtained, carbon disulfide (0.030 mol) is added at +30°. After stirring for 1 h at this temperature, methyl iodide (0.039 mol) is added. After stirring the reaction mixture for 1 h at +30°, the product **8c** is isolated as described above for **4**→**3**. The obtained dithioester is crystallized form methanol.

This investigation was supported by the Netherlands Foundation for Chemical Research (S.O.N.).

Received: January 5, 1979

---

[1] J. Meijer, P. Vermeer, L. Brandsma, *Recl. Trav. Chim. Pays-Bas* **92**, 601 (1973).

[2] P. Gosselin, S. Masson, A. Thuillier, *Tetrahedron Lett.* **1978**, 2715, and references cited therein.

[3] J. F. Normant, G. Cahiez, M. Bourgain, C. Chuit, J. Villieras, *Bull. Chem. Soc. Fr.* **1974**, 1656.

[4] H. Westmijze, J. Meijer, H. J. T. Bos, P. Vermeer, *Recl. Trav. Chim. Pays-Bas* **95**, 299 (1976).

[5] H. Westmijze, J. Meijer, H. J. T. Bos, P. Vermeer, *Recl. Trav. Chim. Pays-Bas* **95**, 304 (1976).

[6] H. Westmijze, H. Kleijn, P. Vermeer, *Tetrahedron Lett.* **1977**, 2023.

[7] A. Marfat, P. R. McGuirk, P. Helquist, *Tetrahedron Lett.* **1978**, 1363.

[8] P. Vermeer, C. de Graaf, J. Meijer, *Recl. Trav. Chim. Pays-Bas* **93**, 24 (1974).

[9] H. Westmijze, H. Kleijn, P. Vermeer, *Synthesis* **1978**, 454.

[10] J. Meijer, H. Westmijze, P. Vermeer, *Recl. Trav. Chim. Pays-Bas* **95**, 102 (1976).

[11] A. C. Brouwer, H. J. T. Bos, *Tetrahedron Lett.* **1976**, 209.

[12] H. Westmijze, J. Meijer, P. Vermeer, *Recl. Trav. Chim. Pays-Bas* **96**, 168 (1977).

[13] H. Westmijze, J. Meijer, P. Vermeer, *Recl. Trav. Chim. Pays-Bas* **96**, 194 (1977).

[14] H. Westmijze, P. Vermeer, *Synthesis* **1977**, 784.

[15] C. Chuit, G. Cahiez, J. F. Normant, J. Villieras, *Tetrahedron* **32**, 1675 (1976).

[16] J. Maignan, J. Vialle, *Bull. Soc. Chim. Fr.* **1973**, 1973.

0039-7881/79/0632-0434 $ 03.00