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Formation of Bis(methylthio)(methylsulfinyl)methane in the Reaction of Methyl (Methylthio)methyl Sulfoxide with Sodium Hydride

Katsuyuki Ogura, Nobuko Katoh, and Gen-ichi Tsuchihashi
Sagami Chemical Research Center, Nishi-Ohnuma Sagamihara, Kanagawa 229

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Treatment of methyl (methylthio)methyl sulfoxide (**1**) with sodium hydride gave bis(methylthio)(methylsulfinyl)methane (**3**) which might be formed by abnormal attack of the carbanion (**2**) of **1** on the sulfide linkage of **1**. The additon of butyl iodide to this system completely suppressed the formation of **3**, showing that **2** reacts faster with butyl iodide than with **1**. The mechanism to account for these phenomena is discussed.

Recently, new synthetic methods using methyl (methylthio)methyl sulfoxide (**1**) have been developed.[1–7] This compound can be converted into the carbanion (**2**) by the action of sodium hydride, potassium hydride, or butyllithium. In tetrahydrofuran (THF), treatment of **1** with either potassium hydride[6,9] or butyllithium[6,7,9] generates **2** instantaneously at from −70 °C to an ambient temperature. On the other hand, when sodium hydride is employed as a base, warming is necessary to form **2**.[2,3,8,10] Thus, alkylation of **1** with an alkyl halide and sodium hydride can be achieved by agitation of these compounds together in THF at an elevated temperature.[2,3,8] During the course of our investigation on the solvent-effect for the formation of **2** using sodium hydride, we have found the following interesting reaction of **1** with **2** to form bis(methylthio)(methylsulfinyl)methane (**3**) and dimethyl sulfoxide.

A solution containing **1** (34.6 mmol) and sodium hydride (22.5 mmol) in hexamethylphosphoric triamide (HMPT; 10 ml) was stirred under cooling with ice-water for 2 h and at room temperature for 36.5 h. A usual work-up gave **3** as colorless crystals, mp 69—70 °C, in 45% yield. The structure of this product was confirmed by its IR and NMR spectra, the elemental analysis, and the independent synthesis achieved by the oxidation of tris(methylthio)methane with hydrogen peroxide and a catalytic amount of sodium tungstate. Even when one equivalent of sodium hydride was employed, the similar result was obtained. The formation of **3** was also observed in THF although the reaction went more slowly than in HMPT. Furthermore, it should be noted that the addition of butyl iodide to the solution containing **1** and sodium hydride in HMPT completely suppressed the formation of **3** and a butylated product, 1-(methylsulfinyl)-1-(methylthio)pentane (**4**) was produced instead.

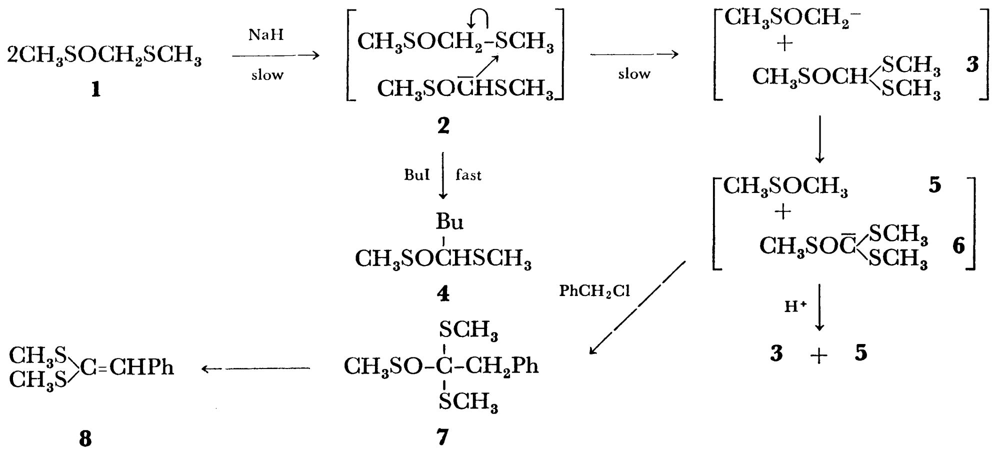
These facts may be reasonably explained by the mechanism depicted in Scheme 1. During the reaction of **1** with sodium hydride, the carbanion (**2**) coexists with the unreacted **1** because of the slow reaction of **1** with sodium hydride. Then, **2** attacks on the sulfide linkage of **1** as shown in Scheme 1, forming the carbanion of dimethyl sulfoxide (**5**) and **3** which are further converted into **5**[11] and the carbanion (**6**) of **3**, respectively, by a proton transfer. When butyl iodide is added to this system, the formed carbanion (**2**) reacts with the iodide faster than with **1** to afford the butylated product (**4**).

Existence of **6** at the final stage of the reaction might be supported by the fact that the addition of benzyl chloride, followed by stirring of the solution at from room temperature to 40 °C gave β,β-bis(methylthio)styrene (**8**) which was very likely formed by dehydrosulfenylation of the benzylated product (**7**) of the carbanion (**6**).

Since the alkylation of **1**, followed by the hydrolysis of the thioacetal *S*-oxide group provides a convenient synthetic route to aldehydes, we would like to emphasize that the necessary conditions for the alkylation of **1** by an alkyl halide–sodium hydride system is to stir a solution containing these reagents together at a temperature of *ca.* 50 °C.

Experimental

Formation of Bis(methylthio)(methylsulfinyl)methane (3) from Methyl (Methylthio)methyl Sulfoxide (1). To a solution



Scheme 1.

containing **1** (4.290 g, 34.6 mmol) in HMPT (10 ml), was added sodium hydride (65% oil-dispersion; 830 mg, 22.5 mmol), and the mixture was stirred under cooling with ice-water for 2 h and at room temperature for 36.5 h. After the addition of dichloromethane (150 ml) and washing with water (100 ml), the organic layer was dried over anhydrous sodium sulfate and evaporated *in vacuo*. The residue was separated by twofold column-chromatography on silica gel (eluted with dichloromethane) to afford **3** (1.337 g, 7.86 mmol; 45%) as colorless crystals. An analytical sample was obtained by recrystallization from diethyl ether–hexane: Mp 69—70 °C; IR (KBr) 1032 cm^{-1}; NMR (CDCl$_3$): δ=2.36 (6H, s), 2.72 (3H, s), and 4.53 (1H, s). Found: C, 28.11: H, 5.90%. Calcd for $C_4H_{10}OS_3$: C, 28.21; H, 5.91%.

This compound is thermally unstable even at room temperature and decomposes completely within 1 h at 50 °C.

*Oxidation of Tris(methylthio)methane into **3**.* To a solution of tris(methylthio)methane(1.505 g, 9.77 mmol) in methanol (10 ml), were added sodium tungstate dihydrate (10 mg) and 30% aqueous solution (1.1 ml, 9.7 mmol) of hydrogen peroxide under cooling with ice–water. Then, the mixture was stirred under cooling with ice–water for 1 h, and water (25 ml) was added. After the extraction with four 30 ml-portions of dichloromethane, the organic layer was dried over anhydrous sodium sulfate and evaporated *in vacuo*. The residue was column-chromatographed on silica gel (eluted with dichloromethane–ethyl acetate) to yield 927 mg (56%) of colorless crystals which were identified with **3** by the comparison of their IR and NMR spectra with those of the product obtained by the reaction of **1** with sodium hydride.

*Reaction of **1** with Sodium Hydride in the Presence of Butyl Iodide.* To a solution of **1** (1.385 g, 11.69 mmol) in HMPT (2 ml) were added sodium hydride (65% oil-dispersion; 538 mg, 14.6 mmol) and butyl iodide (2.888 g, 15.70 mmol). The mixture was stirred under cooling with ice–water for 2 h, at room temperature for 25 h, and at 45 °C for 24 h. After the addition of dichloromethane (30 ml), the deposited solid was filtered off and the filtrate was evaporated *in vacuo*. The residue was separated by column-chromatography on silica gel (eluted with dichloromethane and ethyl acetate) to afford 1.327 g (7.37 mmol: 66%) of **4** which was identified with the product previously reported[8] by the comparison of their NMR spectra.

*Detection of DMSO (**5**) in the Reaction of **2** with **1**.* To a suspension of potassium hydride (24% oil-dispersion; 2.166 g, 13.0 mmol) in THF (10 ml) was added **1** (3.026 g, 24.44 mmol) under cooling with ice–water for 30 min, at room temperature for 16.5 h, and at 40 °C for 9 h. After the addition of dichloromethane (100 ml) and water (1 ml), stirring at room temperature for 5 min, and the addition of anhydrous sodium sulfate, the insoluble matter was filtered off and the filtrate was evaporated *in vacuo*. The residue was separated by column-chromatography on Florisil (eluted with dichloromethane, ethyl acetate, and methanol) to give 203 mg (10%) of **3** and 1.275 g of a colorless oil which was shown by an NMR analysis to consist of **1** (959 mg) and **5** (316 mg; 33%).

*Reaction of **6** with Benzyl Chloride.* A mixture containing **1** (5.159 g, 41.60 mmol) and sodium hydride (65% oil-dispersion; 860 mg, 23.3 mmol) in HMPT (15 ml) was stirred under cooling with ice–water and at room temperature for 49.5 h. After the addition of benzyl chloride (2.818 g, 22.28 mmol), the mixture was further stirred at room temperature for 1 week and at 40 °C for 4 h. Then, water (50 ml) and dichloromethane (100 ml) were added and the solution was shaken. After the organic layer was separated, the aqueous layer was extracted with two 30 ml-portions of dichloromethane. The organic layers were combined, dried over anhydrous sodium sulfate, and evaporated *in vacuo*. The residue was column-chromatographed on silica gel (eluted with hexane–benzene) to give a pale yellow oil which was shown by an NMR analysis(using piperonal as an internal standard) to contain 1.149 g (28%) of β,β-bis(methylthio) styrene (**8**). A pure sample of **8** could be obtained by distillation under reduced pressure and it was identified by comparison of its IR and NMR spectra with those of an authentic sample which was given by reduction of β-(methylsulfinyl)-β-(methylthio)styrene[12] as described in the following.

Reduction of β-(Methylsulfinyl)-β-(methylthio)styrene with Titanium Trichloride. To a solution containing β-(methylsulfinyl)-β-(methylthio)styrene[12] (7.106 g) in 30 ml of dichloromethane and 60 ml of hexane, was added 20% aqueous solution (30 ml) of titanium trichloride and the resulting mixture was stirred at room temperature for 1 h. After the addition of benzene (100 ml), the organic layer was separated, washed with water, dried over anhydrous potassium carbonate, and evaporated *in vacuo*. The residue was column-chromatographed on Florisil to give 1.595 g of a pale yellow oil, whose structure was assigned as **8** by its physical data and an elemental analysis: Bp 104—105 °C/0.3 Torr (lit,[13] bp 94—95 °C/0.25 Torr); NMR (CDCl$_3$): δ=2.27 (3H, s), 2.32 (3H, s), 6.71 (1H, s), and 7.10—7.60 (5H, m); MS(70 eV): *m/e* (rel. intensity) 196 (66), 149 (31), and 134 (100). Found: C, 61.02; H, 6.10; S, 32.56%. Calcd for $C_{10}H_{12}S_2$: C, 61.17; H, 6.16; S, 32.66%.

References

1) K. Ogura, S. Furukawa, and G. Tsuchihashi, *Bull. Chem. Soc. Jpn.*, **48**, 2219 (1975) and the references cited therein.

2) G. Schill and P. R. Jones, *Synthesis*, **1974**, 117.

3) G. R. Newkome, J. M. Robinson, and J. D. Sauer, *J. Chem. Soc. Chem. Commun.*, **1974**, 410.

4) K. Ogura, M. Yamashita, and G. Tsuchihashi, *Synthesis*, **1975**, 385.

5) K. Ogura, I. Yoshimura, N. Katoh, and G. Tsuchihashi, *Chem. Lett.*, **1975**, 803.

6) K. Ogura, M. Yamashita, S. Furukawa, M. Suzuki and G. Tsuchihashi, *Tetrahedron Lett.*, **1975**, 2767.

7) K. Ogura, M. Yamashita, and G. Tsuchihashi, *Tetrahedron Lett.*, **1976**, 759.

8) K. Ogura and G. Tsuchihashi, *Tetrahedron Lett.*, **1971**, 3151.

9) K. Ogura and G. Tsuchihashi, *Tetrahedron Lett.*, **1972**, 2681.

10) K. Ogura and G. Tsuchihashi, *J. Am. Chem. Soc.*, **96**, 1960 (1974).

11) Formation of **5** was confirmed by the experiment using **1** and potassium hydride (0.5 equivalent to **1**) in THF (see Experimental section).

12) K. Ogura and G. Tsuchihashi, *Tetrahedron Lett.*, **1972**, 1383.

13) G. A. Russell and L. A. Ochrymowycz, *J. Org. Chem.*, **35**, 764 (1970).