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Research Article

Sulfated tin oxide (STO)-Catalyzed Efficient Synthesis of *β*-Enaminoesters

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Abstract
Sulfated tin oxide (STO) is characterized as an effective catalytic system for the synthesis of β-enaminoesters from *β*-ketoesters. This method has a number of benefits, including shorter reaction times, use of inexpensive and readily available catalyst, compatible reaction conditions, and high product yields.

Keywords
Amines; *β*-ketoesters; *β*-Enaminoesters; sulfated tin oxide and catalysis

Introduction

β-Enamino esters are useful intermediates for the production of molecules that contain nitrogen[1]. Moreover, they are significant components found in a number of medicinal medications and biologically significant natural products[2]. Organic synthesis has long been interested in the synthesis and uses of *β*-enamino ester derivatives because they are valuable as bioactive leads and versatile building blocks.

Many methods, such as tosyl imines, imidoyl halides, adding enamines or ketimines to activated carboxylic acid derivatives, adding an ester or amide enolate to a nitrile, and directly condensation of *β*-ketoesters with amines, have been reported for the synthesis of *β*-enaminoesters.[3–10] Most of the protocols have extensive documentation, but their broad applicability, harsh reaction conditions, and poor chemical yields are some of their drawbacks. Therefore, the creation of an improved catalyst for the synthesis of *β*-enaminoesters is highly necessary.

Synthetic chemists continue to research novel synthetic methods employing new reagents and catalysts to perform the synthesis of *β*-enaminoesters.[11-19] Solvent-free based synthetic techniques have gained popularity in the creation of pharmacologically significant heterocyclic compounds because of their low production costs and ease of use.[20] Recently, sulfated tin oxide, or STO, has drawn a lot of interest in the disciplines of organic synthesis and catalysis because of its huge surface area, high efficiency, low cost, better stability, non-corrosive nature, reuse, and recyclability. They have therefore been widely employed in a wide range of synthetic transformations as a solid acid heterogeneous catalyst.[21–23]

We present a mild and useful procedure in this article for the synthesis of *β*-enaminoesters from *β*-ketoesters by the reaction of amine and β-ketoester with STO (5 mol%) under solvent-free conditions at room temperature.

Experimental

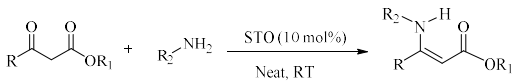
In $CDCl_3$ at 300 MHz, the ^1H NMR spectra were captured using TMS as the internal standard. For solid materials, KBr pellets were used to record IR spectra, and neat was used for liquid samples. Using silica gel, column chromatography was carried out (100-200 mesh). In relation to internal TMS, chemical changes are expressed in ppm, while J values are reported in Hz.

General procedure

The amine (1.5 mmol), *β*-ketoester (1 mmol), and STO (5 mol%) were grounded for the required period of time using a mortar and pestle. The resultant reaction mixture was extracted using ethyl acetate. The organic layer was concentrated and dried (with Na2SO4) at low pressure. The crude product was purified using column chromatography (silica gel 100–120 mesh, petroleum ether: ethyl acetate = 9:1) to obtain the appropriate *β*-enaminoester. All the compound synthesized are known and were compared with literature.

Results and Discussion

Initially, a methodical investigation was carried out to evaluate STO's efficiency as a catalyst for the reaction between aniline and ethylacetoacetate in various conditions (**Scheme 1**).



R/R_1 = alkyl
R_2 = alkyl, aryl

Scheme 1. Synthesis of β-enaminoesters

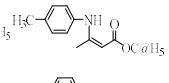
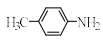
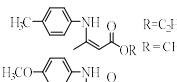
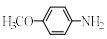
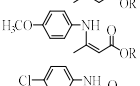
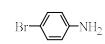
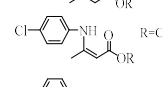
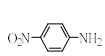
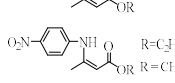
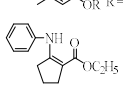
After two days, ethyl acetoacetate and aniline reacted to create a small amount of product (22%, entry 1, Table 1) when no catalyst was present, and poor results when solvents were present (entries 2-3, Table 1). With just 5 mol% of STO, the reaction was finished in 45 minutes, and a great yield of the matching *β*-enaminoester (92%, entry 5, Table 1) was achieved. Then, using no solvent and at room temperature, we determined the ideal amount of STO for this reaction (entries 4-6, Table 1). It's crucial to note that neither yield nor response time were significantly impacted by increasing the amount of STO (entries 6, Table 1). The reaction was not completed with less than 5 mol% STO, even after stirring the reaction mixture for an hour. This resulted in a low yield of the product (80%).

Table 1. Scope of the reaction

Entry	Solvent	Catalyst (mol%)	Time	Yield (%)
1	neat	-	[48]	22
2	$CHCl_3$	5	60 min	58
3	CH_3CN	5	60 min	45
4	neat	2.5	60 min	80
5	**neat**	**5.0**	**45 min**	**92**
6	neat	10	45 min	94

The technique proved effective for primary aromatic amines, as demonstrated by the data shown in Table 2. For example, it was easy to convert methyl and ethyl acetoacetates into the appropriate β-enaminoesters. The present method has many notable advantages over the ones outlined, two of which are moderate to good yields and rapid reaction times. Generally speaking, amines with electron-donating groups (entry 2-4, Table 2) produced higher yields of desired products than amines with electron-drawing groups (entries 6 and 7). Even with cyclic and aromatic *β*-ketoesters, high product yields were obtained (entry 8, Table 2).

Table 2: Synthesis of *β*-enaminoesters from *β*-ketoesters and amines

Entry	Amine	Ketoester R = CH_3/C_2H_5	Product	Time (min)	Yield[a] (%)
1				45	92
2			 R=C_2H_5	45	78
3			R=CH_3	60	85
4				60	89
5			 R=C_2H_5	45	82
6			 R=C_2H_5	60	71
7			R=CH_3	60	68
8				45	67

The catalyst can be filtered, oven dried at 100 ^{0}C and reused for at least three times without losing significant amounts of desired product.

Conclusions

As a result, we have created a novel method for the synthesis of *β*-enaminoesters without the need for solvent. The utilization of an inexpensive and widely available reusable catalyst (STO), ease of experimentation, a simple work-up process, and a prompt response are the main attractive features of this approach.

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Conflicts of interest

The authors declare no potential conflicts of interests on the present work.

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NA

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