Convenient Synthesis of Methyl 3-Alkynedithioates and β,γ-Unsaturated γ-Dithiolactones from Allenyllithium and Allenylsilver(I) Compounds

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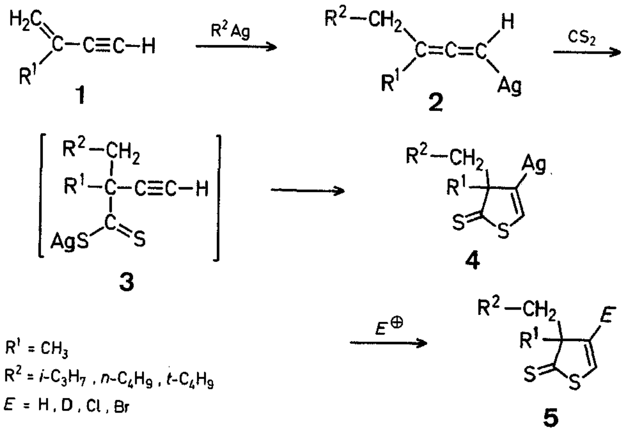
Recently[1], we published some preliminary results for the reaction of allenylsilver(I) reagents with carbon disulfide. We showed that this reaction gives excellent yields of β,γ-unsaturated γ-dithiolactones. In this paper, we report on the results of an extensive study in this area.

A facile approach to β,γ-unsaturated γ-dithiolactones (compounds **5**) is outlined in Scheme **A** (Method A; some of the conversions given in Scheme **A** were already described in Ref.[1]). Method A successively involves addition of alkylsilver compounds to conjugated enynes **1** (→allenylsilver(I) compounds **2**)[2], *in situ* reaction of **2** with carbon disulfide (→**3**), and cyclisation of **3** into the ring compounds **4**. The cyclisation of **3** occurs spontaneously under the conditions of the reaction (*cf.*[1]). It appears that besides protolysis of **4** (→**5**, *E*=H) also the reactions of **4** with *N*-chlorosuccinimide (→**5**, *E*=Cl) and cyanogen bromide (→**5**, *E*=Br) proceed smoothly. The yields of the β,γ-unsaturated γ-dithiolactones **5** via this Method A are good (see Table 1, under Method A).



Scheme A

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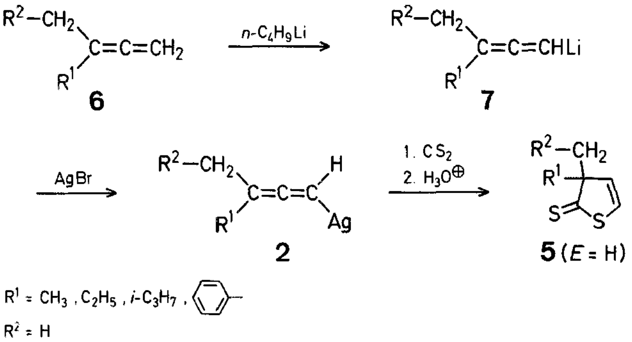
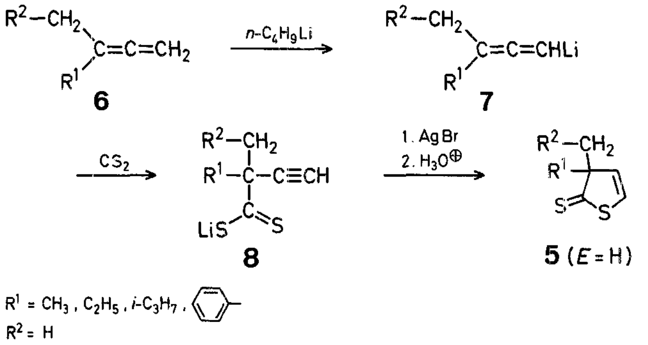
This convenient route to dithiolactones **5** is restricted, however, because of the origin of the allenylsilver(I) compounds **2**. So, Method A is not suited to prepare, for instance, dithiolactones **5** in which R^2 is hydrogen and R^1 is phenyl.

To develop a more general method to prepare compounds of type **5**, it was therefore necessary to search for a more general route to compounds **2**. In view of the fact that allenyllithium compounds (**7**) are easily accessible from allenic hydrocarbons (**6**)[3,4], we decided to use these allenyl-metal reagents for the preparation of **2**. Scheme **B** and Table 1 show that this Method B in which the allenic hydrocarbon is first deprotonated by *n*-butyllithium and subsequently treated with silver(I) bromide [except in Method A, silver(I) bromide is used as the complex silver(I) bromide·3 lithium bromide, *cf.*[2]] (→**2**) and carbon disulfide, is indeed a very useful one to prepare dithiolactones **5**.



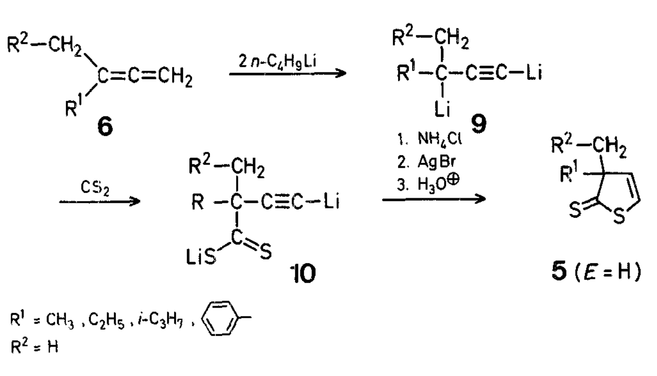
Scheme **B**

The alternative route involving successively lithiation of **6** (→**7**), reaction of **7** with carbon disulfide (→dithioate **8**), and ring closure of **8** by adding silver(I) bromide (see Scheme **C**; Method C) is also possible but does not give yields better than those obtained via Method B (see Table 1). Nevertheless, the observation that **7** smoothly reacts with carbon disulfide to give **8**, a dithioate which is stable under the conditions of the reaction, was useful because it enabled us to apply **8** for the preparation of methyl 3-alkynedithioates (**11**, see below). To our knowledge such compounds have not been described before, except for the one in our preliminary report (*cf.*[1]).



Scheme C

In one case – *viz.* starting from 3-phenyl-1,2-butadiene (**6**; $R^1 = C_6H_5$, $R^2 = H$) – Method B as well as Method C led to **5** ($E = H$) in moderate yield (~50%). Remarkably, this dithiolactone, which is not accessible via Method A, could be obtained in excellent yield when instead of the monolithio derivative **7** the dilithio compound **9**[5] (Scheme **D**) was used. Compound **9** reacted very smoothly with carbon disulfide (→**10** in Scheme **D**). Subsequent addition to **10** of ammonium chloride (→**8**) and silver(I) bromide followed by protolysis furnished the desired dithiolactone **5** ($R^1 = C_6H_5$, $R^2 = H$) in 90% yield. As can be seen from Table 1, this method (Method D) also gives better yields of **5** in other cases.



Scheme **D**

Table 1. Dithiolactones **5** and Methyl 3-Alkynoates **11** prepared

Product[a] No.	R^1	R^2	*E*	Yield [%] (Method)	b.p. [°C]/ torr	n_D^{20}	Molecular formula[b]	
5a	CH_3	H	H	55 (E); 65 (B); 67 (C); 75 (D)	70°/18	1.6121	$C_6H_8S_2$	(144.2)[c]
5b	C_2H_5	H	H	50 (E); 58 (C); 60 (B); 70 (D)	95°/18	1.5970	$C_7H_{10}S_2$	(158.3)
5c	$i\text{-}C_3H_7$	H	H	65 (E); 75 (B); 76 (C); 80 (D)	108°/18	1.5890	$C_8H_{12}S_2$	(172.3)
5d	CH_3	$i\text{-}C_3H_7$	H	95 (A)	60–62°/0.4	1.5695	$C_9H_{14}S_2$	(186.3)
5e	CH_3	$i\text{-}C_3H_7$	Cl	95 (A)	85–86°/0.4	1.6025	$C_9H_{13}ClS_2$	(220.8)
5f	CH_3	$n\text{-}C_4H_9$	H	80 (A)	96–98°/0.6	1.5776	$C_{10}H_{16}S_2$	(200.4)
5g (g′)	CH_3	$t\text{-}C_4H_9$	H (D)	93 (A)	70–71°/0.6	1.5667	$C_{10}H_{16}S_2$	(200.4)
5h	CH_3	$t\text{-}C_4H_9$	Br	92 (A)	m.p. 44–46°	—	$C_{10}H_{15}BrS_2$	(279.3)
5i	C_6H_5	H	H	45 (E); 48 (C); 50 (B); 90 (D)	88°/0.02	1.6597	$C_{11}H_{10}S_2$	(206.3)[d]
11a	CH_3	H	—	78 (F); 80 (G)	80°/18	1.5640	$C_7H_{10}S_2$	(158.3)[e]
11b	C_2H_5	H	—	65 (F); 76 (G)	98°/15	1.5592	$C_8H_{12}S_2$	(172.3)
11c	$i\text{-}C_3H_7$	H	—	74 (F); 86 (G)	75°/0.4	1.5561	$C_9H_{14}S_2$	(186.3)
11d	C_6H_5	H	—	50 (F); 95 (G)	102°/0.001	1.6281	$C_{12}H_{12}S_2$	(220.3)
11e	CH_3	$i\text{-}C_3H_7$	—	75 (F); 85 (G)	51–52°/0.3	1.5432	$C_{10}H_{16}S_2$	(200.4)

[a] Purity ≥95% by G.L.C. (SE 33 column) and ^{1}H-N.M.R. analysis.

[b] Molecular ion peaks observed in the mass spectra.

[c]

	C	H
calc.	C 49.95	H 5.59
found	50.50	5.23

[d]

	C	H
calc.	C 64.04	H 4.89
found	64.60	5.14

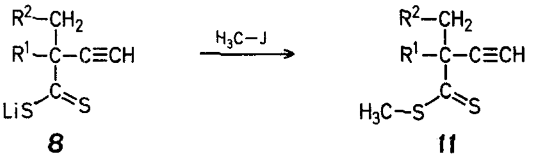
[e]

	C	H	S
calc.	C 53.11	H 6.38	S 40.51
found	53.16	6.87	40.14

For the ring closure of **8** (Scheme C) and **10** (Scheme D) into **5**, it is not necessary to use silver(I) bromide. Treatment of **8** and **10** with 2 normal sulfuric acid (Method E in Table 1) namely also gives compounds **5**, although the yield (not yet optimized) of **5** via this method is lower than that obtained via Methods C and D.

It is noticed that none of the methods A-E is suited to prepare γ-dithiolactones **4** in which R^1 is hydrogen. Several attempts to obtain such dithiolactones (or their 2-mercaptothiophene tautomers) led to tarry products.

As, *in contrast with the silver(I) salts* **3**, *the lithium 3-alkynedithioates* **8** (see Scheme C) are stable under the conditions of the reaction, they can be intercepted by methyl iodide. The yield of the produced methyl 3-alkynedithioates **11** (Scheme E) is generally excellent if, prior to the addition of methyl iodide, an aqueous 2 normal sodium hydroxide solution is added to **8** (Method F in Table 1).



Scheme E

In one case, *viz.* starting from **8** in which R^2 is hydrogen and R^1 is phenyl, the yield of **11** was unsatisfactory. Similar to the preparation of the corresponding dithiolactone **5**, a much better yield of **11** (95%; $R^2=H$, $R^1=C_6H_5$) was obtained in this case when instead of **8** the dilithio derivative **10** (Scheme **D**; $R^2=H$, $R^1=C_6H_5$) was treated with sodium hydroxide solution and methyl iodide. In Table 1 also some other examples involving a preparation of **11** from **10** are given (Method G). It appears that the yields of **11** in these cases are better than those obtained via Method F.

We have already mentioned that we were not able to prepare dithiolactones **5** in which R^1 is hydrogen. Similarly, tarry products were formed when the preparation of dithioesters **11** ($R^1=H$) was attempted.

In conclusion, the ready availability of allenyllithium and -silver(I) compounds *opens attractive synthetic routes to methyl* 3-alkynedithioates and β,γ-unsaturated γ-dithiolactones. To our knowledge, no other routes to both classes of compounds have been reported in the literature. Thus far only α-dialkylaminomethylene analogs of our dithiolactones are known. These analogs are prepared from mercapto-aldimines and dialkylamines[6]. It will not be easy, however, to convert such compounds into the dithiolactones described in this paper.

All operations with organometallic reagents were carried out in an atmosphere of dry nitrogen. The allenes **6** were prepared via addition of alkylsilver compounds to 3-methylbut-1-yn-3-ene ($\rightarrow$**6**; $R^1=CH_3$, $R^2=i\text{-}C_3H_7$)[2], by treatment of 1-ethoxy-2-butyne with phenylmagnesium bromide in the presence of 10 mol% copper(I) bromide in ether ($\rightarrow$**6**; $R^1=C_6H_5$, $R^2=CH_3$)[7], or via a modification of the lithium aluminium hydride-induced S_N2' reaction of 3-bromo-1-alkynes ($\rightarrow$**6**; $R^1=CH_3$, C_2H_5, $i\text{-}C_3H_7$; $R^2=H$)[8] (see below).

Improved Preparation of Allenes 6 ($R^1=CH_3$, C_2H_5, $i\text{-}C_3H_7$; $R^2=H$): To lithium aluminium hydride (0.25 mol) in triethyleneglycol dimethyl ether (200 ml) is dropwise added with stirring the 3-bromo-1-alkyne[9] (0.50 mol) at +60 °C. After the bromide has been added, the mixture is stirred for 1 h at +60 °C. Subsequently, the mixture is cooled to

Table 2. Characteristic Spectral Data for Compounds **5**

Compound	^{1}H-N.M.R. (CDCl$_3$/TMS) δ [ppm][a]		^{13}C-N.M.R. (CDCl$_3$/TMS) δ [ppm][b]			
	H—C-4	*H—C-3 (E)*	*C=S (C-1)*	C-2	C-3	C-4
5a	6.59 (d)[c]	6.18 (d)	249.6	67.1	140.3	121.3
5b	6.68 (d)[d]	6.22 (d)	249.3	72.0	138.8	122.8
5c	6.72 (d)[c]	6.23 (d)	250.6	75.3	136.4	123.8
5d	6.63 (d)[c]	6.32 (d)	242.2	71.3	139.6	121.6
5e	6.74 (s)	—	243.0	72.8	123.1	120.0
5f	6.67 (d)[c]	6.20 (d)	249.6	71.7	139.3	122.5
5g	6.62 (d)[d]	6.42 (d)	242.0	71.1	140.1	120.6
5g′ (*E*=D)	6.62 (s)	—	249.4	71.1	139.8	120.6
5h	6.72 (s)	—	242.4	72.3	123.7	119.8
5i	6.67 (d)[c]	6.30 (d)	247.0	73.7	140.2	123.1

[a] The ^{1}H-N.M.R. spectra were recorded on a Varian EM-390 spectrometer.
[b] The ^{13}C-N.M.R. spectra were recorded on a Varian CFT-20 spectrometer.
[c] $^3J_{(H—C_\beta=C_\gamma—H)}=6.6$ Hz.
[d] $^3J_{(H—C_\beta=C_\gamma—H)}=6.8$ Hz.

Table 3. Characteristic Spectral Data for Compounds **11**

Compound[a]	^{1}H-N.M.R. (CCl$_4$/TMS) δ [ppm][b]		^{13}C-N.M.R. (CDCl$_3$/TMS) δ [ppm][c]			
	H$_3$CS	HC≡C	H$_3$CS	C=S	HC≡<u>C</u>	H<u>C</u>≡C
11a	2.55	2.45	20.6	242.1	37.4	73.9
11b	2.55	2.52	20.8	241.8	86.1	75.7[e]
11c	2.55	2.53	20.6	243.1	84.1	77.1
11d	2.48	2.60	20.8	239.8	86.5	75.5
11e	2.55	2.52[d]	20.8	241.9	86.3	76.4

[a] The I.R. spectra showed inter alia a strong *absorbance at* $\nu=3295$–$3300\ cm^{-1}$ *(H—C≡)*.
[b] The ^{1}H-N.M.R. spectra were recorded on a Varian EM-390 spectrometer.
[c] The ^{13}C-N.M.R. spectra were recorded on a Varian CFT-20 spectrometer.
[d] In C$_6$D$_6$-solution [30% (v/v)] the following data were obtained: $\delta_{CH_3S}=2.22$, $\delta_{HC\equiv C}=2.39$ ppm.
[e] These ^{13}C-N.M.R. data were recorded on a Bruker WP-200 spectrometer.

+25 °C, the reaction flask is evacuated at the water pump, and the volatile allenes **6** are collected in a cold trap at −75 °C. The allenes thus obtained (yield: >95%) are almost pure [>95% according to ^{1}H-N.M.R. and G.L.C. (SE 33 column) analysis] and are used without further purification.

Dithiolactones 5; General Procedures:

Method A: To a stirred solution of silver(I) bromide · 2 lithium bromide (0.030 mol) in a mixture of tetrahydrofuran (100 ml) and hexamethylphosphoric triamide (15 ml) is added the Grignard reagent R^{2}MgCl (0.030 mol; 1 molar solution in tetrahydrofuran) at −60 to −50 °C. After the mixture has been stirred for 15 min at −60 °C, 3-methylbut-1-yn-3-ene (**1**; R^1 = CH$_3$; 0.060 mol) is added. The resulting reaction mixture is then stirred for 3 h (R^2 = *i*-C$_3$H$_7$) or 6 h (R^2 = *n*-C$_4$H$_9$) at 0 °C, or for 3 h (R^2 = *t*-C$_4$H$_9$) at −20 °C. To the allenylsilver(I) reagents **2** thus obtained is added carbon disulfide (0.030 mol), and the mixture is stirred for 1 h at +25 °C (→**3**→**4**). Dithiolactones **5** in which *E* is hydrogen are obtained by treating the mixture with an aqueous solution of ammonium chloride (200 ml), containing sodium cyanide (2 g); the dithiolactone **5** with *E* = D is obtained by treating adduct **4** with a solution of D$_2$SO$_4$ (1 g) in D$_2$O (10 ml) at −20 °C prior to protic work-up; dithiolactones **5** in which *E* = Cl or Br are obtained by treating the silver(I) intermediate with *N*-chlorosuccinimide (0.031 mol) or cyanogen bromide (0.031 mol) for 1 h at +25 °C prior to pouring the mixture into an aqueous ammonium chloride solution (200 ml), containing sodium cyanide (2 g). Dithiolactones **5** are isolated by extraction with pentane (3 × 100 ml). The combined pentane extracts are washed with water (3 × 150 ml) and dried with magnesium sulfate. The solvent is evaporated in vacuo and the residue distilled (*E* = H or Cl) or purified by column chromatography on alumina (deactivated with 5% water) eluting with *n*-hexane (*E* = Br).

Method B: To a stirred solution of allene **6** (0.031 mol) in tetrahydrofuran (60 ml) is added *n*-butyllithium (0.030 mol; 1.6 molar solution in *n*-hexane) at −60 °C. The mixture is stirred for 1 h at −60 °C (→**7**). Subsequently, a solution of silver(I) bromide · 3 lithium bromide (0.030 mol) in tetrahydrofuran (30 ml) is added at −60 °C, the mixture is stirred for 30 min at this temperature (→**2**), and then carbon disulfide (0.030 mol) is added (→**3**→**4**). The temperature is allowed to rise to +25 °C, and stirring is continued for 1.5 h at +25 °C. Dithiolactones **5** are isolated as described under Method A.

Method C: To a stirred solution of **7** (0.030 mol, see Method B) is added carbon disulfide (0.030 mol) at −60 °C. The mixture is stirred for 15 min at −60 °C (→**8**) followed by addition of silver(I) bromide · 3 lithium bromide (0.030 mol) in tetrahydrofuran (30 ml, →**3**→**4**). Subsequently, the mixture is stirred for 1 h at +25 °C. The produced dithiolactones **5** are isolated as described under Method A.

Method D: To *n*-butyllithium (0.060 mol, 1.6 molar solution in *n*-hexane) in tetrahydrofuran (60 ml) is added with stirring allene **6** (0.030 mol) at −60 °C (→**9**). After stirring of the mixture for 1 h at −60 °C, carbon disulfide (0.030 mol) is added at −60 °C (→**10**). Stirring of the mixture at −60 °C is continued for 15 min. Subsequently, dry ammonium chloride (0.030 mol) is added (→**8**). After the mixture has been stirred for 1 h at −60 °C, a solution of the complex silver(I) bromide · 3 lithium bromide (0.030 mol) in tetrahydrofuran (30 ml) is added at −60 °C (→**3**→**4**). The further procedure is identical to that described under Method C.

Method E: To **8** or **10** (0.030 mol) prepared according to Method C or D is added water (20 ml) at 0 °C followed by 2 normal sulfuric acid (30 ml). The mixture is stirred for 15 min at 0 °C, the organic layer is separated and the aqueous layer is extracted with pentane (3 × 50 ml). The combined extracts are added to the organic layer. After washing with water (3 × 100 ml), the extract is dried with magnesium sulfate and the products **5** are isolated as described under Method A.

Methyl 3-Alkynedithioates 11; General Procedures:

Method F: To **8** (0.030 mol, see under Method C) is added at −60 °C at once 2 normal sodium hydroxide solution (30 ml). The mixture is then treated with methyl iodide (0.060 mol) for 30 min at 0 °C. The formed dithioesters **11** are isolated by pouring the mixture in water (150 ml), extracting the aqueous layer with pentane (3 × 50 ml), washing the combined extracts with water (3 × 100 ml), drying the extracts with magnesium sulfate, and evaporating the solvent in vacuo. The residue is distilled.

Method G: The procedure for the conversion of **10** (0.030 mol, see under Method E) into **11** is identical to that described in Method F.

Yields, physical constants, and characteristic spectroscopic data for dithiolactones **5** are given in Tables 1 and 2, for compounds **11** in Tables 1 and 3.

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