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SYNTHESIS OF THIOESTERS AND THIOAMIDES USING POTASSIUM THIOCYANATE UNDER MICROWAVE IRRADIATION

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ABSTRACT
A simple, expedited, and eco-friendly protocol for the synthesis of thioesters and thioamides using Potassium thiocyanate as thionating agent under microwave irradiation method is described. Synthesized compounds are obtained in good yield were analyzed by spectral techniques and matching with the standard compounds made by the reported procedure.
Keywords: Microwave Heating, Thioesters, Thioamides, Potassium thiocyanate
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INTRODUCTION

Microwave-assisted synthesis provides more time for chemists to expand their creativeness, develop new processes and new theories. Recent developments in chemical sciences created microwave energy a new proficient way of heating the reaction.[1] Microwave energy bids abundant benefits for the execution of synthesis comprising enhanced reaction rates, improved yield and cleaner chemistries. Using this technique, reactions can be performed in minutes, instead of spending hours to days in a conventional manner. The difficulty accompanying effluent disposal is overcome by executing the reactions without the use of solvent under microwave irradiation. Microwave irradiation reaction under solvent-free conditions, mineral-supported catalyzed reactions etc. provides better chemical methods with higher reaction rate, improved yield, good selectivity.[2] Chemical reactions that took an hour to days the completion can be performed in minutes. The microwave region is positioned between IR and radio waves in the electromagnetic spectrum. The wavelength of microwave radiation is 1 mm-1 m with the frequencies 0.3-300 GHz. Dielectric heating in microwaves utilizes the capability of various solids and liquids to convert electromagnetic energy into heat to progress the reactions. The microwave technique has been applied in various research technologies like drug release/targeting,[3] polymer technology,[4] waste treatment,[5] ceramics,[6] alkane decomposition,[7] etc. Consequently, microwave technology entertains as a potential method in green chemistry.[8] This technology unlocks new openings as a new heating technique which is very difficult by the regular heating method.[9]
Organosulfur compounds are versatile intermediates in synthetic chemistry, possess many imperative biological properties.[10] The applications and choice of organo-sulfur compounds have augmented enormously as sulfur comprising groups continue to function as an imperative supplementary function in synthetic arrangements.[11] Thiocarbonyl comprising compounds are useful synthetic intermediates, that find numerous uses in the preparation of natural products.[12] Although various reagents are accessible for the preparation of thioesters or thioamides, there are some drawbacks. Some of the important reagents used for thionation comprises lawessons reagent,[13] H_2S,[14] phosphorous pentasulfide,[15] hexamethyldisilathine,[16] R_3OBF_4/NaSH,[17] R_2PSX,[18] $(Et_2Al)_2S$,[19] bis(tricyclcohexylstannyl) sulfide/BCl_3,[20] thiourea,[21] etc. Many of these reagents involve high temperatures, prolonged reaction times, or harsh conditions for reaction execution and frequently require problematic column chromatography to separate and remove the unwanted products. Batool A. et al. described a green procedure for the synthesis of thieranes from oxiranes by using ammonium thiocyanate.[22] Encouraged by this, and in persistence to our work on the development of biologically active heterocycles,[23-26] we thought of using simple and commercially available reagent

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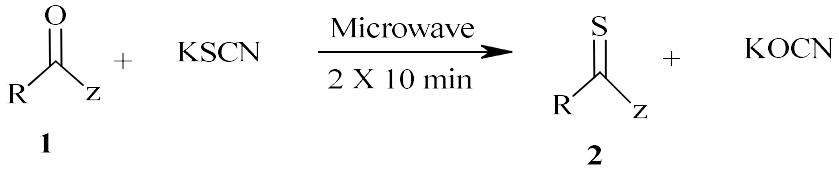
potassium thiocyanate for the transformation of esters into thioesters by making use of microwave irradiation.

EXPERIMENTAL

Material and Methods

The FTIR spectra were performed on Shimadzu IR spectrometer-IRSpirit. ^{1}H NMR and ^{13}C NMR spectra were taken on Bruker AM 400 MHz and 100 MHz spectrometers respectively. TLC was checked on silica gel percolated plates of thickness 0.25 mm.



1 2

a. Z= OEt, b. Z= NH_2

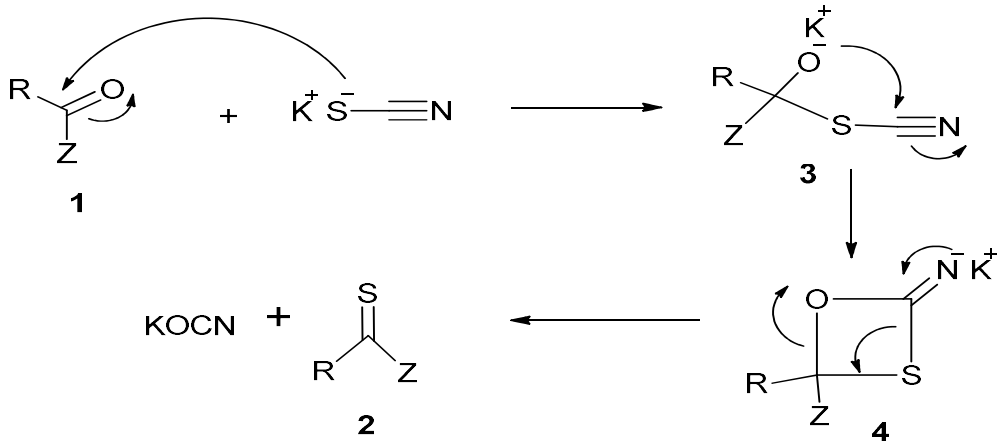
i) R= C_6H_5, Z= OEt ii)R= 2,4-Cl_2-C_6H_3, Z= OEt iii) R= p-NO_2-C_6H_4, Z= OEt
iv) R= 2,3-Cl_2-C_6H_3, Z= OEt v) R= $C_6H_5CH_2$, Z= OEt vi) R= 2-OH-C_6H_4, Z= OEt
vii) R= C_6H_5, Z= NH_2

Scheme-1: Microwave-assisted Synthesis of thioesters/thioamides

Microwave-assisted Synthesis of thioester/thioamide

Synthesis of ethyl thiobenzoate (2aI)

Ethyl benzoate (**1aI**, 1.00 g, 6.67 mmol) and thiourea (1.51 g, 20 mmol) were taken in a microwave vessel and are mixed thoroughly. It was then inserted into a microwave synthesizer (400W) and irradiated for 10 min twice. The reaction mass was cooled to rt. The product formed was then extracted with dichloromethane and washed with distilled water. The organic layer after drying over anhy. Na_2SO_4 and was evaporated in vacuo. The liquid remaining was distilled on an oil bath to yield **2aI** as a colorless oil (1.0 g, 90%), bp 189-191 ^{0}C. IR (neat cm^{-1}) ν 2986 (CH), 1634 (C=S), 1594 (C=C), 1455 ; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.1 (m, 2H, ArH), 7.42 (bm, 3H, ArH), 4.41 (q, 2H, OCH_2), 1.4 (t, 3H, CH_3).



Scheme-2: Plausible Mechanism of Formation of thioesters/thioamides

RESULTS AND DISCUSSION

The reaction sequence is given in Scheme-1. In a distinctive synthesis, ester 1 and 3-4 molar equivalents of potassium thiocyanate were introduced in a glass conical flask and microwave irradiated in the microwave synthesizer for 5-10 min. On usual workup, it yields 88-93% of ethylthiobenzoate (Table-1). Interpretations of conventional thioester synthesis indicate the drawbacks like the involvement of hazardous chemicals, which are damaging the atmosphere. Once the reaction proceeds, the formation of side products or product

mixtures is formed. Subsequently, for a greener practice, it is necessary to develop a quick, easily operated and especially eco-friendly and solvent-free procedure. Based on these interpretations, we assumed to prepare thioesters and amides using potassium thiocyanate as catalyst under microwave conditions. The plausible mechanism of the formation of thioester and thioamide involves the early attack of the sulfur anion of thiocyanate at the electron-deficient carbon atom of the carbonyl group to form intermediate 3, which undergoes cyclization to give oxathietane intermediate 4. The intermediate 4 further undergo ring-opening leading to the creation of anticipated thioester/thioamide and KOCN as the side product (Scheme-2). Endorsement to this mechanism is centered on the previously proposed mechanism.[21] The synthesized products were recognized by comparison (mixed mp/mixed bp, Infrared spectra and ^{1}H NMR spectra) with those of the compounds made using the literature method.[21]

Table-1

Entry	Ester /Amide	Thioester/ Thioamide	Bp/mp (^{0}C)		Yield (%)
			Found	Reported [7,10]	
1.	Ethyl benzoate	2aI	189-191	190-191	90%
2.	Ethyl-2,4-dichlo benzoate	2aII	190-191	191-192	89%
3.	Ethyl-p-nitro benzoate	2aIII	54-56	54-55	93%
4.	Ethyl-2,3-dichlro benzoate	2aIV	185-186	184-185	88%
5.	Ethyl-phenyl acetate	2aV	202-204	202-203	89%
6.	Methyl salicylate	2aVI	199-201	200-201	92%
7.	Benzamide	2bI	180-182	180-181	89%

CONCLUSION

To conclude, we have demonstrated a very effective protocol for the synthesis of various thioester and thioamide using potassium thiocyanate as thionating agent. The advantages of this eco-friendly and safe protocol include quicker reaction, use of commercially available safe reagent, high product yield and elimination of solvents.

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