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A Fast and Solvent-Free Conversion of Thioamides into Thioesters

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Summary. Solvent-free irradiation of thiomorpholides with two kinds of methylating agents under microwave or ultrasonic conditions gave the corresponding thioesters in high yield. The method is simple and avoids prolonged heating with solvents.

Keywords. Thioesters; Thioamides; Solvent-free; Microwave; Ultrasonic.

Introduction

Thioesters are activated carboxylic acid derivatives which are usually prepared by condensation of a thiol and an acid chloride. They exhibit acylating properties similar to those of acid anhydrides [1]. They have therefore found widespread application in synthetic chemistry [2]. A traditional approach to the synthesis of thioesters **1** is the reaction of thiols or their metal salts with acid halides, anhydrides, and esters [3].

Recently, the transformation of a solution of thioamides **2** in THF in presence of water and an alkylating agent yielded thioesters **1** in high yield [3]. However, this method may find only limited application because of the high reaction temperatures and very long reaction periods (15–72 h) required.

As thioamides **2** are part of our project [4–7], we became interested in this reaction to compare the irradiation effects with that of classical heating on the reaction. Herein we wish to report the solvent-free synthesis of thioesters **1** from the reaction of selected methylating agents (dimethylsulfate, *DMS*; methyl iodide) with the corresponding thiomorpholides **2** under both microwave heating and ultrasonic conditions.

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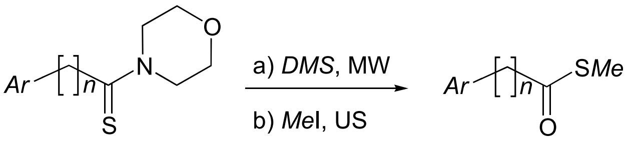

	n	*Ar*		*n*	*Ar*
2a	1	*Ph*	**1a**	1	*Ph*
2b	1	4-Cl-*Ph*	**1b**	1	4-Cl-*Ph*
2c	1	2-*naphth*	**1c**	1	2-*naphth*
2d	0	*Ph*	**1d**	0	*Ph*
2e	0	4-O*Me*-*Ph*	**1e**	0	4-O*Me*-*Ph*

Scheme 1

Table 1. Solvent-free conversion of thiomorpholides into thioesters

Substrate	Product	Microwave (*DMS*) Yield/%	Ultrasonic (CH_3I) Yield/%
2a	**1a**	73	79
2b	**1b**	98	91
2c	**1c**	98	88
2d	**1d**	99	97
2e	**1e**	99	98

Results and Discussion

As shown in Table 1, the yields of the products using microwave irradiation for 40 s are high and comparable to those of the classical reactions which usually require very long refluxing periods [3]. However, using a domestic microwave oven resulted in uncontrolled heating of the reaction mixtures, accompanied by a rapid evaporation of the liquids in open vessels.

Surprisingly, when the same reactions were carried out under ultrasonic conditions at room temperature, similar results were obtained. After 5 h sonication, the temperature was raised to about 35°C. In accord with these facts, we propose that there may be non-thermal effects on the reaction.

In general, we have shown that thioamides can be transformed into the corresponding thioesters under microwave and ultrasonic irradiation condition. Moreover, the method is simple, and avoids prolonged heating with solvents.

Experimental

Caution: *Experiments should be carried out in an efficient hood to avoid exposure to toxic vapors of methylating agents.*

Syntheses under Microwave Condition

A mixture of 1 mmol of thiomorpholines **2**, 2 mmol of *DMS*, and H_2O in an open pyrex glass flask was exposed to microwave irradiation at 900 W for 40 s. The microwave oven used for this study was a domestic National model NN-6755 with 7 power settings (90–900 W). After cooling, the reaction product **1** was washed with H_2O and then purified by flash chromatography on silica gel using ether as eluent. The products are generally pure as judged by TLC, GC-MS, and NMR analysis.

Syntheses under Ultrasonic Condition

A mixture of 1 mmol of thiomorpholines **2**, 2 mmol of methyl iodide, and H_2O in a closed pyrex glass flask was exposed to ultrasonic irradiation for 5 h. The ultrasonic bath used for this study was a Dandelin model Sonorex RK 156 with a power setting (35 KHz). The reaction product **1** was purified by flash chromatography on silica gel using ether as eluent.

Methyl 2-Phenyl ethanethionate (**1a**, $C_{12}H_{15}NOS$)

Colorless oil; ^{1}H NMR (90 MHz, $CDCl_3$): $\delta = 7.20$ (s, 5H), 3.80 (s, 2H), 2.25 (s, 3H) ppm; MS: m/z (rel. intensity %) = 166 (M^+, 20), 119 (45), 91 (100), 47 (15).

Methyl 2-(4-Chlorophenyl)ethanethionate (**1b**, $C_{12}H_{14}ClNOS$)

Colorless oil; ^{1}H NMR (90 MHz, $CDCl_3$): $\delta = 6.80$–7.20 (dd, 4H), 3.85 (s, 2H), 2.28 (s, 3H) ppm; MS: m/z (rel. intensity %) = 200 (M^+, 10), 153 (10), 125 (100), 75 (40), 47 (70).

Methyl 2-(2-Naphtyl)ethanethionate (**1c**, $C_{16}H_{17}NOS$)

Colorless oil; ^{1}H NMR (90 MHz, $CDCl_3$): $\delta = 7.25$–8.05 (m, 7H), 4.80 (s, 2H), 2.29 (s, 3H) ppm; MS: m/z (rel. intensity %) = 216 (M^+, 60), 141 (100), 115 (90), 75 (60), 47 (50).

Methyl phenyl methanethionate (**1d**, $C_{11}H_{13}NOS$)

Colorless oil; ^{1}H NMR (90 MHz, $CDCl_3$): $\delta = 7.20$ (s, 5H), 2.30 (s, 3H) ppm; MS: m/z (rel. intensity %) = 152 (M^+, 70), 105 (90), 74 (100), 46 (80).

Methyl (4-Methoxyphenyl)methanethionate (**1e**, $C_{12}H_{17}NO_2S$)

Colorless oil; ^{1}H NMR (90 MHz, $CDCl_3$): $\delta = 6.70$–7.20 (dd, 4H), 2.28 (s, 3H) ppm; MS: m/z (rel. intensity %) = 196 (M^+, 15), 135 (60), 75 (100), 47 (70).

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