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Journal of Molecular Catalysis A: Chemical 252 (2006) 235–237
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
www.elsevier.com/locate/molcata

Short communication

A rapid and high-yielding synthesis of thiazoles and aminothiazoles using ammonium-12-molybdophosphate☆

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Received 10 February 2006; received in revised form 23 February 2006; accepted 23 February 2006
Available online 3 April 2006

Abstract

A convenient method for the synthesis of thiazoles and aminothiazoles by treatment of phenacyl bromides with thioamides/thiourea in the presence of ammonium-12-molybdophosphate at room temperature has been developed. The products are formed rapidly (within 20 min) and in excellent yields.

Keywords: Thiazole; Aminothiazole; Phenacyl bromide; Thioamide; Thiourea; Ammonium-12-molybdophosphate

The thiazole ring unit is a common structural feature in various bioactive molecules [1]. This heterocyclic system has been employed in the preparation of different important drugs required for treatment of inflammation [2a], hypertension [2b], bacterial [2e] and HIV infections [2d]. Some of the thiazole analogues are used as fungicide, inhibiting in vivo the growth of *Xanthomonas* and as an ingredient of herbicides or an schistosomicidal and anthelmintic drugs [3]. Aminothiazoles are known to be ligands of estrogen receptor and as a novel class of adenosine receptor antagonists [4].

The solid supported synthesis to genarate thiazole libraries [5] and solution phase preparation of 2-aminothiazole combinatorial libraries [6] have previously been reported. These methods require high temperatures and long reaction times. The yields of some of the products are also unsatisfactory. Another synthesis of thiazoles in the presence of β-cyclodextrin was conducted at 50 °C during 1–2.5 h [7].

Recently we have developed an improved method for the synthesis of thiazoles and aminothiazoles by treatment of phenacyl bromides with thioamides/thiourea using ammonium-12-molybdophosphate [AMP], $(NH_4)_3[PMo_{12}O_{40}]$ [8] as a catalyst (Scheme 1).

The reaction was carried out at room temperature and the products were formed within 20 min. Various phenacyl bromides and thioamides or thiourea were applied (Table 1). The yields of thiazoles as well as aminothiazoles were excellent. The structures of the products were settled from their spectral (^{1}H NMR and MS) data.

The catalyst, AMP, the ammonium salt of a heteropoly acid, works under heterogeneous conditions. It can easily be handled and removed from the reaction mixture by simple filtration. Heteropoly acids and their salts have gained much importance in recent years because of their interesting catalytic activity and capability of conducting the reaction in cleaner manner compared to conventional liquid acid catalysts [9]. They have found industrial applications in various important procedures. However, the synthetic utility of these catalysts has not yet been fully explored. The present catalyst (AMP) is highly effective for the synthesis of thiazoles and aminothiazoles at room temperature. Possibly, it activates the carbonyl group of phenacyl bromides for rapid formation of thiazole derivatives. In absence of this catalyst the yields were lower (52–58%) even after 1 h.

In conclusion, we have developed a novel, mild, efficient and rapid method for the synthesis of thiazoles and aminothiazoles using ammonium salt of a heteropoly acid. We feel the method

☆ Part 86 in the series, "Studies on Novel Synthetic Methodologies". IICT Communication No. 060328.

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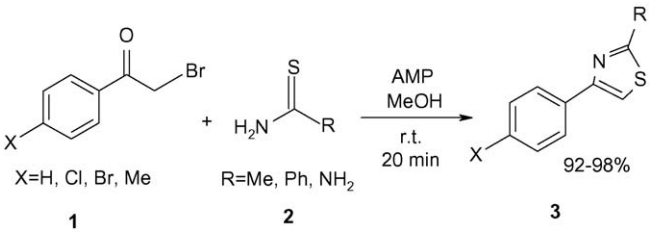
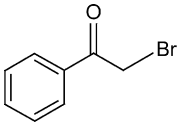
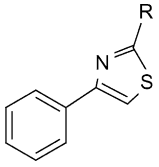
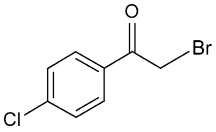
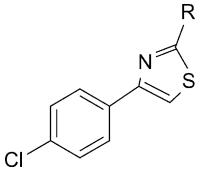
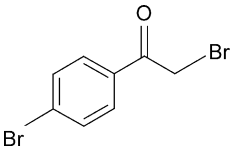
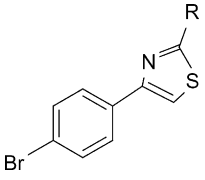
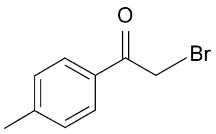
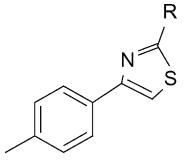
doi:10.1016/j.molcata.2006.02.065



Scheme 1.

Table 1
Synthesis of thiazoles and aminothiazoles using AMP[a]

Entry	Phenacyl bromide (**1**)	Thiazole/aminothiazole (**3**)	Isolated yield (%)
			
a		R = Me	95
b		R = Ph	94
c		R = NH_2	97
			
d		R = Me	92
e		R = Ph	95
f		R = NH_2	98
			
g		R = Me	96
h		R = Ph	97
i		R = NH_2	94
			
j		R = Me	93
k		R = Ph	95
l		R = NH_2	97

[a] The structures of the prepared thiazoles/aminothiazoles were settled from their spectral (^{1}H NMR and MS) data.

will find practical applications for the synthesis of these compounds.

1. Experimental

1.1. General procedure for the synthesis of thiazole derivatives

To a mixture of a phenacyl bromide (1 mmol) and thioamide/thiourea (1.2 mmol) in MeOH (5 ml) AMP (10 mol%) was added. The mixture was stirred at room temperature and the reaction was monitored by TLC. After 20 min the mixture was filtered. The filtrate was concentrated and the residue was subjected to column chromatography over silica gel using hexane-EtOAc (4:1) as eluent to afford pure thiazole/aminothiazole.

The Spectral (^{1}H NMR and MS) data of some representative compounds are given below.

3e: ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.05–7.84 (4H, m), 7.46–7.32 (6H, m); FABMS: *m/z* 274, 272 $[M+H]^+$.

3f: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.74 (2H, d, $J = 8.0$ Hz), 7.38 (2H, d, $J = 8.0$ Hz), 6.70 (1H, s), 5.29–5.11 (2H, brs); FABMS: *m/z* 213, 211 $[M+H]^+$.

3g: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.76 (2H, d, $J = 8.0$ Hz), 7.51 (2H, d, $J = 8.0$ Hz), 7.28 (1H, s), 2.77 (3H, s); FABMS: *m/z* 256, 254 $[M+H]^+$.

3l: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.60 (2H, d, $J = 8.0$ Hz), 7.17 (2H, d, $J = 8.0$ Hz), 6.58 (1H, s), 5.72–5.40 (2H, brs), 2.40 (3H, s); FABMS: *m/z* 191 $[M+H]^+$.

Acknowledgement

The authors thank CSIR and UGC, New Delhi for Financial assistance.

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