HX-DMSO: A novel liquid halogenating system for synthesis of 2-aminothiazoles via Csp3—H bond functionalization

Zohre Zarnegar, Masoud Sadeghi, Roghayeh Alizadeh, Javad Safai *

Laboratory of Organic Compound Research, Department of Organic Chemistry, College of Chemistry and Biochemistry, University of Kashan, P.O. Box: 87317-51167, Kashan, Islamic Republic of Iran

ARTICLE INFO
Article history:
Received 7 October 2017
Received in revised form 22 December 2017
Accepted 20 January 2018
Available online xxxx

Keywords:
Methylcarbonyl
2-Aminothiazole
Thiourea
Catalytic system
DMSO

ABSTRACT
A new protocol developed for the synthesis of some 2-aminothiazoles from methylcarbonyl compounds using HX/DMSO liquid system as halogenating agent. This protocol provides an interesting new metal-free pathway for synthesis of 2-aminothiazole derivatives using Csp3—H bond functionalization of simple methylcarbonyls as substrates and HX/DMSO (X = Br or I) as the best halogenating catalytic system. Different methylcarbonyls such as aldehyde, aromatic ketones, β-diketone, and β-ketoesters were used and gave the products in good yields without any catalyst. The mild and simple conditions make this strategy extremely attractive in the development of efficient synthesis of 2-aminothiazoles and other analogous heterocycles.

© 2017 Published by Elsevier B.V.

1. Introduction

The thiazole structure (1,3-thiazole), a five membered heterocyclic ring with sulfur and nitrogen, is found in natural products such as thiamine (vitamin B1). Thiazoles are present in many natural and synthetic products with wide range of pharmacological activities such as anticancer, antiviral, antibacterial, antifungal, antiparkinsonian, anticonvulsant, and anti-inflammatory activities [1].

2-Aminothiazole and its derivatives are an important class of heterocyclic compounds in medicinal and organic chemistry due to their considerable pharmaceutical and chemical properties [2]. 2-Aminothiazoles derivatives have been used as disperse dyes in cotton industries for many years. 2-Amino-5-nitrothiazole based blue dis-chargeable monoazo dyes have been used by dye chemists since 1950 [3].

There are a large number of medicinal compounds containing 2-aminothiazole moiety such as talipexole (dopamine agonist), meloxicam (nonsteroidal anti-inflammatory drug) and niridazole (antihelmintic agent) [4].

In 1887, Hantzsch and Weber reported the first synthesis of 2-aminothiazole and 2-methylthiazole using halo ketones, thiourea, and thioamides as precursors [5]. After the first report presented by Hantzsch, many reports have been provided for the synthesis of 2-aminothiazoles [6]. However, there are few protocols for the synthesis of 2-aminothiazoles through unfunctionalized methylcarbonyl. Concerning the importance of Csp3—H bond functionalization area, it seems that the use of simple methylcarbonyls is an important issue in the synthesis of 2-aminothiazoles (Fig. 1).

To date, two methods have been introduced for the converting of the unfunctionalized methy lacarbonyl to 2-aminothiazoles. These methods include the use of halogenated agents and oxidant reagents. King and Dodson disclosed the first oxidative procedure for preparation of 2-amino-1,3-thiazole derivatives [7]. To our knowledge, there is no other protocol based on using oxidant reagents in this field.

However, various methods have been developed for the halogenating of methylcarbonyls. Among the family of halogen compounds, iodine reagents like I2 [8], PhI(OH)OTs [9], NaICl2 [10], KIO3/NH4NO3/H2SO4 [11], and chitosan NPs/I2 [12] have been introduced as good halogenating sources. There are two proposed brominating agents for the synthesis of 2-aminothiazole such as NBS [13] and CBr4/ Et3N [14]. In addition to above halogens (I and Br), researchers have been considered chlorine reagent based protocols as new methods for synthesis 2-aminothiazole derivatives using Csp3—H bond functionalization of simple methylcarbonyls (Scheme 1).

Recently, Nagarajaiah and co-workers reported mechanocchemical solid-state synthesis of 2-aminothiazole derivatives using trichloroisocyanuric acid as first organic chlorinating reagent in this field [15]. Very recently, our group introduced 1,3-dichloro-5,5-dimethylhydantoin (DCDMH) as another promising organic chlorinating reagent in this field [16]. Up to now, there is no report based on using fluorine reagent (organic and inorganic) as halogenating agent in this field.

* Corresponding author.  
E-mail address: safai@kashanu.ac.ir (J. Safai).

https://doi.org/10.1016/j.molliq.2018.01.119  
0167-7322/© 2017 Published by Elsevier B.V.
2. Experimental

2.1. Chemicals and apparatus

All chemicals were purchased from the Merck, Aldrich and Sigma Chemical Companies. Melting points were determined on an Electrothermal MK3 apparatus using an open-glass capillary and are uncorrected. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker DRX-400 spectrometer at 400 and 100 MHz respectively. FT-IR spectra were obtained with KBr pellets in the range 400–4000 cm$^{-1}$ with a Perkin-Elmer 550 spectrometer.

2.2. General procedure for the synthesis of 2-aminothiazole

A mixture of methylcarbonyl (0.5 eq.), HBr or HI (0.6 eq.) and DMSO (0.6 eq.) in EtOAc (2 mL) at 60 °C was stirred for 2 h. Then, thiourea (0.5 eq.) was added to the mixture and was stirred for 2 h. After the completion of reaction, the solvent was evaporated under vacuum and the crude was washed by sodium bicarbonate solution. The solid obtained was crystallized from a mixture of water and ethanol.

2.3. Spectroscopic data of representative products

2.3.1. Thiazole-2-amine

Pale yellow powder; m.p. = 89–90; Yield: 98 mg (98%); IR (KBr): 3410, 3289, 3084, 1629, 1512, 1491, 698 (cm$^{-1}$); $^1$H NMR (400 MHz, DMSO $d_6$): $\delta = 6.52$ (d, $J = 3.7$ Hz, 2H); 6.75 (s, 2H, NH$_2$), 2.08 (s, 3H, D$_2$O exchangeable), 6.90 (d, $J = 3.7$ Hz, 1H).

2.3.2. 4-Phenylthiazol-2-amine

Yellow crystal, m.p. = 151–153; Yield: 163 mg (93%); IR (KBr): 3424, 3256, 2856, 1623, 1519, 1336, 728 (cm$^{-1}$); $^1$H NMR (400 MHz, DMSO $d_6$): $\delta = 6.92$ (s, 1H, thiazole), 7.22 (s, 2H, NH$_2$), 2.08 (s, 3H, D$_2$O exchangeable), 7.32 (t, $J = 7.9$ Hz, 1H, Ar-H), 7.69 (t, $J = 7.9$ Hz, 2H, Ar-H), 7.71 (m, $J = 7.05$ Hz, 2H, Ar-H).

2.3.3. 4-(4-Nitrophenyl)thiazol-2-amine

Yellow crystal; m.p. = 285–286; Yield: 212 mg (96%); IR (KBr): 3400, 3115, 1626, 1596, 1507, 1331, 722 (cm$^{-1}$); $^1$H NMR (400 MHz, DMSO $d_6$): $\delta = 7.45$ (s, 1H, thiazole), 8.00 (d, $J = 8.6$ Hz, 2H, Ar-H), 8.28 (d, $J = 8.6$ Hz, 2H, Ar-H).

3. Results and discussion

To optimization of reaction condition, acetophenone and thiourea were selected as raw materials (Table 1). To initiate our work, at first, the reaction between acetophenone, HBr-DMSO system and thiourea surveyed in H$_2$O as solvent without using catalyst at 60 °C (one-pot and one-step). The results showed that the bromination of acetophenone occurred (Entry 1). However, the trace amount of thiazole product was detectable. The addition of catalyst to reaction mixture did not increased reaction efficiency (Entries 2–4). In the next step, the one-pot and two-step reaction condition was used which led to improved results (Entries 5–22). The addition of thiourea to the reaction vessel was delayed and it was allowed to be performed methylcarbonyl bromination step without thiourea. Then, different solvents and equivalent ratios of HBr-DMSO were evaluated, and then ethylacetate and 1.2/1.2 ratios (HBr-DMSO) were chosen as the best solvent and equivalent ratios, respectively. In addition to the solvent, some promising catalysts were screened for the reaction. The use of different catalysts such as Fe$_3$O$_4$ NPs, starch NPs, MMT, Al$_2$O$_3$, SiO$_2$, CuO NPs and CuFe$_2$O$_4$ NPs did not improve the yield of product (Entries 12–22). The above results showed that without assistance from catalyst, better results could be achieved in a two-step reaction (Entry 7).

To compare the type of HX-DMSO and their effects on the model reaction process and yield, and to choose the best condition and reagent, a series of experiments were carried out (Table 2). For this purpose, 1.2 eq. of HX and DMSO as the halogenating reagents were selected (Entries 1–7). Inspired by the above bromination reaction, we expected that if HI-DMSO was used, the iodination of methylcarbonyls would be possible. As expected, with 1.2 eq. of HI and DMSO in EtOAc at 60 °C, the corresponding 2-aminothiazole afforded in 95% yield in a two-step reaction (Entry 7). It is noteworthy that when HI-DMSO was used in a one-pot process, 93% yield was obtained (Entry 8), with the
دریافت فوری متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات