November, 1983] © *1983 The Chemical Society of Japan* NOTES *Bull. Chem. Soc. Jpn.*, ***56***, *3543—3544 (1983)* 3543

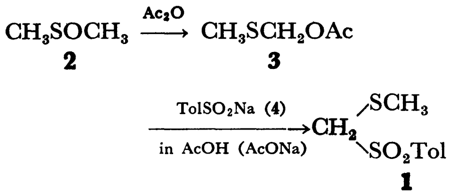
Convenient Preparation of Methylthiomethyl *p*-Tolyl Sulfone Starting from Dimethyl Sulfoxide

Katsuyuki Ogura,* Nobuhiro Yahata, Jun-ichi Watanabe,
Kazumasa Takahashi, and Hirotada Iida
Department of Synthetic Chemistry, Faculty of Engineering, Chiba University,
Yayoicho 1-33, Chiba 260

(Received June 4, 1983)

Synopsis. An efficient method for preparing methylthiomethyl *p*-tolyl sulfone was accomplished by the Pummerer reaction of dimethyl sulfoxide with acetic anhydride followed by treatment of the resulting acetoxymethyl methyl sulfide with sodium *p*-toluenesulfinate in the presence of sodium acetate in acetic acid.

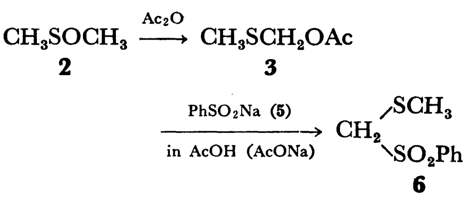
In a previous paper,[1] methylthiomethyl *p*-tolyl sulfone (**1**) was shown to be one of the most useful reagents for preparation of *S*-methyl α-oxo thiocarboxylates, carboxylic esters, five- and six-membered cycloalkanones, and α-methoxy-α-arylacetic esters.[2] With regard to formation of **1**, there has been only one report which describes the reaction of (*p*-tolylsulfonyl)acetone with *S*-methyl *p*-toluenethiosulfonate in the presence of sodium carbonate followed by hydrolysis to give **1**.[3] However, this does not seem to be suitable as a preparative method of **1** because these starting materials are not easily available. Hence, our effort was devoted to exploiting a convenient method for its synthesis; we have found an efficient route from inexpensive dimethyl sulfoxide (**2**) to **1** *via* acetoxymethyl methyl sulfide (**3**) in a "one-pot" fashion, as outlined in the following scheme.



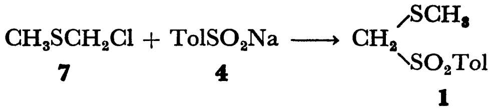
$$\underset{\mathbf{2}}{CH_3SOCH_3} \xrightarrow{Ac_2O} \underset{\mathbf{3}}{CH_3SCH_2OAc} \xrightarrow[\text{in AcOH (AcONa)}]{\text{TolSO}_2\text{Na } (\mathbf{4})} \underset{\mathbf{1}}{CH_2\genfrac{}{}{0pt}{}{\diagup SCH_3}{\diagdown SO_2Tol}}$$

First, the substitution of acetoxymethyl methyl sulfide (**3**)[4] with *p*-toluenesulfinate anion was investigated. Heating **3** together with sodium *p*-toluenesulfinate (**4**) in DMF at 80—90 °C afforded only a trace of **1**. Efforts were made to achieve a higher yield of **1** by variation of reaction conditions (solvent, temperature, time). Acetic acid was found to be the most suitable solvent. In acetic acid, the substitution reaction occurred at 100 °C, and **1** was produced in 65% yield after heating for 48 h. It may be reasonable to assume that acetic acid not only serves as an appropriate solvent for **4**, but enhances the capability of the acetoxyl group as a leaving group by protonation. Since **3** was obtained by the Pummerer reaction of dimethyl sulfoxide (**2**) with acetic anhydride where acetic acid is the only by-product, the employment of acetic acid as a solvent in the above substitution allows the synthesis of **1** from **2** to perform in one flask without isolation of the intermediate **3**. Thus, a mixture of **2** and acetic anhydride (1.3 mol-equiv. to **2**) was heated at 80 °C for 24 h, and, after addition of acetic acid and sodium *p*-toluenesulfinate (1.5 mol-equiv. to **2**), the resulting mixture was further heated at 100 °C for 26 h to give **1** in 57% yield. It was also found that the presence of sodium acetate (1 mol-equiv. to **2**) in the substitution step (**3**→**1**) increased the yield of **1** to 71%. Sodium acetate is thought to prevent production of *p*-toluenesulfinic acid, which affords *S*-*p*-tolyl *p*-toluenethiosulfonate and di-*p*-tolyl disulfide at an elevated temperature.

It should be noted that a combination of acetic anhydride, acetic acid, and sodium *p*-toluenesulfinate was crucial to the above reaction. As mentioned above, DMF is not suitable as a solvent. When propionic anhydride and propionic acid were employed, the yield of **1** was 15%. The use of sodium benzenesulfinate (**5**) in place of **4** gave methylthiomethyl phenyl sulfone (**6**), but the yield was lower (25—38% overall yield from **2**) in the presence or absence of sodium acetate. Furthermore, the reaction of chloromethyl methyl sulfide (**7**) with **4** in THF, DMF, or diglyme met with no success. In spite of many efforts, the maximum yield (22%) of **1** was attained when the reaction was carried out by stirring **4** and **7** in DMF at room temperature for 44 h (see also Experimental section).



$$\underset{\mathbf{2}}{CH_3SOCH_3} \xrightarrow{Ac_2O} \underset{\mathbf{3}}{CH_3SCH_2OAc} \xrightarrow[\text{in AcOH (AcONa)}]{\text{PhSO}_2\text{Na } (\mathbf{5})} \underset{\mathbf{6}}{CH_2\genfrac{}{}{0pt}{}{\diagup SCH_3}{\diagdown SO_2Ph}}$$



$$\underset{\mathbf{7}}{CH_3SCH_2Cl} + \underset{\mathbf{4}}{TolSO_2Na} \longrightarrow \underset{\mathbf{1}}{CH_2\genfrac{}{}{0pt}{}{\diagup SCH_3}{\diagdown SO_2Tol}}$$

Thus we have found that **1** can be conveniently prepared from inexpensive dimethyl sulfoxide by successive treatment with acetic anhydride and with commercially available sodium *p*-toluenesulfinate in one flask.

Experimental

Melting points were determined on a hot-stage microscope (Yanagimoto) and were uncorrected. ^{1}H NMR spectra were obtained on a Hitachi R-600 spectrometer. Infrared spectra were determined with a JASCO A-200 spectrometer.

One-pot Preparation of Methylthiomethyl p-*Tolyl Sulfone (1) from Dimethyl Sulfoxide (2)*: A mixture of **2** (9.25 g: 0.118 mol) and freshly distilled acetic anhydride (15.60 g: 0.153 mol) was heated at 80 °C for 24 h and then cooled to ambient temperature. Acetic acid (90 ml), sodium acetate (9.70 g: 0.118 mol), and sodium *p*-toluenesulfinate[5] (31.60 g: 0.178 mol) were successively added to the mixture, and the resulting mixture was again heated at 100 °C for 26 h. After addition of brine (150 ml), the mixture was extracted with five 70-ml portions of dichloromethane. The extracts were combined, dried over anhydrous sodium sulfate, and evaporated under reduced pressure to give 27.20 g of pale yellow crystals containing a small amount of an oil. Recrystallization of these crystals from 95% ethanol afforded 13.31 g of **1** as colorless needles. The mother liquor was evaporated and subjected to a column chromatography on silica gel using hexane and benzene as eluents to give 4.88 g of **1** as colorless crystals. The total yield of **1** was 71%: mp 82—83 °C (lit,[3] 80 °C); ^{1}H NMR ($CDCl_3$) δ=2.29 (3H, s), 2.46 (3H, s), 3.93 (2H, s), 7.37 (2H, d, J=8 Hz), and 7.87 (2H, d, J=8 Hz); IR (KBr) 1295, 1160, 1117, 1018, 740, 542, and 507 cm^{-1}.

Calcd for $C_9H_{12}O_2S_2$: C, 49.98; H, 5.59%. Found: C, 50.09; H, 5.56%.

*Preparation of Methylthiomethyl Phenyl Sulfone (**6**)*: A mixture of dimethyl sulfoxide (1.04 g: 13.3 mmol) and acetic anhydride (1.76 g: 17.3 mmol) was heated at 80 °C for 24 h. After the mixture was cooled to ambient temperature, acetic acid (10 ml), sodium acetate (1.09 g: 13.3 mmol), and sodium benzenesulfinate (**5**) (3.27 g: 19.9 mmol) were added and the resulting mixture was heated at 100 °C for 26 h. The usual workup [addition of water and extraction with dichloromethane] and column chromatography on silica gel (eluted with hexane and benzene) gave 1.01 g (38% yield) of methylthiomethyl phenyl sulfone (**6**) as colorless crystals: mp 86.5—87.5 °C (from 95% ethanol); ^{1}H NMR ($CDCl_3$): δ=2.32 (3H, s), 3.96 (2H, s), and 7.48—8.09 (5H, m); IR (KBr) 1292, 1160, 1116, 1080, 741, 544, and 520 cm^{-1}.

Calcd for $C_8H_{10}O_2S_2$: C, 47.50; H, 4.98%. Found: C, 47.62; H, 4.96%.

*Conversion of Dimethyl Sulfoxide (**2**) to **1** Using Propionic Anhydride, Propionic Acid, and **4***: A mixture of **2** (1.27 g: (16.3 mmol) and propionic anhydride (2.84 g: 21.8 mmol) was heated at 80 °C for 24 h. After being cooled to room temperature, propionic acid (20 ml) and **4** (4.35 g: 24.4 mmol) were added and the resulting mixture was heated at 100 °C for 48 h. Water (40 ml) was added and the reaction mixture was extracted with five 40-ml portions of dichloromethane. The extracts were combined, washed with water, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. Column chromatography on silica gel using hexane and benzene as eluents afforded 518 mg (15% yield) of **1**.

*Reaction of Chloromethyl Methyl Sulfide (**7**) with Sodium* p-*Toluenesulfinate (**4**)*: A mixture containing 7 (5.65 g: 58.6 mmol) and **4** (15.72 g: 88.3 mmol) in DMF (60 ml) was stirred at room temperature for 44 h. After addition of water (100 ml), the mixture was extracted with four 40-ml portions of dichloromethane. The extracts were combined, washed with water, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel using hexane and benzene as eluents to give 2.84 g (22% yield) of **1**.

Several reaction conditions were also examined for the reaction of **7** with **4** (1.2—1.75 mol-equiv.), but the yields of **1** were low [70 °C/28 h in DMF, 19%; 40 °C/116 h in THF in the presence of *n*-$Bu_4N\cdot HSO_4$ (0.2 mol-equiv.), 11%; r.t./70 h in diglyme, 10%; r.t./70 h without solvent, 10%]

References

1) K. Ogura, N. Yahata, K. Hashizume, K. Tsuyama, K. Takahashi, and H. Iida, *Chem. Lett.*, **1983**, 767.

2) Formylation of **1** with methyl formate in the presence of potassium *t*-butoxide in THF was reported: G. Ferdinand and K. Schank, *Synthesis*, **1976**, 406.

3) D. T. Gibson, *J. Chem. Soc.*, **1932**, 1819.

4) L. Horner and P. Kaiser, *Justus Liebigs Ann. Chem.*, **626**, 19 (1959).

5) Sodium *p*-toluenesulfinate (**4**) was dried over phosphorus pentaoxide prior to use.