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Synthesis of thioesters and thioamides under solvothermal condition using thiourea as thionating agent

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A simple, rapid, high-yielding and environmentally benign method for the conversion of esters and amides to the corresponding thio compounds was carried out using thiourea as thionating agent under solvothermal reaction. All the compounds isolated in good yields were characterized both by spectral analysis and comparing them with the authentic samples synthesized using the literature method.

1. Introduction

Thiocarbonyl containing molecules are versatile synthetic intermediates which find many applications in the synthesis of complex natural products [1]. Though there are a number of reagents available for the thionation of esters or amides, they have some disadvantages. The various thionating reagents used for thionation reaction includes Lawesson's reagent [2], hydrogen sulfide [3], phosphorous pentasulfide [4], hexamethyldisilathiane [5], R_3OBF_4/NaSH [6], R_2PSX [7], $(Et_2Al)_2S$ [8], bis(tricyclohexylstannyl)sulfide/boron trichloride [9], thiourea [10] etc. For instance, many of these reagents require more reaction times, high temperatures, or inconvenient reaction condition for their execution and are often accompanied by painful chromatographic separation to remove spent reagents from desired products. Recently Rai and Linganna [11] successively used thiourea as thionating agent for the conversion of 1, 3, 4-oxadiazole to 1, 3, 4-thiadiazole under solvothermal reaction condition. The development of solvothermal reaction is of interest because they offer the possibility of environmentally benign reaction conditions by reducing the burden of organic solvent disposal. Solvothermal process involve the heterogeneous chemical reaction, which occur at solid-liquid or solid-liquid-gas interfaces under high temperature and high pressure. For instance, conversion of lactone to amide [12] was achieved by heating the amide with liquor ammonia in a sealed glass tube on water bath for 10–12 h. Intramolecular 1,3-dipolar cycloaddition of oxime with olefins via nitrone intermediate was carried out successfully in a sealed tube at 100°C using benzene as solvent [13], while conversion of aldehyde semicarbazones to bishydrazones by thermolysis under reduced pressure was achieved in 90–95% yield using ethanol as solvent [14]. This prompted us to use simple easily available reagent thiourea for the conversion of esters to thioesters under solvothermal condition.

In a typical synthesis, equimolar quantities of thiourea and ester (**1**) were taken in a stainless steel SS316 Morey type of autoclave provided with a teflon liner of 30 ml capacity. On usual workup, it yields 85 to 90% of ethylthiobenzoate.

2. Experimental section

Melting points were recorded in open capillaries using Thomus Hoover apparatus and were uncorrected. The compounds were routinely checked for their purity by TLC using silica gel-G as adsorbent. IR spectra were recorded on Shimadzu FT 8300 spectrometer. ^{1}H NMR spectra were recorded on a Jeol 60 MHz FT NMR spectrometer using $CDCl_3$ as solvent.

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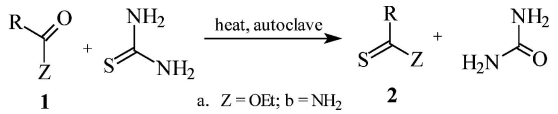


i) R=C_6H_5; ii) R=2,4-$Cl_2C_6H_3$; iii) R=p-NO_2-C_6H_4;
iv) R=2,3-$Cl_2C_6H_3$; v) R=$C_6H_5CH_2$;
vi) R=2-HO-C_6H_3; vii) R=C_6H_5.

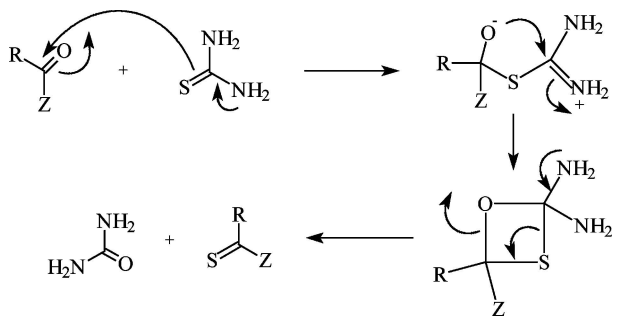
Figure 1

2.1. General procedure for the preparation of thioester/amide

Typical procedure for the preparation of o-ethyl thiobenzoate (**2a-i**):- A mixture of ethyl benzoate (1.00 g) and thiourea (5.00 g) was loaded in Teflon liner, the lid was closed and liner was placed in the autoclaves, the plates were kept on the liner and autoclave was closed and was tightened and was kept in oven for about 4 h. The autoclave was then opened and the product was extracted into ether, washed thoroughly with water to remove unreacted thiourea and the side product urea. TLC of this solution shows single spot, which is different from the starting material. It was dried over anhydrous sodium sulphate and the solvent was removed by distillation in the water bath. The oily product thus obtained was then purified by distillation using oil bath and yielded the desired product as colourless oil in 92% yield (0.99 g); b.p. = 190°C; IR (neat): $\surd$ 2983 (CH), 1632 (C=S), 1592 (C=C), 1453 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.0 (bm, 2H, ArH), 7.4 (bm, 3H, ArH), 4.40 (q, 2H, OCH_2), 1.4 (t, 3H, CH_3).

3. Discussion

The synthetic sequence is outline in Fig. 1. Observations shows that in the conventional method for the synthesis of thioesters, the limitations have been the use of toxic reagents, which is detrimental to the environment, and as the reaction progresses a mixture of product arises. Consequently, for a more green procedure it is desirable to develop a rapid, easily manipulated and preferentially environmentally benign solvent free protocol. In view of the above observations, we thought of synthesizing thioesters and amides using thiourea as thionating agent



Scheme 1

TABLE I

Entry	Ester/amide 1	Thioester /Thioamide	B.P./ M.P. (°C) Found	Reported[2,5]	Yield (%)
1.	Ethyl benzoate	2a–i	189	190–191	92
2.	Ethyl-2,4-dichlorobenzoate	2a–ii	190	191–192	90
3.	Ethyl-p-nitrobenzoate	2a–iii	54	54–55	95
4.	Ethyl-2,3-dichlorobenzoate	2a–iv	185	184–185	89
5.	Ethyl-phenyl acetate	2a–v	203	202–203	91
6.	Methyl salicylate	2a–vi	200	200–201	92
7.	Benzamide	2a–vii	180	180–181	88

under solovothermal condition. Here the reagent itself acts as solvent. The probable mechanism for the formation of thioester and thioamides involves the initial attack of sulphur atom of thiourea assisted by the lone pair of electron on the nitrogen at carbonyl carbon atom of the ester/amide gave oxathietane as intermediate (Scheme 1). These intermediates undergo ring-opening reaction leading the formation of desired thioester/thiamide and urea as the side product. Evidence for this mechanism is based on the mechanism put forwarded by Bordwell and et al.[10] for the conversion of oxiranes to thiranes using thiourea.

Products were identified by direct comparison (mixed m.p./mixed b.p., I.R. and ^1H NMR) with those of the samples prepared using literature procedures[2].

4. Conclusion

We have described a highly efficient solvothermal procedure for the preparation of various thioesters and thioamide starting from corresponding esters and amide respectively using thiourea as thionating reagent. The advantages of this environmentally benign and safe prorocol include a simple reaction set-up, application of commercially available reagents, high product as well as elimination of solvents.

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