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$MgCl_2 \cdot 6H_2O$: An Efficient And Economic Catalyst For Three Component One-Pot Synthesis Of 3,4-Dihydropyrimidin-2(1H)-Ones And Thiones

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ABSTRACT

We synthesized 3,4-dihydropyrimidin-2(1H)-ones and thiones by $MgCl_2 . 6H_2O$ as an efficient, inexpensive and available catalyst under reflux condition in high yield.

KEYWORDS

$MgCl_2.6H_2O$;
Dihydropyrimidin-2(1H)-ones and thiones;
Biginelli reaction;
One-pot synthesis.

INTRODUCTION

In recent years, dihydropyrimidin-2(1H)-ones and thiones have occupied an important place in synthetic organic chemistry due to their pharmacological and therapeutic properties[1]. They have served as integral backbones of several calcium channel blockers, antihypertensive agents, a-1a-antagonists and neuropeptideY(NPY) antagonists[2] several isolated marine alkaloids with biological activities have been also found to contain the dihydropyrimidinones-5-carboxylate core[3]. Due to the importance of these compounds as synthons in organic synthesis, many methods for preparing such compounds have been developed, and the Biginelli reaction has gained particular importance for ongoing research programs[4].

Recently, $MgCl_2$ has reported for promoted aldol reaction of alpha-dimethylsilylesters with aldehydes, ketones and alpha-enones[5] theoretical study on dehydration process of $MgCl_2 \cdot 6H_2O$[6], synthesis of branched polyethylene from stock by an interference free tandem catalyst of $TiCl_4/MgCl_2$ and iron catalyst[7] and ethylene polymerization[8] In this communication, we report a simple, an efficient and economic method for the synthesis of dihydropyrimidinones and thiones using a catalytic amount(2 mol%) of $MgCl_2$ under reflux conditions (SCHEME 1).

Several activated and deactivated aromatic and

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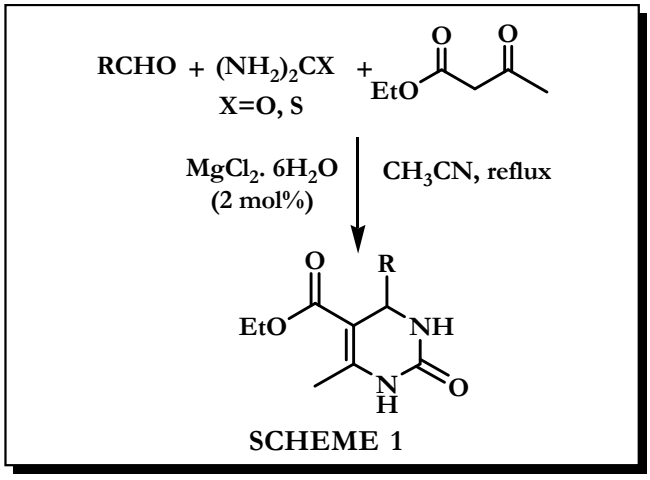
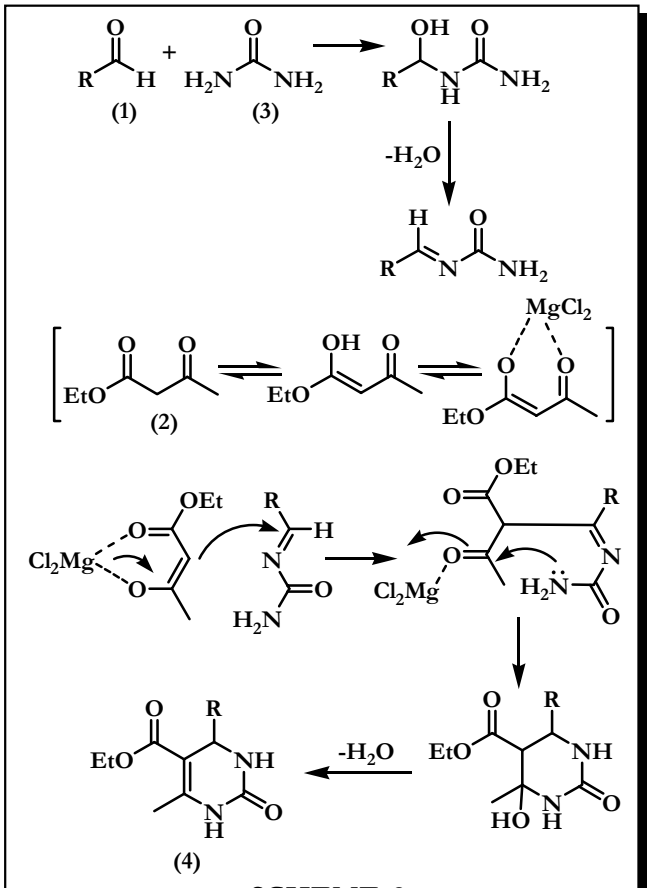


SCHEME 1

aliphatic aldehydes underwent the reaction to give the corresponding dihydropyrimidinones and thiones in good yields. The experimental procedure is very simple, convenient and has the ability to tolerate a variety of other functional groups such as methoxy, nitro, halide and olefins under the reaction conditions. Thiourea was used as one of the ingredients with similar success to provide the corresponding 3,4-dihydropyrimidin-2(1H)-thiones (TABLE 1).

The proposed mechanism shows that at first step of the reaction between aldehyde 1 and urea 3 is the formation of Schiff's base on the α-olefinic carbon of the tautomer followed by β-arbonyl carbon attack on imine-carbon to give a six-membered heterocyclic compound, which on dehydration leads to the target DHPMs 4 (SCHEME 2).



SCHEME 2

EXPERIMENTAL

Preparation of 3,4-dihydropyrimidin-2(1H)-ones and thiones: a typical procedure. In three-neck round bottomed flask equipped with condenser and thermometer, benzaldehyde(5mmol, 0.53cc), ethyl

TABLE 1: $MgCl_2.6H_2O$, catalyzed synthesis of dihydropyrimidinones and thiones

Entry	Aldehyde	X	Product	Time(h)	M.p(^{0}C)		Yield%[a]
					Observed	Reported	
1	PhCHO	O	4a	1.3	201-204	200-202[9]	90
2	4-Cl-PhCHO	O	4b	1.5	214-217	215-216[9]	87
3	3-Nitro-PhCHO	O	4c	0.7	225-228	226-227[10]	91
4	4-MeO-PhCHO	O	4d	3.5	202-204	201-202[11]	86
5	Ph-CH=CH-CHO	O	4e	3.0	158-160	157-159[13]	85
6	$CH_3CH_2CH_2CHO$	O	4f	0.7	152-154	153-155[12]	88
7	CH_3CH_2CHO	O	4g	1.0	171-174	170-172[14]	93
8	$(CH_3)_2CH$-CHO	O	4h	0.5	170-173	170-172[12]	85
9	PhCHO	S	4i	2.0	209-211	208-210[11]	84
10	4-Cl-PhCHO	S	4j	1.0	191-195	192-195[11]	82
11	4-MeO-PhCHO	S	4k	4.1	153-156	153-155[11]	88

a. Isolated yields

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acetate(5mmol, 0.5cc), urea(7.5mmol, 0.46g), $MgCl_2 \cdot 6H_2O$(0.1mmol, 0.02g), in acetonitrile(2.5ml) was stirred at reflux temperature for 75 minute (TABLE 1). Upon completion of the reaction, as indicated by TLC(eluent:n-hexane:ethyl acetate, 4:1), the solvent was removed under reduced pressure. The residue was poured on crushed ice and filtered to give crude the product, which was purified by re-crystallization from MeOH.

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