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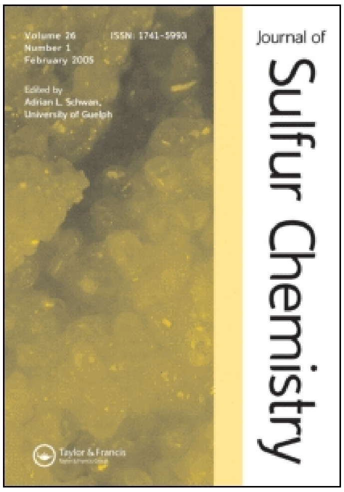

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A convenient, one-step synthesis of 1,4-dithiin

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A convenient, one-step synthesis of 1,4-dithiin

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A practical, high-yielding, one-step synthesis of 1,4-dithiin is described starting from commercially available 1,4-dithiane-2,5-diol.

Keywords: 1,4-dithiane-2,5-diol; 1,4-dithiin; double dehydration

1. Introduction

The chemistry of 1,4-dithiins continues to generate interest from both material chemists and medicinal chemists (*1*). Our interest is in the chemistry of 1,4-dithiin itself, and to this end we wish to report a convenient, one-step synthesis of this simple but elusive target.

Previous synthesis of 1,4-dithiin have been reported by Parham in 1953 (*2*), Russell in 1972 (*3*) and Brandsma and co-workers in 1973 (*4*), but the reported yields were not sufficient for the project we had in mind. It so happened that we had been using 1,4-dithiane-2,5-diol in our lab for other purposes so we made attempts to carry out the double dehydration of this readily available starting material.

2. Results and discussion

Heating 1,4-dithiane-2,5-diol with various acids, both in solution and neat, under a variety of temperatures and conditions, resulted in complex mixtures of product as determined by ^{1}H-nuclear magnetic resonance (NMR). Attempts at converting the hydroxyl groups into better leaving groups under basic conditions, for eventual thermolysis or E2-type elimination, led to substantial quantities of ring-opened products, as evidenced by the presence of aldehydes in the ^{1}H-NMR.

Eventually, we found that distilling a mixture of 1,4-dithiane-2,5-diol in N,N-dimethyl formamide (DMF) in the presence of three equivalents of thionyl chloride and two equivalents of pyridine, followed by extraction of the DMF distillate with ether and evaporation of the ether gave, almost pure, 1,4-dithiin in approximately 65% yield, as evidenced by the clean singlet at

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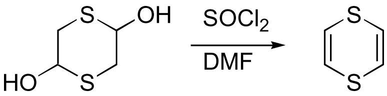
6.2 ppm in the ^{1}H-NMR. This result gave us ample 1,4-dithiin to work with, but we were not thrilled at using so much pyridine. The reaction did not work using N,N-diisopropylethylamine (DIPEA) in place of pyridine, but worked well using solid Na_2CO_3, $NaHCO_3$ and solid NaOH.

It turns out that the reaction works best with no added base at all. Excellent yields of 1,4-dithiin are obtained by heating a dry DMF solution of 1,4-dithiane-2,5-diol and 2.5 equivalents of thionyl chloride to reflux and distilling off most of the DMF at 155°C . The 1,4-dithiin co-distills with the DMF. The DMF is diluted with diethyl ether, which is washed several times with water to remove the DMF. Evaporation of ether results in 1,4-dithiin pure enough for most uses. We have run the reaction starting with 15 g of 1,4-dithiane-2,5-diol and obtained 1,4-dithiin in 80–85% yield as a dark yellow oil.



Moderate yields were obtained using methylchloroformate in place of thionyl chloride.

The identity of the 1,4-dithiin obtained was established by its mass spectrum, by comparison with the reported ^{1}H-NMR chemical shift, and from additional chemistry performed on 1,4-dithiin that resulted in solid material for which X-ray structures were obtained.

3. Experimental

Thionyl chloride (17 ml, 230 mmol) was added via Pasteur pipette to a magnetically stirred solution of 1,4-dithiane-2,5-diol (10 g, 65.8 ml) in dry DMF (500 ml, distilled under N_2 from CaH_2) in a 1 l flask maintained in an ice bath. After the addition of thionyl chloride, the solution was allowed to warm to room temperature. The reaction was set up for simple distillation and heated with a Bunsen burner. Approximately 400 ml of distillate was collected between 140–160°C. The reaction pot was allowed to cool somewhat, and another 200 ml of dry DMF was added to the pot and subsequently distilled off. The 1,4-dithiin co-distills with the DMF. (A thick black residue is left in the reaction flask, to which ice water is added for eventual cleaning.)

The distilled DMF was added to a separatory funnel, and diethyl ether (500 ml) was added to it. The organic layer was washed with distilled water (3 × 200 ml), saturated sodium bicarbonate (2 × 150 ml) and brine (1 × 150 ml). The organic layer was dried ($MgSO_4$), filtered and evaporated to yield pure 1,4-dithiin (6.3 g, 54 mmol). ^{1}H-NMR ($CDCl_3$, 270 MHz): 6.21 (s); ^{13}C-NMR ($CDCl_3$, 67.5 MHz); 121.3; EIMS ($r_t = 4.73\,\text{min}$) $M + 116$.

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