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# Reaction of Methyl (Phenylhydrazonomethylthio)acetate with Sodium Methoxide

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The reaction of methyl (phenylhydrazonomethylthio)acetate **1** with sodium methoxide in methanol at 30 °C was found to give initially 5-oxo-4-phenyl-5,6-dihydro-1,3,4-thiadiazine **2**, which then rearranged to 2-(phenylimino)-4-oxothiazolidine **3** in quantitative yield *via* cleavage of the nitrogen–nitrogen bond.

**Keywords**——methyl (phenylhydrazonomethylthio)acetate; 5-oxo-4-phenyl-5,6-dihydro-1,3,4-thiadiazine; 2-(phenylimino)-4-oxothiazolidine; ring contraction; nitrogen–nitrogen bond cleavage

Sato and Ohta described the synthesis of 5-oxo-4-phenyl-5,6-dihydro-1,3,4-thiadiazine **2** (mp 181 °C) by the reaction of methyl (phenylhydrazonomethylthio)acetate **1** with sodium methoxide in methanol.[1] However, our recent work has revealed that the compound obtained by Sato *et al.* is not **2** but 2-(phenylimino)-4-oxothiazolidine **3** and that **2** can be alternatively

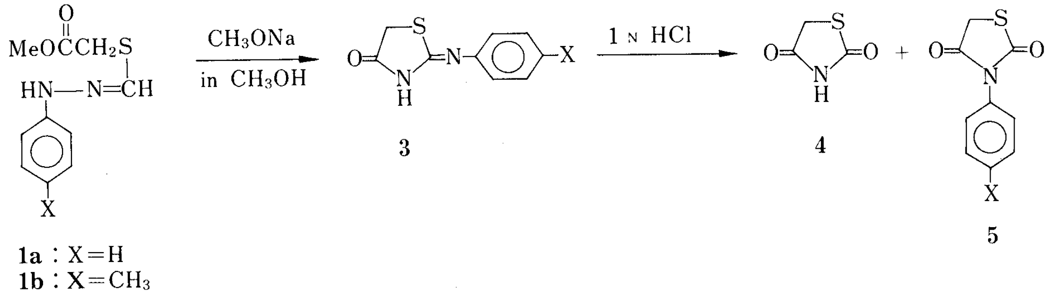

Chart 1

TABLE I. Results for **3**, **4** and **5**

| Compound | mp (°C) | Formula | Elemental analysis (%) Calcd (Found) | | | IR spectra (cm$^{-1}$)[a] | | $^1$H-NMR spectra (ppm)[b] | |
|---|---|---|---|---|---|---|---|---|---|
| | | | C | H | N | C=O | C=N | Ph | CH$_2$ |
| **3a** | 180—182 | | (56.20 | 4.38 | 14.46) | 1680 | 1640 | 7.23 (s) | 3.80 (s) |
| | (178)[4] | $C_9H_8N_2OS$ | 56.23 | 4.19 | 14.58 | | | | |
| **3b** | 190—191 | | (58.15 | 4.95 | 13.49) | 1678 | 1637 | 7.06 (s) | 3.20 (s) |
| | | $C_{10}H_{10}N_2OS$ | 58.23 | 4.89 | 13.58 | | | | |
| **4** | 146—147 | | (30.83 | 2.64 | 11.81) | 1690 | — | — | 3.91 (s) |
| | (147)[5] | $C_3H_3NO_2S$ | 30.76 | 2.58 | 11.96 | | | | |
| **5** | 124—125 | | (55.69 | 3.62 | 7.42) | 1700 | — | 7.28 (s) | 4.04 (s) |
| | (125—126)[6] | $C_9H_7NO_2S$ | 55.94 | 3.65 | 7.25 | | | | |

*a*) KBr disk. *b*) In CD$_3$OD. (s): singlet.

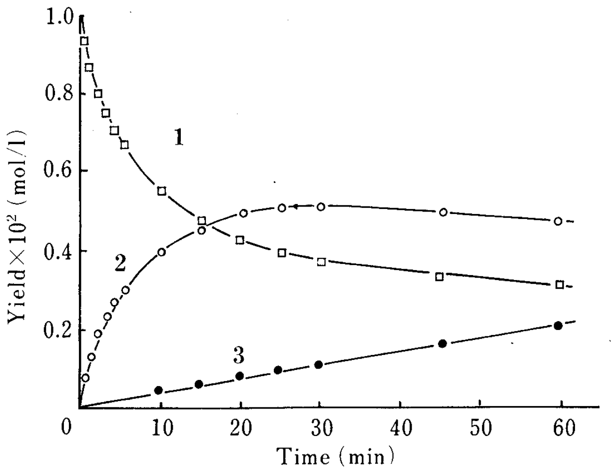

Fig. 1. Time–Yield Curves for the Reaction of **1b** with $CH_3ONa$

[**1b**] = $1\times10^{-2}$ mol/l, [$CH_3ONa$] = $1\times10^{-2}$ mol/l at 35 °C in methanol.

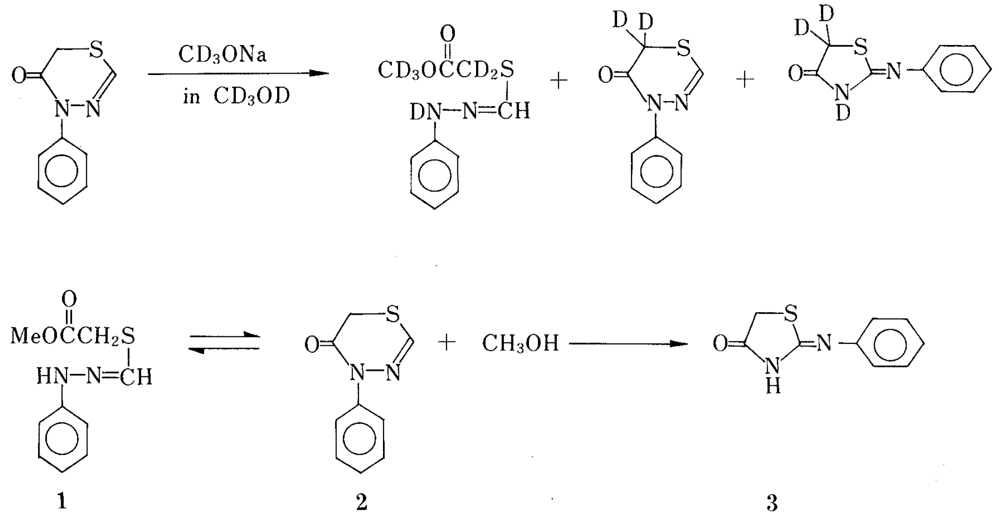

Chart 2

prepared by the reaction of **1** in the presence of triethylamine in methanol or by the reaction of (phenylhydrazonomethylthio)acetic acid with *N*,*N*′-dicyclohexylcarbodiimide in chloroform.[2,3] The present paper deals with the experimental findings that **3** may be obtained from **2** formed by a reversible reaction of **1**.

Reaction of methyl (phenylhydrazonomethylthio)acetates **1a** and **1b** with sodium methoxide in methanol at 30 °C gave **3a** (mp 180—182 °C) and **3b** (mp 190—191 °C) in quantitative yields, respectively. The melting point and proton nuclear magnetic resonance ($^1$H-NMR) and infrared (IR) spectroscopic data of **3a** and **3b** thus obtained are in complete agreement with those of authentic samples[4] (Table I). Compound **3a** was heated in an 1 N HCl aqueous solution to give **4** and **5** in good yield. These results are summarized in Chart 1 and Table I.

The structural identification of **4** and **5** by $^1$H-NMR and IR spectral analysis and also by comparison with authentic samples[5,6] revealed that **4** is 2,4-thiazolidinedione and **5** is 3-phenyl-2,4-thiazolidinedione. The progress of the reaction of **1b** at low concentration ($1\times10^{-2}$ mol/l) was monitored by high performance liquid chromatography (HPLC) on a reversed-phase column with methanol as a solvent (Fig. 1). Rapid disappearance of **1b**, with simultaneous formation of **2b**, was initially detected and then the amount of **3b** gradually increased. The total amount of **1b**, **2b** and **3b** was always constant. On the other hand, the reaction of **2a** with sodium $d_3$-methoxide in $d_4$-methanol, when stopped in the course of the reaction process, gave **1a**, **2a** and **3a** having deuterated methylene groups, as determined by $^1$H-NMR spectroscopy and HPLC. These observations suggest that the reaction of **1** with methoxide proceeds through two steps; initial formation of **2** by a ring closure reaction through a reversible reaction, as shown in Chart 2, and a secondary conversion of **2** to **3** by ring contraction (Chart 2).

## Experimental

Melting points were obtained on a Yanaco hot-stage apparatus and are uncorrected. The $^1$H-NMR spectra were recorded on a JEOL FX-200 NMR spectrometer at 200 MHz with tetramethylsilane as an internal standard. IR spectra were run on a JASCO IRA-1 spectrometer with the samples in potassium bromide pellets. HPLC was run on a Yanaco L-2000 unit using a pre-packed column of Yanaco GEL-5510 (4 mm × 250 mm) with methanol as a solvent. Thin-layer chromatography and column chromatography were done on precoated Kieselgel 60-F254 sheets and Kieselgel 60 (240—400 mesh), respectively.

**Preparation of Materials**——Methyl (Phenylhydrazonomethylthio)acetate **1** and 5-Oxo-4-phenyl-5,6-dihydro-1,3,4-thiadiazine **2**: These compounds were prepared as described in the preceeding papers.[2,3]

Product **1a**: mp 63—64 °C. Product **1b**: mp 72—73 °C.

Product **2a**: mp 77—78 °C. Product **2b**: mp 95—97 °C.

**Reaction of 1 with Sodium Methoxide**——A mixture of **1** (1 mmol) and sodium methoxide (1 mmol) in methanol (10 ml) was stirred for 1 h at 30 °C. The reaction mixture was neutralized with concentrated hydrochloric acid. The precipitate was filtered off to give almost pure **3** in quantitative yield and this product was recrystallized from a methanol–water mixture. The properties are summarized in Table I.

**Treatment of 3 with Hydrochloric Acid**——A mixture of **3** (1 mmol) in 1 N HCl (5 ml) was refluxed for 1 h and cooled in an ice bath. The white powder precipitate was filtered off and recrystallized from water to give **4** in 21% yield. The filtrate was evaporated *in vacuo* and the residue was recrystallized from benzene to give **5** in 65% yield. The properties are summarized in Table I.

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