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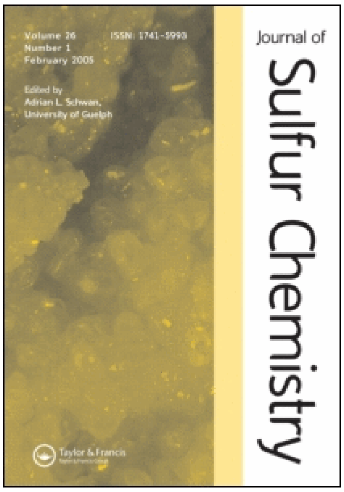

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Solvent-free synthesis of tri-substituted thiophenes via thio-Claisen rearrangement under microwave irradiation: A convenient route to novel tertiary 2-thienyl amines

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Solvent-free synthesis of tri-substituted thiophenes via thio-Claisen rearrangement under microwave irradiation: A convenient route to novel tertiary 2-thienyl amines

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A solvent-free, solid-supported, and microwave-assisted thio-Claisen rearrangement of *S*-propargylated thioamides having an activated α-methylene group has been developed. The methodology could be used successfully for the synthesis of tri-substituted thiophenes and sulfur containing triarylamines. The reaction takes place in short time and in good isolated yield.

Keywords: Thio-Claisen rearrangement; Thiophene; Microwave irradiation; Tertiary amine

1. Introduction

Highly substituted thiophenes have attracted a great deal of interest, due to their presence in natural products [1], as novel conducting polymers [2], isosteric replacements for phenyl groups in medicinal chemistry [3] and as optical chromophores [4]. The thio-Claisen rearrangement has been an excellent method for the formation of C−C bonds and is useful for the construction of heterocyclic ring system [5] and has been reviewed in the literature [6]. In continuation of our work on microwave-assisted Claisen rearrangement of propargyl naphthyl ethers to pyrans and furans [7], we report a simple and one-pot method for the preparation of tri-substituted thiophenes via thio-Claisen rearrangement of thiomorpholides [8]. In most cases, the Claisen rearrangement requires a high boiling solvent such as *o*-dichlorobenzene [8], N,N-diethyl aniline [9], or quinoline [10] and a long reflux time. These are not eco-friendly reaction conditions and moreover, there are problems in the work-up of the reaction mostly pertaining to the removal of the solvent. Therefore there is a demand for performing such a rearrangement under solvent-less conditions and in one-step and such treatment has not been previously reported in the literature. Herein, we report a solvent-free solid supported microwave assisted thio-Claisen rearrangement of thioacetamide derivatives to the corresponding tri-substituted thiophenes.

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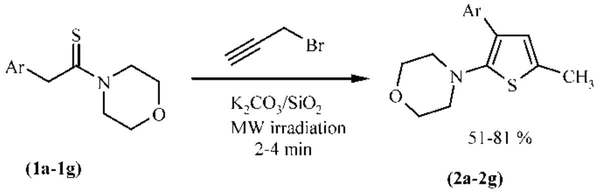
2. Results and discussion

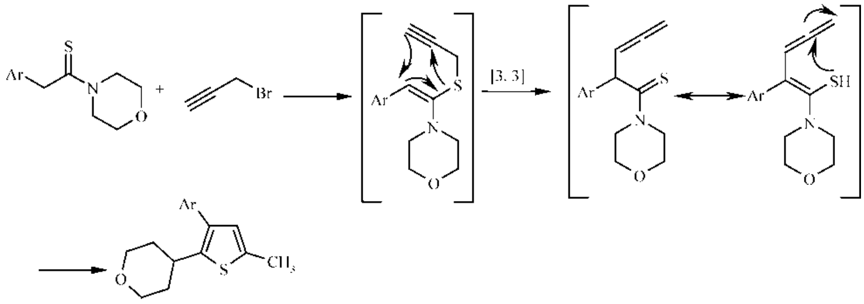
When thioamide and propargyl bromide was supported on a mixture of anhydrous K_2CO_3, silica-gel, and irradiated in a microwave oven, a rapid and clean thio-Claisen rearrangement was takes place and tri-substituted thiophenes were obtained in good isolated yields (51–81%, scheme 1).



a: Ar= phenyl, b: Ar= 4-tolyl, c: Ar= 4-chorophenyl, d: Ar= 4-bromophenyl
e: Ar= 4-methoxyphenyl, f: Ar=4-biphenyl, g: Ar= 2-naphthyl

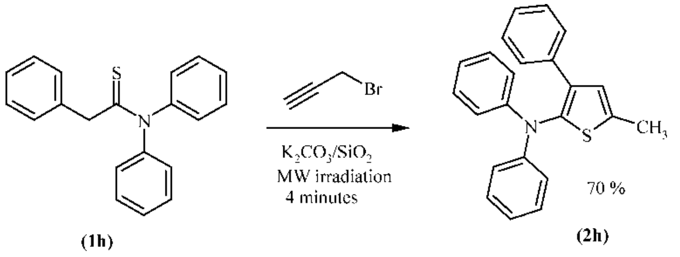
SCHEME 1

A mechanism has been proposed for this type of transformation and is shown in scheme 2.



SCHEME 2

The thioamide undergoes an initial enolization, and then *S*-propargylation followed by the Claisen rearrangement, and finally cyclization leads to the thiophene ring. In a typical procedure, N,N,2-triphenyl thioacetamide (2 mmol) and propargyl bromide (4 mmol) were supported on K_2CO_3/SiO_2 (50:50, 2 g) and irradiated in a single-mode microwave oven (at 300 W) for 4 minutes [11]. After conventional work-up the residue was subjected to flash chromatography (silica-gel, ethyl acetate/hexane, 1:4) to afford the desired product in 70 % isolated yield (scheme 3).



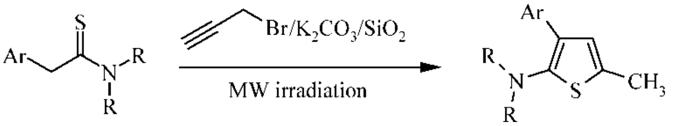
SCHEME 3

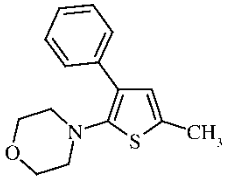
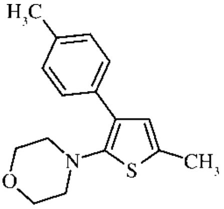
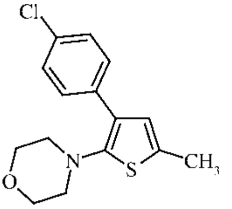
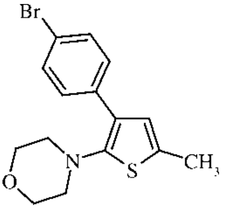
Several examples have been investigated and the results of the conventional thermal heating are compared with those of the microwave heating. Table 1 summarizes our results along with the isolated yields of the compounds.

It is clearly shown that for the same yield in both methods (table 1, entry 4), the use of microwave dielectric heating increases the relative rate of the reaction by 180 times. This methodology could be used for the synthesis of sulfur containing triarylamines (compound **h**), which could be used as hole transport material in electroluminescent display devices [12]. Also these materials have the potential of being used as drugs [13].

In conclusion a solvent-free, solid-supported, and microwave-assisted thio-Claisen rearrangement has been developed. The methodology is quite simple and fast with a straightforward work-up. Using this methodology, the sulfur containing triarylamines (which is hardly prepared by other methods) is readily prepared. The ease of work-up is another advantage of this new methodology.

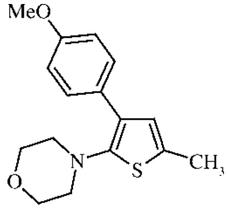
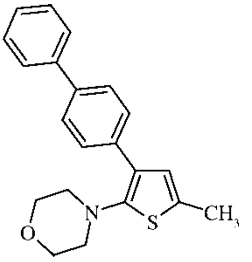
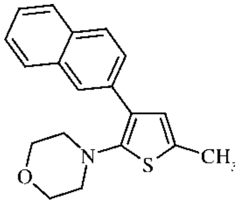
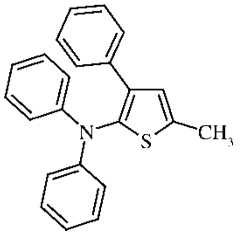
Table 1. Solvent-free synthesis of tri-substituted from thioacetamide derivaties



		Conventional heating		MW heating	
Entry	Product[1]	Time (h)[2]	Yield (%)	Time (min)[2]	Yield (%)
a		5	76	2	81
b		5	70	2	75
c		6	50	3	54
d		6	66	2	65

(*continued*)

Table 1. Continued.

Entry	Product[1]	Conventional heating Time (h)[2]	Conventional heating Yield (%)	MW heating Time (min)[2]	MW heating Yield (%)
e		5	65	3	68
f		6	62	3	71
g		6	53	3	51
h		6	61	4	70

[1] For full spectroscopic data for compounds (**a** and **c**–**g**) see reference [8].

[2] Yields refer to pure isolated products.

3. Experimental

The compounds gave satisfactory all spectroscopic data. FT IR spectra were recorded as KBr pellets on a Nicolet spectrometer (Magna 550). A Bruker (DRX-500 Avance) NMR was used to record the ^{1}H NMR spectra. All ^{1}H NMR spectra were determined in $CDCl_3$ at ambient temperature. Melting points were determined on a Büchi B540 apparatus.

The thioacetomorpholides were prepared from substituted styrene or aryl ketones by our previously published procedures [14, 15].

3.1 *General procedure for the solid-supported microwave-assisted synthesis of tri-substituted thiophenes*

Thioamide (2 mmol) was dissolved in 10 ml dry acetone and K_2CO_3/SiO_2 (50:50, 2 g) was added. Then propargyl bromide (4 mmol) was added dropwise with vigorous stirring. Stirring was continued for 10 minutes and the solvent evaporated under vacuum. The solid supported mixture was subjected to microwave heating for the times cited in table 1. The reaction mixture was extracted with dichloromethane and the solvent was removed under vacuum. Then the residue was introduced to flash chromatography (silica-gel, ethyl acetate/hexane, 1:4), and the product was obtained as almost colorless crystals.

3.1.1 Spectroscopic data for the compounds (b, h). Compound **b**: colorless crystals (EtOH), mp: 103 °C, ^{1}H-NMR ($CDCl_3$, 500 MHz) 7.67 (d, $J = 7.8$ Hz, 2 H), 7.21 (d, $J = 7.8$ Hz, 2 H), 3.80 (t, $J = 4.1$ Hz, 4 H), 2.93 (t, $J = 4.1$ Hz, 4 H), 2.47 (s, 3 H), 2.40 (s, 3 H); IR (KBr) 2964, 2907, 2860, 1643, 1501, 1429, 1117 (cm^{-1}).

Compound **h**: white crystal (EtOH), mp: 114 °C, ^{1}H-NMR ($CDCl_3$, 500 MHz) 7.43 (d, $J = 8.1$ Hz, 2 H), 7.18–7.25 (m, 7 H), 7.11 (d, $J = 8.6$ Hz, 4 H), 6.96 (t, d, $J = 7.3, 0.8$ Hz, 2 H), 6.85 (s, 1 H), 2.52 (s, 3 H); IR (KBr) 2959, 2912, 2851, 1640, 1511, 1449, 1115 (cm^{-1}).

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