

A Convenient Synthesis of 1,3-Dithiane Derivatives by Reaction of 4-Methyl-1,3-dithiane-2-thione with Grignard Reagents and Butyllithium

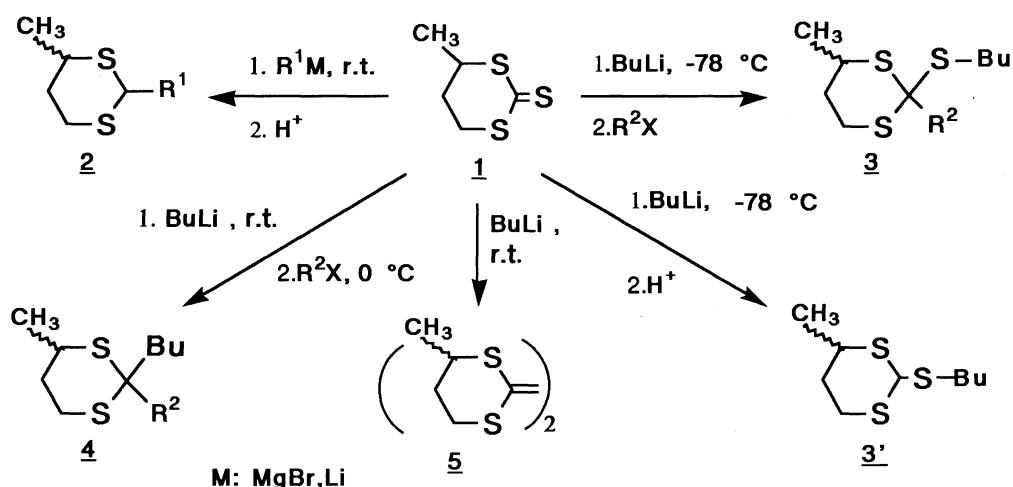
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The reaction of 4-methyl-1,3-dithiane-2-thione with alkyl Grignard reagents or butyllithium (BuLi) at room temperature gave 2-alkyl-4-methyl-1,3-dithianes in good yields. High yields of 2-alkyl-2-butylthio-4-methyl-1,3-dithianes and 2,2-dialkyl-4-methyl-1,3-dithianes were obtained by treatment with BuLi at -78 °C and room temperature followed by alkylation with alkyl halides, respectively.

Much attention has been focused on the synthesis of trithiocarbonates, which are very important intermediates for the preparation of insecticides and oil additives.¹⁾ Recently, we also reported a convenient synthesis and reactions of a variety of trithiocarbonates.²⁾ During the course of our investigation on the reactivity of trithiocarbonates, we found some interesting chemical behaviors of trithiocarbonates.³⁾ In this paper, we wish to report a convenient synthesis of 1,3-dithiane derivatives by reaction of six-membered cyclic trithiocarbonates such as 4-methyl-1,3-dithiane-2-thione (1) with Grignard reagents or butyllithium (BuLi) (Scheme 1).



Scheme 1.

A typical procedure is as follows: A solution of **1** (0.5 mmol) in THF (20 ml) was added to a solution of BuLi (1.5 mmol) in THF at -78 °C, and then the mixture was stirred for 1 h at room temperature. After the usual workup, the obtained reaction mixture was chromatographed on silica gel using a mixture of hexane-CH₂Cl₂ (v/v, 5/2) as an eluent to give **2b** in 82% yield.

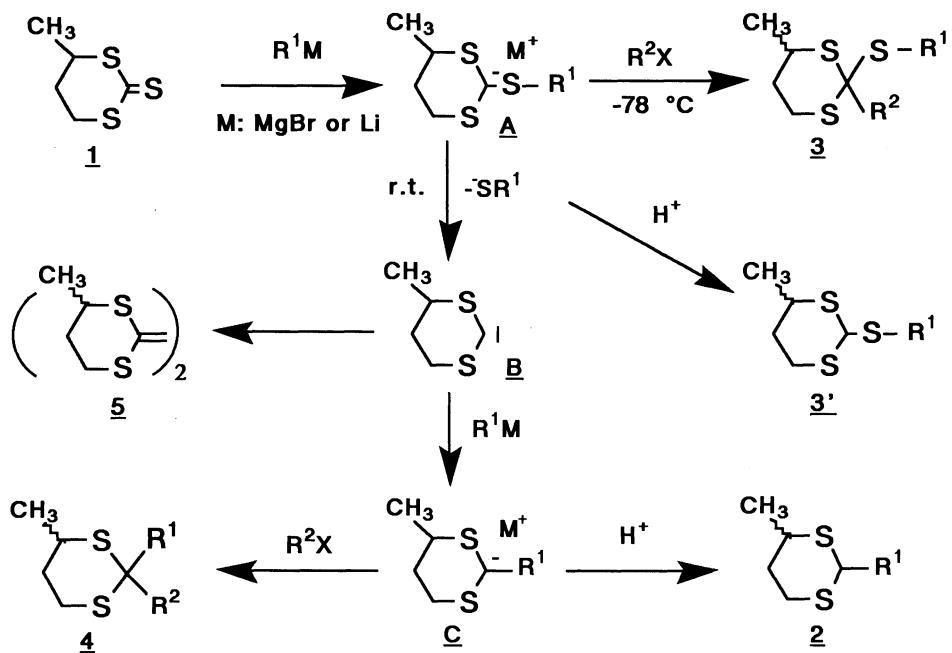
Table 1. Reactions of **1** with Organometallic Compounds

Run ^{a)}	Reagent	Alkylation agent	Reaction temp/°C	Yield of products/% ^{b)}				
				2	3	3'	4	5
1	C ₂ H ₅ MgBr	-	r.t.	62	2a	-	-	-
2	C ₂ H ₅ MgBr	-	-78	7	2a	-	-	-
3	n-C ₄ H ₉ MgBr	-	r.t.	63	2b	-	-	-
4	i-C ₄ H ₉ MgBr	-	r.t.	61	2c	-	-	-
5	BuLi ^{c)}	-	r.t.	-	-	-	-	66
6	BuLi ^{d)}	-	r.t.	82	2b	-	-	-
7	BuLi	CH ₃ Br	0	-	-	-	60	4a
8	BuLi	C ₂ H ₅ Br	0	-	-	-	60	4b
9	BuLi	C ₂ H ₅ Br	-78	-	-	89	3a	-
10	BuLi	C ₂ H ₅ Br	-78	-	-	75	3a	-
11	BuLi	n-C ₃ H ₇ Br	-78	-	-	81	3b	-
12	BuLi	n-C ₄ H ₉ Br	-78	-	-	89	3c	-
13	BuLi	i-C ₄ H ₉ Br	-78	-	-	84	3d	-
14	BuLi	C ₅ H ₁₁ Br	-78	-	-	81	3e	-
15	BuLi	s-C ₄ H ₉ Br	-78	-	-	-	92	-
16	BuLi	s-C ₄ H ₉ Br	r.t.	11	2b	-	-	8

a) **1**, 0.5 mmol; RMgBr, 2.5 mmol and BuLi, 1.5 mmol. b) Isolated yield based on **1**. c) **1**, 0.5 mmol; BuLi, 0.5 mmol. d) **1**, 0.5 mmol; BuLi, 2.5 mmol.

The reactions of the trithiocarbonate **1** with various Grignard reagents at room temperature gave selectively 2-alkyl-4-methyl-1,3-dithianes (**2**)^{4,5)} in moderate yields as shown in Table 1. The reaction at -78 °C resulted in formation of **2** in low yield (Run 2). Surprisingly, the use of butyllithium (0.5 mmol) instead of a Grignard reagent afforded an interesting coupling product bis(4-methyl-1,3-dithiane-2-ylidene) (**5**)⁶⁾ in 66% yield (Run 5) and the reaction with excess BuLi (2.5 mmol) gave **2b** in 82% yield (Run 6). On the other hand, the reaction of **1** with BuLi in THF followed by treatment with an appropriate alkylation agent at -78 °C and 0 °C afforded 2-alkyl-2-alkylthio-4-methyl-1,3-dithianes (**3**)⁷⁾ and 2,2-dialkyl-4-methyl-1,3-dithianes(**4**)⁸⁾ in high yields, respectively (Runs 7-14). When s-butyl bromide as an alkylation agent was employed at -78 °C, 2-butylthio-4-methyl-1,3-dithiane (**3'**)⁹⁾ was obtained in 92% yield (Run 15), while at room temperature **2b** (11%) and **5** (8%) were obtained (Run 16).

On the basis of the formation of the dithianes 2, the dithianes 4, the thiophilic adducts 3, and carbenoid-coupling product 5, the reaction pathway is illustrated as shown in Scheme 2. 10) In the initial step, an organometallic compound attacks the sulfur atom of the thiocarbonyl group of 1 to give a carbanion intermediate A, which reacts readily with an alkyl halide at -78 °C to afford compound 3. On the other hand, at room temperature, the intermediate A releases an alkyl thiolate anion to yield a carbenoid intermediate B. The intermediate B gives a carbenoid-coupling product 5 or an alkylated product 2 and 4 via the intermediate C.



Scheme 2.

As mentioned above, we were able to obtain different products from those reported previously by Hatanaka et al. who showed that the reaction of five-membered cyclic trithiocarbonates with an organic lithium compound such as BuLi or lithium diisopropylamide affords olefins and vinyl alkyl trithiocarbonates.¹¹⁾ Thus, we found a novel reaction of six-membered cyclic trithiocarbonates. Furthermore, it is well known that dithiane is an important intermediate in many synthetic reactions¹²⁾ and has been used as a synthetic equivalent of carbonyl dianion in the synthesis of natural products.¹³⁾

In conclusion, we succeeded in obtaining the dithianes 2, the dithianes 4, and the thioldithianes 3, which have great synthetic potential, from six-membered cyclic trithiocarbonates 1 by the reaction initiated by the thiophilic attack of alkyl Grignard reagent or BuLi followed by alkylation.

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- 4) The products **2**, **3**, **3'**, and **4** were shown by their ^1H NMR spectra to consist of almost one diastereomer. The major isomer in each case was isolated in a pure form by column chromatography, but its stereochemical structure was not determined at the present time.
- 5) Product **2a**: Colorless oil; ^1H NMR (200 MHz, CDCl_3) δ 1.07 (t, $J=7.3$ Hz, 3H), 1.31 (d, $J=7.0$ Hz, 3H), 1.77 (dd, $J=14.6$, 8.3, 6.0, 5.4 Hz, 1H), 1.98 (qd, $J=7.3$, 7.3 Hz, 2H), 2.14 (dd, $J=14.6$, 5.5, 4.0, 3.1 Hz, 1H), 2.85 (m, 2H), 3.09 (qdd, $J=8.3$, 7.0, 3.1 Hz, 1H), and 3.78 (t, $J=7.3$ Hz, 1H); IR (neat) 2900, 1440, 1370, 1250, 890, and 800 cm^{-1} ; MS (70 eV) m/z 161 (M^+-1).
- 6) Product **5** : Colorless crystals; mp, 98-108 °C (CDCl_3); ^1H NMR (200 MHz, CDCl_3) δ 1.30 (d, $J=7.0$ Hz, 3H), 1.80 (m, 1H), 2.25 (m, 1H), 2.95 (m, 2H), and 3.20 (m, 1H); IR (neat) 2900, 1450, 1420, 1300, 1250, and 860 cm^{-1} ; MS (20 eV) m/z 264 (M^+); Anal. Found: C, 45.48; H, 6.19%. Calcd for $\text{C}_{10}\text{H}_{16}\text{S}_4$: C, 45.41; H, 6.10%.
- 7) Product **3a**: Colorless oil; ^1H NMR (200 MHz, CDCl_3) δ 0.92 (t, $J=7.2$ Hz, 3H), 1.17 (t, $J=7.4$ Hz, 3H), 1.20 (d, $J=6.9$ Hz, 3H), 1.30-1.60 (m, 4H), 2.05 (q, $J=6.9$ Hz, 2H), 2.10 (m, 2H), 2.48 (t, $J=7.0$ Hz, 2H), 2.71 (dt, $J=14.0$, 3.2 Hz, 1H), and 3.30 (m, 2H); IR (neat) 2950, 1450, 1410, 1370, and 1250 cm^{-1} ; MS (20 eV) m/z 250 (M^+).
- 8) Product **4a** : Colorless oil; ^1H NMR (200 MHz, CDCl_3) δ 0.93 (t, $J=7.0$ Hz, 3H), 1.18 (d, $J=7.0$ Hz, 1.3-1.5(m, 4H), 1.45(s, 3H), 1.9-2.0(m, 2H), 2.0-2.8(m, 1H), and 2.8-3.1(m, 2H); IR (neat) 2900, 1450, 1380, and 1250 cm^{-1} ; MS (20 eV) m/z 204 (M^+).
- 9) Product **3'**: Colorless oil; ^1H NMR (200 MHz, CDCl_3) δ 0.92 (t, $J=7.0$ Hz, 3H), 1.19 (d, $J=7.0$ Hz, 3H), 1.30-1.60 (m, 4H), 1.70 (m, 1H), 2.1 (m, 1H), 2.60 (t, $J=7.2$ Hz, 2H), 2.68 (m, 1H), 3.38 (m, 2H), and 4.96 (s, 1H); IR (neat) 2900, 1450, 1410, 1250, 900, and 730 cm^{-1} ; MS (20 eV) m/z 222 (M^+).
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