

Convenient Synthesis of *N*-Methylpyrrolidine-2-thione and Some Thioamides

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Abstract—The synthesis of thioamides and thiolactams, which are used as important organic intermediates, has attracted great attention. However, expensive reagents, severe reaction conditions and low yields of the target products made conventional methods inconvenient and economically infeasible. To overcome these disadvantages, we investigated a new process for synthesizing thioamides and thiolactams. We examined thermal reactions of CS₂ with *N*-methyl-2-pyrrolidinone, formylamide, acetamide and *N,N*-dimethylformylamide, respectively. The results show that under optimum conditions *N*-methylpyrrolidine-2-thione and the corresponding thioamides can be obtained in good to excellent yields by the above thionation reactions.

Key words: CS₂, Amides, Thionation, *N*-Methylpyrrolidine-2-thione, Thioamides

INTRODUCTION

Much work has been directed towards the synthesis of thioamides and thiolactams because of their importance as synthetic intermediates [Lubosch and Seebach, 1980; Borthakur and Goswami, 1995], a medium in CO₂ sensor [Yamaguchi et al., 1986] and ligands for a variety of complexes [Rechberger and Gritzner, 1978; Senyel and Kurcuoglu, 2001; Dunstan, 2002].

P₄S₁₀ was widely used as a thionating reagent for the synthesis of thioamides [Hurd and DeLaMeter, 1961] from amides. Conventional experiments were conducted by refluxing an amide with excess P₄S₁₀ in a solvent, usually requiring a large excess of P₄S₁₀ and prolonged time. Raucher and Klein improved the procedure by ultrasonic irradiation [Raucher and Klein, 1981]. Harpp and MacDonald investigated the reactions of 1,1'-thiocarbonyldiimidazole and 1,1'-thiocarbonylbis(1,2,4-triazole) with some aldonitrone [Harpp and MacDonald, 1983]. Although thioamides can be obtained in good yields (67-75%), use of expensive heterocyclic thiocarbonyl transfer reagents makes the reaction difficult in practical applications. Thioamides and thiolactams were also synthesized by using Lawesson reagents [Thomsen et al., 1984; Xie and Lightner, 1991; Sakamoto et al., 2000; Olsson et al., 2000] and by the reactions of thiuram monosulfides with organolithium derivatives [Gronowitz et al., 1993] and of carboxylic acids and amines with *O,O*-diethyl di-thiophosphoric acid [Borthakur and Goswami, 1995]. These methods, however, still require expensive thionating reagents.

Taking the disadvantages of previous synthetic procedures into account, we used CS₂ as a thionating reagent for the synthesis of thioamides and thiolactams from amides and lactams. Here we re-

port our results about the synthesis of *N*-methylpyrrolidine-2-thione (MPT), thioformamide (TFA), thioacetamide (TAA) and *N,N*-dimethylthioformamide (DMTFA) by thermal reactions of CS₂ with *N*-methyl-2-pyrrolidinone (MP), formamide (FA), acetamide (AA) and *N,N*-dimethylformamide (DMFA), respectively.

EXPERIMENTAL

1. Chemicals

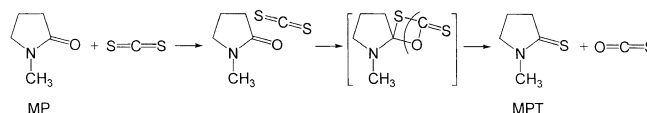
CS₂, MP, FA, AA and DMFA were reagent grade and purchased from Aldrich Chemical Company, Inc.

2. Reactor and Analytical Instruments

A 100 mL stainless steel, magnetically stirred autoclave was used as a reactor for all the reactions. Analytical instruments included a Hewlett Packard 6890/5973 GC/MS, a Hewlett Packard 6890/Nicolet Magna IR-560 GC/FTIR and a Hewlett Packard 6890 GC with FID.

3. Reaction and Analysis Procedures

Prescribed amounts of CS₂ and MP (5 mL) or an amide (5 mL) were put into an autoclave. After being pressurized with nitrogen to 5 MPa at room temperature, the autoclave was heated to an indicated temperature within 10 min and kept at the temperature for a prescribed period of time. Then the autoclave was immediately cooled to room temperature in an ice-water bath. After being taken out from the autoclave, the reactants and products were identified with GC/MS and GC/FTIR and quantified with GC.



Scheme 1. Mechanism for MPT formation from thermal reaction of MP with CS₂.

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[‡]This paper is dedicated to Professor Baik-Hyon Ha on the occasion of his retirement from Hanyang University.

Table 1. Mass and FTIR spectral data of MPT

| Mass (m/e, %) | FTIR (ν , cm^{-1}) |
|--|---|
| 115 (M^+ , 100), 100 (17.1), 87 (26.7), 85 (19.6), 82 (58.8), 73 (49.8), 58 (31.5), 42 (29.6), 30 (21.0) | 856, 937, 1,088, 1,142, 1,223, 1,296, 1,317, 1,404, 1,462, 1,508, 2,877, 2,931, 2,970 |

RESULTS AND DISCUSSION

1. Synthesis of MPT

The reaction of MP with CS_2 under milder conditions only afforded MPT, indicating the thionation of MP by CS_2 selectively proceeded, i.e., as Scheme 1 shows, the oxygen atom in carbonyl group of MP was substituted by a sulfur atom in CS_2 during the thermal reaction.

Table 1 lists mass and FTIR spectral data of MPT. It is noteworthy that FTIR spectral data of MPT are much more complicated than those (990, 1,103, 1,290, 1,404, 1,725, 2,902 cm^{-1}) of MP, implying the interaction between C=S group and other moiety in MPT is stronger than that between C=O group and other moiety in MP.

Table 2 summarizes MPT yields obtained under different conditions. First, fixing the volume ratio of CS_2 to MP to 2, we examined the effects of reaction temperature and time on MPT yield. MPT was not detected from the thermal treated mixture heated up to 180 °C. In 3 h reaction at 185 °C, only 2% of MP was converted to MPT. MPT yield increased with raising reaction temperature, but the increase is not remarkable above 225 °C. In 1 h reaction at 220 °C, more than 60% of MP was converted to MPT. MPT yield steadily increased with reaction time until 4 h reaction. The volume ratio of CS_2 to MP also affected the reaction significantly. MPT yield in-

creased from 68 to 85% by increasing the ratio from 1 to 2, but subsequent increase in the ratio led to the decrease in MPT yield. The reason for the decrease remains unclear.

Under the conditions shown in Table 2, no peaks were found by GC analysis for products other than MPT and the reaction mixture was observed to be a solution. However, at higher temperatures than 250 °C a significant amount of black solid was observed. This solid is not dissolved either in CS_2 /MP mixed solvent or in many other solvents and not melted or volatile even at 300 °C in vacuo. It may result from MPT polymerization, but its detailed structure needs to be investigated.

H_2S was also used as a thionating agent for converting MP to MPT, but MP conversion to MPT was only ca. 25% even though the reaction was performed at much higher temperature and in the presence of a $\gamma\text{-Al}_2\text{O}_3$ [Eastman et al., 1990]. An alternative method for MPT synthesis from MP was to use Lawesson reagent [Thomson et al., 1984], but the method lacks economical feasibility due to the costliness of the reagent. Other than these, benzyltriethylammonium tetrathiomolybdate was also used as a sulfur transfer reagent for the conversion of amides and lactams to thioamides and thiolactams, respectively, including MPT [Iankumaran et al., 1995]. However, in addition to the use of expensive tetrathiomolybdate, the need to convert the reactants to chloro iminium salts by using $(\text{COCl})_2$ or POCl_3 made the method inconvenient. Hence, thermal reaction of MP with CS_2 provides a convenient approach to MPT synthesis.

Although the synergic effect of CS_2 /MP mixed solvent on coal extraction was found more than 10 years ago [Iino et al., 1988], its mechanism is still not clarified. According to the above results, we consider that the synergic effect may be related to the π - π interaction between CS_2 and MP, by which MP reacts with CS_2 at high temperatures. Our results also suggest that CS_2 /MP mixed solvent is not appropriate for coal extraction at high temperatures because of the reaction between the two compounds.

2. Synthesis of Some Thioamides

At elevated temperatures, CS_2 can also react with FA, AA and DMFA to afford TFA, TAA and DMTEFA, respectively. Table 3 displays mass and FTIR spectral data of the thioamides. Similar to MPT, all the molecular ion peaks for the thioamides are base peak, showing the high stabilities of the compounds. The thioamides show different FTIR spectral data, but FTIR spectral data of TFA is very similar to those of MPT.

Table 4 exhibits the yields of the thioamides obtained under dif-

Table 2. Effects of reaction temperature, time and volume ratio of CS_2 to MP on MPT formation

| Temperature (°C) | Time (h) | CS_2 /MP (vol/vol) | MPT yield (mol%) |
|------------------|----------|-----------------------------|------------------|
| 180 | 3.0 | 2 | 0 |
| 185 | 3.0 | 2 | 2 |
| 195 | 2.0 | 2 | 30 |
| 210 | 2.0 | 2 | 74 |
| 225 | 2.0 | 2 | 85 |
| 250 | 2.0 | 2 | 87 |
| 220 | 1.0 | 2 | 60 |
| 220 | 2.0 | 2 | 70 |
| 220 | 4.0 | 2 | 89 |
| 225 | 2.0 | 1 | 68 |
| 225 | 2.0 | 4 | 82 |
| 225 | 2.0 | 8 | 14 |

Table 3. Mass and FTIR spectral data of some thioamides

| Thioamides | Mass (m/e, %) | FTIR (ν , cm^{-1}) |
|------------|--|---|
| TFA | 61 (M^+ , 100), 45 (15.7), 32 (31.7) | 855, 945, 1,095, 1,140, 1,232, 1,300, 1,315, 1,400, 1,465, 1,505, 1,737, 2,880, 2,930 |
| TAA | 75 (M^+ , 100), 60 (31.8), 42 (22.5), 28 (35.6), 18 (22.1) | 1,098, 1,210, 1,354, 1,450, 1,560, 1,655, 1,865, 2,203, 3,005 |
| DMTEFA | 89 (M^+ , 100), 74 (25.8), 56 (2.2), 44 (57.8), 30 (23.3) | 900, 1,000, 1,135, 1,400, 1,510, 1,720, 2,810, 2,940 |

Table 4. Effects of reaction temperature, time and volume ratio of CS₂ to amides on the formation of thioamides

| Amide | CS ₂ /Amide (vol/vol) | Time (h) | Yield (mol%) | | | | |
|-------|-------------------------------------|-------------|--------------|--------|--------|--------|--------|
| | | | 110 °C | 125 °C | 150 °C | 175 °C | 200 °C |
| FA | 3 | 1 | - | 2 | 9 | 20 | 5 |
| FA | 3 | 2 | - | 5 | 25 | 35 | 13 |
| FA | 3 | 4 | - | 31 | 60 | 73 | 45 |
| AA | 2 | 1 | - | 6 | 20 | 15 | 10 |
| AA | 2 | 2 | - | 12 | 38 | 27 | 21 |
| AA | 2 | 4 | - | 20 | 55 | 44 | 35 |
| DMFA | 2 | 1 | 1 | 2 | 7 | 25 | - |
| DMFA | 2 | 2 | 2 | 6 | 12 | 49 | - |
| DMFA | 2 | 4 | 11 | 21 | 34 | 78 | - |
| DMFA | 3 | 2 | - | - | 12 | - | - |
| DMFA | 4 | 2 | - | - | 6 | - | - |
| DMFA | 8 | 2 | - | - | 2 | - | - |

ferent reaction conditions. The reactions of the amides with CS₂ proceeded much more readily than that of MP with CS₂. The higher reactivities of the amides with CS₂ than that of MP with CS₂ may be in part related to their difference in volatility, i.e., significant amounts of the reactants may be converted in gas-phase reaction. The yields of the thioamides increased with reaction time but did not monotonically increase with reaction temperature. For example, in the reaction of FA with CS₂, TFA yield increased with raising reaction temperature from 125 °C to 175 °C but decreased at 200 °C. Maximum yield of TAA was obtained at 150 °C. The reaction of DMFA with CS₂ proceeded at a temperature as low as 110 °C, and the yield of the resulting DMTFA increased with reaction temperature up to 175 °C, but some by-products were detected from the reaction mixture obtained from the reaction at 175 °C (Table 5). The formation of the by-products should be related to DMTFA decomposition, so we did not perform the reaction at higher temperatures. Similar to the reaction of MP with CS₂, increasing volume ratio of CS₂ to DMFA from CS₂/DMFA=2 also inhibited DMFA thionation.

Many efforts have been made to improve the syntheses of TFA [Ogata et al., 1996; Rohaly et al., 1999], TAA [Williams, 1994] and DMTFA [Ilankumaran et al., 1995], but all the improvements involved the use of expensive and/or very hazardous reagents. Compared to the previously reported methods, thermal reactions of amides with CS₂ should be better choices for the syntheses of thioamides

Table 5. Mass spectral data of by-products from the reaction of DMFA with CS₂

| Structure | Mass (m/e, %) |
|---|---|
| $\begin{array}{c} \text{S} \\ \\ (\text{CH}_3)_2\text{NCCH}_3 \end{array}$ | 103 (M ⁺ , 100), 88 (17.4), 70 (28.6), 59 (50.2), 44 (49.8) |
| $\begin{array}{c} \text{S} \\ \\ (\text{CH}_3)_2\text{NCNH}_2 \end{array}$ | 104 (M ⁺ , 100), 87 (2.0), 77 (30.1), 60 (28.5), 52 (1.2), 44 (62.4), 30 (5.2) |
| $(\text{CH}_3\text{NH})_2\text{C}=\text{S}$ | 104 (M ⁺ , 100), 74 (26.4), 60 (12.7), 51 (2.0), 30 (20.5) |
| $\begin{array}{c} \text{S} \\ \\ (\text{CH}_3)_2\text{NCNHCH}_3 \end{array}$ | 118 (M ⁺ , 100), 104 (0.2), 88 (29.4), 74 (50.0), 44 (64.5), 30 (18.6) |

and thiolactams.

SUMMARY

CS₂ is a commonly used organic compound. In the reactions of MP and amides with CS₂, CS₂ acts both as a reactant and as a solvent. Because of its low boiling point, residual CS₂ can be easily separated from reaction mixture and reused. Therefore, our work provides a convenient method for the synthesis of thioamides and thiolactams.

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