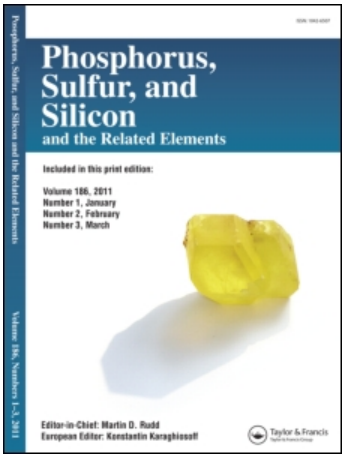


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

REACTION OF POLYMERIZATION-RESISTANT 1,2-DITHIOLANES WITH SULFOXONIUM YLIDES. NEW METHOD FOR 1,3-DITHIANE SYNTHESIS

Masato Tazaki[a]; Michihiro Yamada[a]
[a] Department of Industrial Chemistry, Kumamoto Institute of Technology, Kumamoto, Japan

To cite this Article Tazaki, Masato and Yamada, Michihiro(1996) 'REACTION OF POLYMERIZATION-RESISTANT 1,2-DITHIOLANES WITH SULFOXONIUM YLIDES. NEW METHOD FOR 1,3-DITHIANE SYNTHESIS', Phosphorus, Sulfur, and Silicon and the Related Elements, 116: 1, 253 — 259
To link to this Article: DOI: 10.1080/10426509608040486
URL: http://dx.doi.org/10.1080/10426509608040486

Phosphorus, Sulfur, and Silicon, 1996, Vol. 116, pp. 253–259
Reprints available directly from the publisher
Photocopying permitted by license only

REACTION OF POLYMERIZATION-RESISTANT 1,2-DITHIOLANES WITH SULFOXONIUM YLIDES. NEW METHOD FOR 1,3-DITHIANE SYNTHESIS

MASATO TAZAKI* and MICHIHIRO YAMADA

Department of Industrial Chemistry, Kumamoto Institute of Technology, Ikeda 4-22-1, Kumamoto 860, Japan

(Received 28 March 1996; In final form 4 June 1996)

Reaction of polymerization-resistant 1,2-dithiolanes **1** with dimethylsulfoxonium methylide **3** was developed for the synthesis of the corresponding 1,3-dithianes **4** by a high-dilution method. Oxygen did not prevent the formation of **4**, but facilitated the product separation leading to a good yield and the excellent purity of **4**.

Keywords: 1,2-Dithiolanes; nucleophilic S–S bond cleavage; sulfoxonium ylide; methylene insertion of cyclic disulfides; 1,3-dithiane formation

INTRODUCTION

Reaction of polymerization-resistant 1,2-dithiolanes **1** with carbon nucleophiles has been studied in elucidating the intrinsic reactivity of the enzyme-bound lipoic acids[1] and developing selective syntheses of monosubstituted 1,3-propanedithiol derivatives.[2] It was previously found that their reaction with sulfonium ylide, a carbanion stabilized by the neighboring sulfonium group, is different from that of the linear disulfides,[3] and resulted in the formation of 1,3-dithianes via a methylene-insertion type reaction.[4] Only the sulfonium benzylides are, however, useful for the synthesis of 2-aryl-1,3-dithianes, since the yield of 2-alkyl-1,3-dithianes is insufficient in the case of the sulfonium alkylides. In the linear disulfide system, the use of sulfoxonium ylide in place of

*Corresponding author.

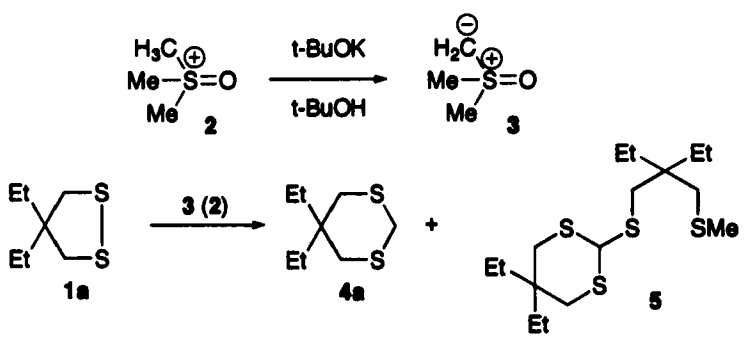
sulfonium ylide improved the yield of the methylene insertion products.[3] The reaction of the 1,2-dithiolanes **1** with dimethylsulfoxonium methylide **3** was studied in order to improve the yield of 1,3-dithianes **4** and develop the selective synthesis of 1,3-dithianes **4**.

Results and Discussion

For comparison with the sulfonium ylide system,[4] we started to react the polymerization-resistant 1,2-dithiolane **1a** with dimethylsulfoxonium methylide **3** which was generated *in situ* by a deprotonation of trimethylsulfoxonium iodide **2** with *t*-BuOK in a protic solvent *t*-BuOH (see Scheme 1). The product **4** was separated by simple Kugelrohr distillation after the usual workup, and in some cases the product distribution was monitored by glc before distillation. The results were rather disappointing (Table I, entries 1–6), and similar to that of the sulfonium ylide;[4] 5,5-diethyl-1,3-dithiane **4a**[4] and higher 1,3-dithiane **5**[4] were produced. The yield of the desired **4a** did not exceed 50%, even when the reaction was optimized by changing the molar ratio of **1a**:**2**:*t*-BuOK (entries 1–6).

The rather complicated nature of the reaction mechanism may be simplified as shown in Scheme 2; the first step of the reaction may be a bimolecular reaction between **1a** and **3**, and the second step for the formation of **4a** may be an unimolecular degradation, competing with bimolecular step(s) for the formation of **5**. Under these conditions, the formation of **4a** would be improved by a high dilution method which favors the unimolecular process.

The high dilution method was carried out conveniently by adding a solution (5 ml) containing **1a** and **2** dropwise to a heated solution (5 ml) of *t*-BuOK over a period of 1 h (Table I, entries 7–9). The yield and purity of the isolated **4a**



SCHEME 1

TABLE I Optimization of the Reaction of **1a** and **2**[a)]

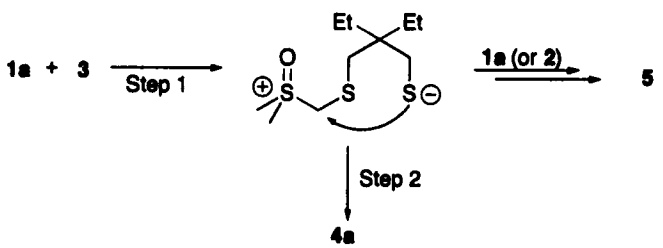
entry	***1a*** : ***2*** : *t-BuOK*	*method*[b]	*time/h*[c]	*composition/%*[d,e]			*isolation of* ***4a***[f]	
				1a	***4a***	***5***	*yield/%*	*purity/%*[e]
1	1:1.2:1.2	A	1	–	–	–	80	41.7
2	1:2.1:2.1	A	1	–	–	–	24	53.3
3	1:2.1:2.1	A	4	–	–	–	26	91.6
4	1:3.0:3.0	A	4	5	28	64	27	77.6
5	1:1.1:3.0	A	4	25	31	39	–	–
6	1:2.0:6.0	A	4	19	45	30	–	–
7	1:1.5:6.0	B, C	0.5	5	81	11	50	89.7
8	1:1.5:6.0	B, C	2	4	61	6	62	92.6
9	1:1.5:6.0	B, D	2	1	85	6	63	97.4

[a]Reaction described in Scheme 1. Substrate **1a** 1.0 mmol. Solvent t-BuOH-THF (4:1).
[b]Method A: **1a**, **2**, and t-BuOK were mixed in the solvent 5 ml under Ar at room temp.
B: A solution of **1a** and **2** in the solvent 5 ml was added to the solution of t-BuOK (5 ml).
C: Reaction under argon at 40°C. D: Reaction under dry air at reflux temp.
[c]Reaction time after the complete addition. d) composition before distillation.
[e]Estimated by glc. f) Separation of **4a** by Kugelrohr distillation.

were effectively improved. Interestingly, oxygen (dry air) did not prevent the formation of **4a** (entry 9), but apparently suppressed the formation of by-products and facilitated the separation of **4a**.

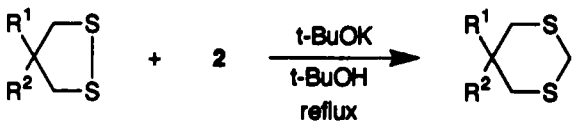
The separation of **4a** was further improved by column chromatography before the Kugelrohr distillation (Table II). Under the optimized conditions, various 1,2-dithiolanes **1a–d** were reacted to produce the corresponding 1,3-dithianes **4a–d**, and the results are summarized in Table II. Fairly good yields and excellent purities of **4a–d** resulted.

In this study we have developed a new method for the synthesis of 1,3-dithianes which are useful as a masked formyl anion equivalent for C-C bond forming reactions.[5] The nature of this reaction is closely related to that of the sulfonium ylide reported earlier;[4] the reaction proceeds under basic conditions



SCHEME 2

TABLE II Synthesis of 1,3-dithianes by high dilution method



1 R^1, R^2	*4*	*Yield/%*	*Purity/%*
a Et, Et	**a**	83	100
b $(CH_2)_5$	**b**	85	99
c Me, Pr	**c**	78	99
d Et, Me	**d**	70	98
e $(CH_2)_4$	**e**	74	99

quite different from the ordinary 1,3-dithiane synthesis.[5] The use of a sulfoxonium ylide in place of a sulfonium ylide is successful in the preparation of 1,3-dithianes containing no substituents on the C-2 position.

EXPERIMENTAL

Melting points were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL EX-90 instrument operating at 89.5 and 22.5 MHz, respectively. DEPT methods using 90 and 135 degree pulses were employed to determine the number of proton(s) attached to the carbon. The resolution in these measurements is 0.0025 ppm (0.22 Hz) for ^{1}H and 0.015 ppm for ^{13}C NMR. IR spectra were obtained by using a JASCO FT/IR-7000 spectrometer.

Dithiolanes **1** were prepared from the corresponding 1,3-propanediols according to the reported method.[6]

Reaction of 4,4-Diethyl-1,2-dithiolane 1a with Dimethylsulfoxonium Methylide 3

A solution of potassium *tert*-butoxide 673.6 mg (6.00 mmol) in a mixture of *tert*-butyl alcohol (4 ml) and benzene (1 ml) was refluxed under dry air. A solution containing trimethylsulfoxonium iodide **2** 330.5 mg (1.50 mmol) and 4,4-diethyl-1,2-dithiolane **1a** 162.1 mg (1.00 mmol) dissolved in a mixture of *tert*-butyl alcohol (4 ml) and benzene (1 ml) was added to the refluxing solution from a dropping funnel during 1 h. The mixture was further refluxed for 2 h, cooled, diluted with water (10 ml), and extracted with hexane (10 ml). The organic layer was washed with 1% NaOH solution (10 ml) and then with 10% NaCl solution (10 ml), and evaporated. The residue was chromatographed on a

silica gel column (Wakogel C-200) with an eluent of hexane-dichloromethane (1:1), and further purified by Kugelrohr distillation to give 5,5-Diethyl-1,3-dithiane **4a** 135.8 mg (77%) as a colorless liquid, ot (oven temp) 80–140°C/20 mmHg, purity 100% by glc. The spectral data of **4a** were identical to those of the authentic sample[4] within the experimental errors. Some chemical shift data in the NMR spectra proved to be misreported in the previous paper,[4] and are corrected as follows; ^{1}H NMR ($CDCl_3$, 89.5 MHz) δ 0.802 (6H, t, J = 7.4 Hz, $2CH_3$), 1.602 (4H, q, J = 7.4 Hz, $2CH_2$), 2.574 (4H, s, $2CH_2S$, previously reported as 2.24 ppm[4]), and 3.636 ppm (2H, s, CH_2). ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 6.92 ($2CH_3$), 27.42 ($2CH_2$), 31.24 (C, previously reported as 21.28 ppm[4]), 31.80 (CH_2), and 38.80 ppm ($2CH_2$).

Reaction of 4,4-Pentamethylene-1,2-dithiolane 1b with Dimethylsulfoxonium Methylide 3

A solution of trimethylsulfoxonium iodide **2** 330.0 mg (1.50 mmol) and 4,4-pentamethylene-1,2-dithiolane **1b** 174.6 mg (1.00 mmol) in a mixture of *tert*-butyl alcohol (4 ml) and benzene (1 ml) was added from a dropping funnel to a refluxing solution of *t*-BuOK 673.3 mg (6.00 mmol) in *tert*-butyl alcohol (4 ml) and benzene (1 ml) during 1 h. The mixture was refluxed further 2 h, diluted with water (10 ml), and extracted with hexane (10 ml). The organic layer was washed with 1% NaOH solution (10 ml) and with 10% NaCl solution (10 ml), filtered and evaporated. The residue was chromatographed on Wakogel C-200 using hexane-dichloromethane (1:1) as eluent, and purified by Kugelrohr distillation to give 2,4-dithiaspiro[5.5]undecane **4b** 160.5 mg (85%).

2,4-Dithiaspiro[5.5]undecane **4b**. Yield 160.5 mg (85%), ot 110–160°C/20 mmHg, purity 99.2% by glc. Colorless crystal, mp 48–49.5°C. Found: C, 57.31; H, 8.55%. Calcd for $C_9H_{16}S_2$: C, 57.39; H, 8.56%. ^{1}H NMR ($CDCl_3$) δ 1.450 (6H, broad s, $3CH_2$), 1.580 (4H, broad s, $2CH_2$), 2.634 (4H, s, $2CH_2S$), and 3.656 ppm (2H, s, CH_2). ^{13}C NMR ($CDCl_3$) δ 20.96 ($2CH_2$), 26.44 (CH_2), 28.72 (C), 32.16 (CH_2), 35.50 ($2CH_2$), and 40.06 ppm ($2CH_2$). IR (KBr)ν 2922 (s), 2858 (m), 1454 (m), 1294 (m), 1191 (m), 965 (m), and 716 cm^{-1} (m).

Reaction of 4-Methyl-4-propyl-1,2-dithiolane 1c with Dimethylsulfoxonium Methylide 3

A mixture of freshly distilled 4-methyl-4-propyl-1,2-dithiolane **1c** 162.3 mg (1.00 mmol, ot 90–130°C/20 mmHg), trimethylsulfoxonium iodide **2** 330.4 mg (1.50 mmol), *t*-BuOH (4 ml), and benzene (1 ml) was added dropwise over a

period of 1 h to a solution of *t*-BuOK 673.5 mg (6.0 mmol) in *t*-BuOH (5 ml) with refluxing under dry air. The mixture was refluxed further 2 h, diluted with water (10 ml), and extracted with hexane (10 ml). The organic layer was washed with 1% NaOH solution (10 ml) and with 10% NaCl solution (10 ml), filtered and evaporated. The residue was chromatographed on Wakogel C-200 using hexane-dichloromethane (1 : 1) as eluent, and purified by Kugelrohr distillation to give 5-methyl-5-propyl-1,3-dithiane **4c** 137.3 mg (78%).

4c. Yield 137.3 mg (78%), colorless liquid ot 80–165°C/20 mmHg, purity 99.2% by glc. Found: C, 54.27; H, 9.01%. Calcd for $C_8H_{16}S_2$: C, 54.49; H, 9.14%. ^{1}H NMR ($CDCl_3$) δ 0.946 (3H, m, CH_3 in Pr), 1.100 (3H, s, CH_3), 1.18–1.68 (4H, m, $2CH_2$ in Pr), 2.564 (4H, s, $2CH_2S$), and 3.636 ppm (2H, s, CH_2). ^{13}C NMR ($CDCl_3$) δ 14.80 (CH_3), 16.20 (CH_2), 24.96 (CH_3), 29.26 (C), 31.68 (CH_2), 40.76 ($2CH_2$), and 41.42 ppm (CH_2). IR (neat)ν 2960 (s), 2934 (s), 2892 (s), 1458 (m), 1377 (m), 1292 (m), 1189 (m), 1168 (m), and 716 cm^{-1} (m).

Reaction of 4-Ethyl-4-methyl-1,2-dithiolane 1d with Dimethylsulfoxonium Methylide 3

A mixture of freshly distilled 4-ethyl-4-methyl-1,2-dithiolane **1d** 149.0 mg (1.00 mmol, ot 60–120°C/20 mmHg), trimethylsulfoxonium iodide **2** 330.5 mg (1.50 mmol), *t*-BuOH (4 ml), and benzene (1 ml) was added dropwise over a period of 1 h to a solution of *t*-BuOK 673.2 mg (6.0 mmol) in *t*-BuOH (5 ml) with refluxing under dry air. The mixture was refluxed further 2 h, diluted with water (10 ml), and extracted with hexane (10 ml). The organic layer was washed with 1% NaOH solution (10 ml) and with 10% NaCl solution (10 ml), filtered and evaporated. The residue was chromatographed on Wakogel C-200 using hexane-dichloromethane (1 : 1) as eluent, and purified by Kugelrohr distillation to give 5-ethyl-5-methyl-1,3-dithiane **4d** 114.5 mg (70%).

5-Ethyl-5-methyl-1,3-dithiane **4d**, colorless liquid, ot 60–130°C/20 mmHg, yield 114.5 mg (70%), purity 98.3% by glc. Found: C, 51.58.; H, 8.61%. Calcd for $C_7H_{14}S_2$: C, 51.80; H, 8.69%. ^{1}H NMR ($CDCl_3$) δ 0.850 (3H, t, J = 7.2 Hz, CH_3 in Et), 1.082 (3H, s, CH_3), 1.636 (2H, q, *J* = 7.4 Hz, CH_2 in Et), 2.560 (4H, s, $2CH_2S$), and 3.630 ppm (2H, s, CH_2). ^{13}C NMR ($CDCl_3$) δ 7.36 (CH_3), 24.28 (CH_3), 29.22 (C), 31.42 (CH_2), 31.66 (CH_2), and 40.42 ppm ($2CH_2$). IR (neat)ν 2966 (s), 2892 (s), 1458 (m), 1427 (m), 1408 (m), 1383 (m), 1290 (m), 1189 (m), 1170 (m), 760 (m), and 716 cm^{-1} (m).

Reaction of 4,4-Tetramethylene-1,2-Dithiolane 1e with Dimethylsulfoxonium Methylide 3

A mixture of freshly distilled 4,4-tetramethylene-1,2-dithiolane **1e** 160.3 mg (1.00 mmol, ot 80–140°C/20 mmHg), trimethylsulfoxonium iodide **2** 330.7 mg (1.50 mmol), *t*-BuOH (4 ml), and benzene (1 ml) was added dropwise over a period of 1 h to a solution of *t*-BuOK 673.5 mg (6.0 mmol) in *t*-BuOH (5 ml) with refluxing under dry air. The mixture was refluxed further 2 h, diluted with water (10 ml), and extracted with hexane (10 ml). The organic layer was washed with 1% NaOH solution (10 ml) and with 10% NaCl solution (10 ml), filtered and evaporated. The residue was chromatographed on Wakogel C-200 using hexane-dichloromethane (1 : 1) as eluent, and purified by Kugelrohr distillation to give 7,9-dithiaspiro[4.5]decane **4e** 129.3 mg (74%).

7,9-Dithiaspiro[4.5]decane **4e**, colorless liquid, ot 90–145°C/20 mmHg. Yield 129.3 mg (74%), purity 98.9% by glc. Found: C, 54.88.; H, 7.99%. Calcd for $C_8H_{14}S_2$: C, 55.12; H, 8.09%. ^{1}H NMR ($CDCl_3$) δ 1.671 (8H, broad s, $4CH_2$), 2.632 (4H, broad s, $2CH_2S$), and 3.645 ppm (2H, s, CH_2). ^{13}C NMR ($CDCl_3$) δ 24.64 ($2CH_2$), 31.30 (CH_2), 38.24 ($2CH_2$), 39.50 (C), and 40.94 ppm ($2CH_2$). IR (neat)ν 2948 (s), 2890 (s), 1450 (m), 1425 (m), 1408 (m), 1280 (m), 1187 (m), 1174 (m), 758 (m), and 717 cm^{-1} (m).

References

[1] M. Tazaki, S. Nagahama and M. Takagi, *Chem. Lett.*, 1339 (1988); M. Tazaki, H. Tanabe, S. Nagahama and M. Takagi, *J. Chem. Soc., Chem. Commun.*, 291 (1994); M. Tazaki, M. Kumakura, S. Nagahama and M. Takagi, *J. Chem. Soc., Chem. Commun.*, 1763 (1995).

[2] M. Tazaki, H. Tanabe, T. Hieda, S. Nagahama, K. Inoue and M. Takagi, *Phosphorus Sulfur Silicon*, **88**, 189 (1994); M. Tazaki, S. Okai, T. Hieda, S. Nagahama and M. Takagi, *Phosphorus Sulfur Silicon*, **112**, 101 (1996).

[3] L. Field and H. -K. Chu, *J. Org. Chem.*, **42**, 1768 (1977).

[4] M. Tazaki, M. Kumakura, S. Nagahama and M. Takagi, *Phosphorus Sulfur Silicon*, **106**, 227 (1995).

[5] D. J. Ager, "*Umpoled Synthons*," ed. by T. A. Hase, Ch. 2, Wiley-Interscience, New York (1987).

[6] G. Bergson and A. Biezais, *Arkiv. Kemi*, **22**, 475 (1964).