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A Facile Conversion of Amides and Lactams to Thioamides and Thiolactams using Tetrathiomolybdate

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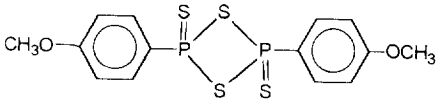
Abstract: Chloro iminium salts generated *in situ* from amides and lactams using $(COCl)_2$ or $POCl_3$ reacted very readily with the new sulfur transfer reagent, benzyltriethylammonium tetrathiomolybdate to afford the corresponding thioamides and thiolactams in exellent yields under mild reaction conditions.

The utility of thioamides as synthetic intermediates[1] and in heterocyclic synthesis[2] is well documented in the literature. Hence a large amount of work has been directed towards the synthesis of thioamides. Thionation of corresponding amides is certainly of great interest because of their easy availability. Lawesson's reagent **1** is normally the reagent of choice for effecting this transformation.[3]



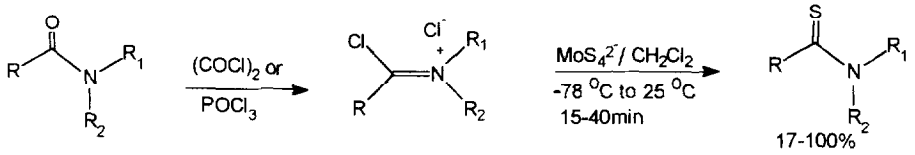
1

Other than this P_2S_5,[4] $R_3OBF_4/NaSH$,[5] R_2PSX,[6] and $(Et_2Al)_2S$[7] have also been used. Most of these methods require very long reaction times, high temperatures, difficuty in handling the reagents, tedious work up and chromatographic seperation of products from the reagents used. Recently while exploring the scope and utility of benzyltriethylammonium tetrathiomolybdate, $(PhCH_2NEt_3)_2MoS_4$, **2** as a sulfur transfer reagent in organic synthesis, we observed that **2** is very effective for the synthesis of alkyl disulfides from alkyl halides.[8] Herein, we report that tetrathiomolybdate **2** is a useful thionating reagent for the conversion of amides and lactams to thioamides and thiolactams respectively.

In our initial studies, the reaction of tetrathiomolybdate **2** directly with the amides was attempted. Since the electrophilicity of the carbonyl carbon in amide is low, no reaction was observed. When the reaction of tetrathiomolybdate **2** with amides and lactams in the presence of Lewis acids like $CoCl_2$, $BF_3.Et_2O$ etc. was carried out, it led to the decomposition of the reagent and starting material was

recovered unchanged. Recently Fuchs et al. reported that if the amide is first converted to the Vilsmeyer intermediate it reacted readily with hexamethyldisilathiane to form the corresponding thioamides in good yields.[9] This strategy was adopted in the present case and when the amides and lactams were reacted with $(COCl)_2$ (method A) or $POCl_3$ (method B) in CH_2Cl_2 to generate the chloro iminium salts *in situ*, they reacted readily with tetrathiomolybdate **2** (-78 to 25°C, 15-40 min) to afford the corresponding thioamides and thiolactams in excellent yields (Scheme **1**). The results of this new methodology of thionation of amides and lactams are summerized in Table I.

Scheme 1



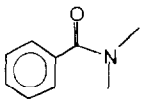
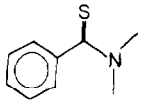
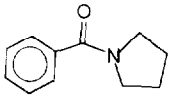
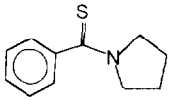
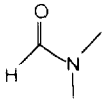
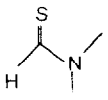
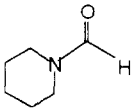
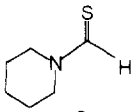
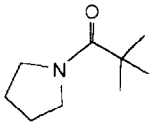
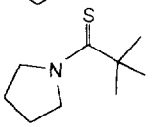
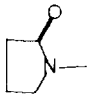
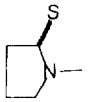
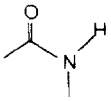
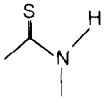
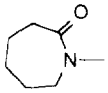
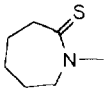
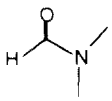
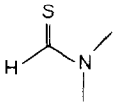
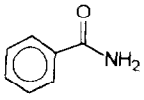
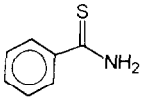
The yields of thioamides obtained using this methodology are comparable to those reported using Lawesson's reagent, excepting the case of primary amides (e.g. benzamide, entry 10 in Table I).[3] The advantage of the present methodology is the isolation of products by simple extraction with diethylether compared to the tedious chromatographic seperation that is often needed while using Lawesson's reagent. Although the methodology reported by Fuchs et al.[9] for thionation using hexamethyldisilathiane is good, the reagent is expensive and has an obnoxious odour. In the present methodology, the tetrathiomolybdate **2** is easily prepared, inexpensive and does not have offensive smell and hence is convenient to use even for large scale preparations.

Typical Procedure:

Procedure A: To a stirred solution of amide or lactam (2mmol) in dry CH_2Cl_2 (2ml) cooled to -78°C was added oxalyl chloride (0.28ml, 1.5mmol) over a period of 5 min. After stirring for 5 min the solution was allowed to warm to 0°C and left at this temperature for 30 min. During this period the solution turned pale amber in color with the evoluion of CO_2 and CO. The solution was again cooled to -78°C and tetrathiomolybdate **2** (1.5g, 3mmol) was added at once. The reaction mixture was allowed to come to room temperature (25°C) and was stirred (15-40 min). The solvent was evaporated and the residue was extracted with ether (3×30ml) and the organic extract was filtered through a pad of Celite. The solvent was evaporated to reveal the thioamide or thiolactam. The products were purified by recrystallisation or distillation.

Procedure B: In the formation of chloro iminium salt from amides, the same molar ratio of $POCl_3$ was used instead of $(COCl)_2$.

Table 1. Reaction of amides and lactams with tetrathiomolybdate 2

Entry	Substrate	Product[a]	Method	Time(min)	Yield(%)[b]
1			A	30	82
2			A	20	96
3			A	20	93
4			A	25	100
5			A	20	100
6			B	40	80
7			B	40	81
8			B	15	94
9			B	25	89
10			B	25	17

a All the products gave satisfactory spectral data

b Yield refers to isolated products

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