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An efficient synthesis of 4-substituted pyrazolyl-3,4-dihydropyrimidin-2(1H)-(thio)ones catalyzed by $Mg(ClO_4)_2$ under ultrasound irradiation

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Abstract

A simple method for the one-pot, three-component Biginelli condensation reaction of 5-chloro/phenoxyl-3-methyl-1-phenyl-4-formylpyrazole, a 1,3-dicarbonyl compound and urea or thiourea is described, employing Magnesium perchlorate [$Mg(ClO_4)_2$] as an efficient catalyst under ultrasound irradiation. A novel series of 4-substituted pyrazolyl-3,4-dihydropyrimidin-2(1H)-(thio)ones have been synthesized in moderate yields. The catalyst exhibited remarkable reactivity and can be recycled.

Keywords: Biginelli reaction; Magnesium perchlorate; Ultrasound irradiation; Dihydropyrimidinone; Pyrazole

1. Introduction

3,4-Dihydropyrimidin-2(1H)-ones are well known heterocyclic units in the realm of natural and synthetic organic chemistry due to their therapeutic and pharmacological properties including antiviral, antitumor, antibacterial and anti-inflammatory activities [1,2] and are medicinally important as calcium channel blockers, antihypertensive agents, α-1a-antagonists and neuropeptide Y (NPY) antagonists [3].

The Biginelli reaction was first reported by the Italian chemist Pietro Biginelli in 1893 and recently reviewed [4,5], and involves the synthesis of 3,4-dihydropyrimidin-2(1H)-ones by a very simple one-pot condensation reaction of an aldehyde, β-ketoester and urea in the presence of a strongly acid catalyst. However, this reaction suffers from the harsh conditions, long reaction time and frequently low yields of the desired target molecules, in particular when substituted aromatic or aliphatic aldehydes are employed.

In recent years, new methods for preparation of dihydropyrimidinones have been the subject of research for organic chemists. Consequently, several improved procedures have been reported, either by modification of the classical one-pot Biginelli approach itself [6], such as the use of a number of Lewis acid catalysts as well as protic acids including $FeCl_3$ [7], $ZnCl_2$, $CuCl_2$ and $NiCl_2$ [8], ZnI_2 [9], VCl_3 [10], Indium(III) halides [11], NH_4Cl [12], $ZrCl_4$ [13], H_3BO_3 [14], $Mn(OAc)_3{\cdot}2H_2O$ [15], silica sulfuric acid [16], $LiClO_4$ [17], $Sr(OTf)_2$ [18], $In(OTf)_3$ [19], SiO_2–$NaHSO_4$ [20], NH_2SO_3H [21]. In addition, ionic liquids [22], polymer-supported reagents [23] and polymer–metal complexes [24] have also been utilized as catalyts.

As increasing environmental consciousness in chemical research and industry, the challenge for a sustainable environment calls for clean procedures. Ultrasound as a green synthetic approach has gradually been used in organic synthesis over the last three decades. Compared with the traditional methods, it is more convenient, easier to be controlled, and consumes less power. With use of ultrasound irradiation, a large number of organic reactions can be carried out in milder conditions with shorter reaction time and higher product yields [25].

In the past works, some other groups used conventional substituted aliphatic and aromatic aldehydes as substrates. Due to the biological properties of pyrazole derivatives [26], in this work, we studied the possibility to synthesize 4-substituted pyrazolyl-3,4-dihydropyrimidin-2(1H)-(thio)ones

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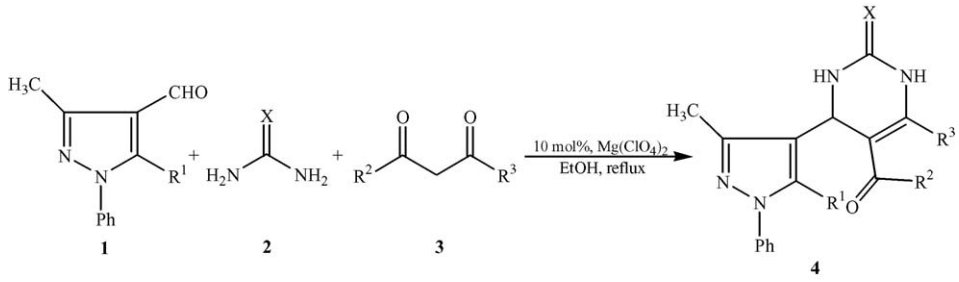


Scheme 1.

by the Biginelli reaction under ultrasound irradiation using 5-chloro/phenoxyl-3-methyl-1-phenyl-4-formylpyrazole instead of the ordinary aldehydes as substrates and employing $Mg(ClO_4)_2$ as the catalyst. Here, an efficient and practical method for the synthesis of target compounds is described and none of them has yet been reported in the literature.

2. Experiments

All compounds were characterized by IR, ^{1}H NMR spectra and elemental analysis. The IR spectra were obtained as potassium bromide pellets with a FTS-40 spectrometer (BIO-RAD, U.S.A). The ^{1}H NMR spectra were obtained on a Varian Inova-400 spectrometer using $CDCl_3$ or DMSO-d_6 as solvent (shown in details in data part) and TMS as an internal standard, chemical shifts are given in ppm. Elemental analysis (C, H, N) was performed on a Perkin-Elmer Analyzer 2400. Melting points were determined using a Büchi B-540 instrument. All melting points are uncorrected. Sonication was performed in a Kunshan ultrasonic cleaner with a frequency of 40 K Hz and a nominal power of 200 W (KQ5200B, Kunshan ultrasonic instrument Co. Ltd.).

2.1. General procedure for the synthesis of 4-substituted pyrazolyl-3,4-dihydropyrimidin-2(1H)-(thio)ones

General procedure for one-pot preparation of 4-substituted pyrazolyl-3,4-dihydronpyrimidin-2(1H)-(thio)ones **4** using $Mg(ClO_4)_2$ as a catalyst is that a mixture of 5-chloro/phenoxyl-3-methyl-1-phenyl-4-formylpyrazole (1 mmol), 1,3-dicarbonyl compound (1 mmol), urea or thiourea (1.2 mmol) and $Mg(ClO_4)_2$ (0.1 mmol) was refluxing at 80 °C in EtOH (Scheme 1) for a few hours (Table 1) without stirring. After the completion of the reaction (indicated by TLC on silica gel), most products crystallized spontaneously at room temperature, while products **4k** and **4p** crystallized after ethyl acetate was introduced to the reaction mixture and the mixture was concentrated. After filtration, the collected solid was washed with a little amount of ethanol, and then dried. The products were pure enough and were analyzed

Table 1
Magnesium perchlorate catalyzed one-pot synthesis of 4-substituted pyrazolyl-3,4-dihydropyrimidin-2(1H)-(thio)ones

Entry	R^1	R^2	R^3	X	Yields (%)		Time (h)[a]		Mp (°C)
					A[b]	B[b]	A[b]	B[b]	
4a	Cl	OEt	CH_3	O	86.5	87.2	4.0	2.0	242–243
4a	Cl	OEt	CH_3	O	92.5[c]		4.0		242–243
4b	Cl	OEt	CH_3	S	89.5	91.2	4.5	2.5	238–240
4c	Cl	OEt	Ph	O	72.1	75.4	5.5	3.0	233–235
4d	Cl	OEt	Ph	S	69.8	73.2	6.0	3.0	245–247
4e	Cl	CH_3	CH_3	O	83.4	86.4	4.0	2.0	236–240
4f	Cl	CH_3	CH_3	S	84.2	87.5	4.5	2.5	220.4[d]
4g	Cl	Ph	CH_3	O	73.0	76.4	6.0	3.0	242–244
4h	Cl	Ph	CH_3	S	74.8	77.1	5.0	2.5	208–210
4i	OPh	OEt	CH_3	O	80.2	82.8	5.0	2.5	209–211
4j	OPh	OEt	CH_3	S	78.4	80.2	6.5	3.0	245–246
4k	OPh	OEt	Ph	O	60.7	63.5	8.0	3.5	172–173
4l	OPh	OEt	Ph	S	58.4	60.4	8.0	3.5	147–149
4m	OPh	CH_3	CH_3	O	76.4	79.5	5.0	2.5	259–260
4n	OPh	CH_3	CH_3	S	73.6	75.0	6.5	3.0	242–243
4o	OPh	Ph	CH_3	O	59.2	60.5	8.0	3.5	204–206
4p	OPh	Ph	CH_3	S	57.3	59.7	8.5	3.5	200–202

[a] Reactions were finished until the TLC shown the starting materials disappeared.
[b] Method A: $Mg(ClO_4)_2$ as catalyst in EtOH refluxing at 80 °C without ultrasound. Method B: $Mg(ClO_4)_2$ as catalyst in EtOH refluxing at 80 °C under ultrasound irradiation.
[c] Yield of **4a** in CH_3CN for the first use of $Mg(ClO_4)_2$.
[d] Charring point of **4d,** which did not melt at 380 °C.

by ^{1}H NMR, IR and elemental analysis without further purificaton.

To investigate the generality of the catalyst, 5-chloro/phenoxyl-3-methyl-1-phenyl-4-formylpyrazole, a various of 1,3-dicarbonyl compounds and urea or thiourea were used to prepare the corresponding Biginelli products in moderate yields under both conventional condition and ultrasound irradiation condition. The results are showed in Table 1.

2.2. Physical and spectroscopic data of products

Compound **4a**: white powder. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.19 (t, J = 7.2 Hz, 3H, $CH_3{}^*CH_2O$), 2.30 (s, 3H, CH_3 on dihydropyrimidione ring), 2.41 (s, 3H, CH_3 on pyrazole ring), 4.13 (q, J = 7.2 Hz, 2H, OCH_2), 5.40 (s, 1H, CH), 5.58 (bs, 1H, NH), 7.26–7.48 (m, 5H, arom CH), 7.74 (bs, 1H, NH). IR (KBr): 3317, 3257, 3114, 2963, 2916, 1964, 1682, 1589, 1262, 1168, 756, 693 cm^{-1}. Anal. calcd. for $C_{18}H_{19}N_4O_3Cl$: C, 57.74; H, 5.12; N, 14.97. Found: C, 57.81; H, 5.05; N, 14.86.

Compound **4b**: light yellow powder. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.12 (t, J = 7.2 Hz, 3H, $CH_3{}^*CH_2O$), 2.09 (s, 3H, CH_3 on dihydropyrimidithione ring), 2.27 (s, 3H, CH_3 on pyrazole ring), 3.98 (q, J = 7.2 Hz, 2H, OCH_2), 5.28 (s, 1H, CH), 5.47 (bs, 1H, NH), 7.44–7.56 (m, 5H, arom CH), 7.79 (bs, 1H, NH). IR (KBr): 3378, 3233, 3181, 2988, 2902, 1949, 1686, 1574, 1219, 1206, 764, 696 cm^{-1}. Anal. calcd. for $C_{18}H_{19}N_4O_2SCl$: C, 55.37; H, 4.91; N, 14.36. Found: C, 55.48; H, 4.87; N, 14.44.

Compound **4c**: light yellow powder. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.82 (t, J = 7.2 Hz, 3H, $CH_3{}^*CH_2O$), 2.35 (s, 3H, CH_3 on pyrazole ring), 3.75 (q, J = 7.2 Hz, 2H, OCH_2), 5.43 (s, 1H, CH), 5.56 (bs, 1H, NH), 7.32–7.63 (m, 10H, arom CH), 7.81 (bs, 1H, NH). IR (KBr): 3389, 3279, 3137, 2975, 2912, 1962, 1671, 1590, 1229, 1158, 768, 698 cm^{-1}. Anal. calcd. for $C_{23}H_{21}N_4O_3Cl$: C, 63.28; H, 4.85; N, 12.84. Found: C, 63.39; H, 4.78; N, 12.94.

Compound **4d**: yellow powder. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 0.73 (t, J = 7.2 Hz, 3H, $CH_3{}^*CH_2O$), 2.32 (s, 3H, CH_3 on pyrazole ring), 3.74 (q, J = 7.2 Hz, 2H, OCH_2), 5.38 (s, 1H, CH), 5.53 (bs, 1H, NH), 7.29–7.58 (m, 10H, arom CH), 7.76 (bs, 1H, NH). IR (KBr): 3384, 3262, 3123, 2958, 2912, 1927, 1682, 1596, 1256, 1204, 757, 691 cm^{-1}. Anal. calcd. for $C_{23}H_{21}N_4O_2SCl$: C, 61.05; H, 4.68; N, 12.39. Found: C, 61.17; H, 4.62; N, 12.49.

Compound **4e**: light brown powder. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.83 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3 on dihydropyrimidione ring), 2.48 (s, 3H, CH_3 on pyrazole ring), 5.42 (s, 1H, CH), 5.54 (bs, 1H, NH), 6.79–7.58 (m, 5H, arom CH), 7.98 (bs, 1H, NH). IR (KBr): 3329, 3208, 3112, 2946, 2919, 1953, 1693, 1595, 1274, 1198, 748, 697 cm^{-1}. Anal. calcd. for $C_{17}H_{17}N_4O_2Cl$: C, 59.28; H, 4.98; N, 16.28. Found: C, 59.37; H, 5.06; N, 16.35.

Compound **4f**: red powder. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.82 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3 on dihydropyrimidithione ring), 2.46 (s, 3H, CH_3 on pyrazole ring), 5.39 (s, 1H, CH), 5.48 (bs, 1H, NH), 6.72–7.53 (m, 5H, arom CH), 7.92 (bs, 1H, NH). IR (KBr): 3351, 3220, 3109, 2937, 2906, 1953, 1693, 1585, 1224, 1204, 759, 703 cm^{-1}. Anal. calcd. for $C_{17}H_{17}N_4OSCl$: C, 56.65; H, 4.76; N, 15.56. Found: C, 56.76; H, 4.81; N, 15.47.

Compound **4g**: yellow powder. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.83 (s, 3H, CH_3 on dihydropyrimidione ring), 2.33 (s, 3H, CH_3 on pyrazole ring), 5.37 (bs, 1H, CH), 5.84 (s, 1H, NH), 7.39–7.67 (m, 10H, arom CH), 7.72 (bs, 1H, NH). IR (KBr): 3367, 3227, 3198, 2951, 2918, 1963, 1689, 1592, 1296, 1134, 743, 698 cm^{-1}. Anal. calcd. for $C_{22}H_{19}N_4O_2Cl$: C, 65.01; H, 4.72; N, 13.79. Found: C, 65.12; H, 4.65; N, 13.87.

Compound **4h**: brown powder. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.80 (s, 3H, CH_3 on dihydropyrimidithione ring), 2.29 (s, 3H, CH_3 on pyrazole ring), 5.33 (bs, 1H, CH), 5.78 (s, 1H, NH), 7.37–7.62 (m, 10H, arom CH), 7.69 (bs, 1H, NH). IR (KBr): 3373, 3252, 3136, 2962, 2907, 1952, 1687, 1582, 1238, 1208, 761, 692 cm^{-1}. Anal. calcd. for $C_{22}H_{19}N_4OSCl$: C, 62.54; H, 4.54; N, 13.27. Found: C, 62.67; H, 4.59; N, 13.38.

Compound **4i**: yellow powder. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.24 (t, J = 7.2 Hz, 3H, $CH_3{}^*CH_2O$), 1.87 (s, 3H, CH_3 on dihydropyrimidione ring), 2.42 (s, 3H, CH_3 on pyrazole ring), 4.14 (q, J = 7.2 Hz, 2H, OCH_2), 5.38 (s, 1H, CH), 5.47 (bs, 1H, NH), 6.79–7.58 (m, 10H, arom CH), 7.68 (bs, 1H, NH). IR (KBr): 3386, 3265, 3197, 2972, 2913, 1927, 1683, 1584, 1221, 1149, 749, 692 cm^{-1}. Anal. calcd. for $C_{24}H_{24}N_4O_4$: C, 66.64; H, 5.60; N, 12.96. Found: C, 66.81; H, 5.53; N, 12.85.

Compound **4j**: light yellow powder. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.24 (t, J = 7.2 Hz, 3H, $CH_3{}^*CH_2O$), 1.84 (s, 3H, CH_3 on dihydropyrimidithione ring), 2.38 (s, 3H, CH_3 on pyrazole ring), 4.12 (q, J = 7.2 Hz, 2H, OCH_2), 5.34 (s, 1H, CH), 5.42 (bs, 1H, NH), 6.77–7.55 (m, 10H, arom CH), 7.64 (bs, 1H, NH). IR (KBr): 3385, 3221, 3178, 2983, 2914, 1943, 1686, 1582, 1236, 1206, 761, 694 cm^{-1}. Anal. calcd. for $C_{24}H_{24}N_4O_3S$: C, 64.26; H, 5.40; N, 12.50. Found: C, 64.37; H, 5.44; N, 12.61.

Compound **4k**: white powder. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.16 (t, J = 7.2 Hz, 3H, $CH_3{}^*CH_2O$), 2.29 (s, 3H, CH_3 on pyrazole ring), 3.69 (q, J = 7.2 Hz, 2H, OCH_2), 5.27 (s, 1H, CH), 5.41 (bs, 1H, NH), 6.66–7.52 (m, 15H, arom CH), 7.59 (bs, 1H, NH). IR (KBr): 3396, 3218, 3126, 2976, 2924, 1938, 1692, 1592, 1242, 1142, 764, 689 cm^{-1}. Anal. calcd. for $C_{29}H_{26}N_4O_4$: C, 70.42; H, 5.30; N, 11.33. Found: C, 70.59; H, 5.37; N, 11.42.

Compound **4l**: yellow powder. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.24 (t, J = 7.2 Hz, 3H, $CH_3{}^*CH_2O$), 2.50 (s, 3H, CH_3 on pyrazole ring), 3.88 (q, J = 7.2 Hz, 2H, OCH_2), 5.51 (s, 1H, CH), 6.78 (bs, 1H, NH), 6.86–7.41 (m, 15H, arom CH), 7.58 (bs, 1H, NH). IR (KBr): 3312, 3234, 3114, 2987, 2907, 1956, 1697, 1595, 1249, 1203, 768, 697 cm^{-1}. Anal. calcd. for $C_{29}H_{26}N_4O_3S$: C, 68.21; H, 5.14; N, 10.98. Found: C, 68.37; H, 5.08; N, 11.12.

Compound **4m**: yellow powder. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.85 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3 on dihydropyrimidione ring), 2.41 (s, 3H, CH_3 on pyrazole ring), 5.37 (s, 1H, CH), 5.44 (bs, 1H, NH), 6.77–7.55 (m, 10H, arom CH), 7.94 (bs, 1H, NH). IR (KBr): 3395, 3232, 3117, 2976, 2932, 1938, 1699, 1596, 1240, 1172, 752, 691 cm^{-1}. Anal. calcd. for $C_{23}H_{22}N_4O_3$: C, 68.63; H, 5.51; N, 13.93. Found: C, 68.79; H, 5.46; N, 13.84.

Compound **4n**: yellow powder. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.80 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3 on dihydropyrim-

idithione ring), 2.43 (s, 3H, CH_3 on pyrazole ring), 5.41 (s, 1H, CH), 5.53 (s, 1H, NH), 6.77–7.55 (m, 10H, arom CH), 7.78 (bs, 1H, NH). IR (KBr): 3312, 3230, 3118, 2967, 2912, 1928, 1694, 1593, 1247, 1207, 762, 692 cm^{-1}. Anal. calcd. for $C_{23}H_{22}N_4O_2S$: C, 66.01; H, 5.30; N, 13.40. Found: C, 66.17; H, 5.38; N, 13.51.

Compound **4o**: yellow powder. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.07 (s, 3H, CH_3 on dihydropyrimidione ring), 2.47 (s, 3H, CH_3 on pyrazole ring), 5.48 (s, 1H, CH), 5.92 (bs, 1H, NH), 6.94–7.67 (m, 15H, arom CH), 8.22 (bs, 1H, NH). IR (KBr): 3384, 3224, 3117, 2956, 2917, 1962, 1695, 1592, 1235, 1173, 759, 693 cm^{-1}. Anal. calcd. for $C_{28}H_{24}N_4O_3$: C, 72.38; H, 5.21; N, 12.07. Found: C, 72.55; H, 5.17; N, 12.16.

Compound **4p**: light yellow powder. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.05 (s, 3H, CH_3 on dihydropyrimidithione ring), 2.55 (s, 3H, CH_3 on pyrazole ring), 5.47 (s, 1H, CH), 5.86 (bs, 1H, NH), 6.97–7.62 (m, 15H, arom CH), 8.17 (bs, 1H, NH). IR (KBr): 3398, 3227, 3119, 2974, 2921, 1960, 1685, 1594, 1257, 1202, 762, 694 cm^{-1}. Anal. calcd. for $C_{28}H_{24}N_4O_2S$: C, 69.98; H, 5.04; N, 11.67. Found: C, 70.14; H, 5.11; N, 11.78.

3. Results and discussion

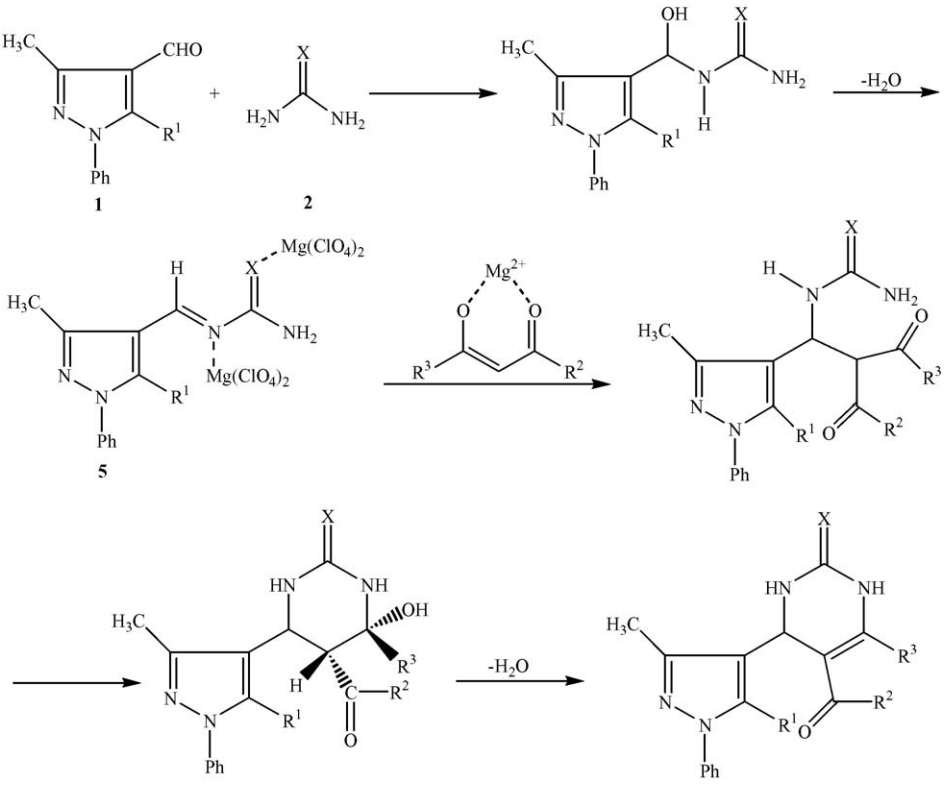
Data in Table 1 clearly shows that the condensation of 5-chloro/phenoxyl-3-methyl-1-phenyl-4-formylpyrazole with a 1,3-dicarbonyl compound and urea or thiourea employing $Mg(ClO_4)_2$ as a catalyst leading to 4-substituted pyrazolyl-3,4-dihydropyrimidin-2(1H)-(thio)ones was carried out smoothly under both conventional and ultrasound irradiation conditions. As a catalyst, $Mg(ClO_4)_2$ exhibited a remarkable reactivity in both methods. Comparing to the conventional heating method, the achieved yields under ultrasound irradiation increase two or three percent with only half reaction time needed.

In order to get the best molar ratio of reaction materials, we also did the experiment with different ratios of 5-chloro/phenoxyl-3-methyl-1-phenyl-4-formylpyrazole, 1,3-dicarbonyl compounds, urea or thiourea and $Mg(ClO_4)_2$. We found that the reaction gave the best results when the molar ratio of reactants was 1:1:1.2:0.1, respectively.

Through all the experiments, we found that when $PhCOCH_2COCH_3$ or $PhCOCH_2COOEt$ was used as 1,3-dicarbonyl compounds, especially when $R^1 = -Oph$, it was difficult to get the target compounds and the yields were lower than others. This may be because of the steric hindrance between the aromatics.

As a model reaction, the condensation reaction of 5-chloro-3-methyl-1-phenyl-4-formylpyrazole, ethyl acetoacetate and urea in thermal conditions was repeated three times through the reuse of filter liquor containing the used catalyst. To study reusability of the catalyst, we did the same reaction in ethanol and acetonitrile. When ethanol was used as solvent, the yields were 86.5%, 80.8%, 76.4%, respectively, indicating that the catalyst was recyclable. While, when we did this reaction in acetonitrile, the yields were 92.5%, 87.8%, 85.5%, respectively. It is apparent that the yields were higher using CH_3CN than using EtOH as solvent. This is an obvious solvent effect. Developing a polar aproter solvent provides higher reactivity.

A proposed reaction mechanism of Biginelli condensation via acyl imine intermediate **5** is presented in Scheme 2, this intermediate is formed by the reaction of the 5-chloro/phenoxyl-



Scheme 2.

3-methyl-1-phenyl-4-formylpyrazole **1** and urea or thiourea **2** and then stabilized by $Mg(ClO_4)_2$. Subsequent addition of a 1,3-dicarbonyl compound enolate to the acyl imine, followed by cyclization and dehydration, producing the corresponding 4-substituted pyrazolyl-3,4-dihydropyrimidin-2(1H)-(thio)ones.

4. Conclusion

Here, we reported a catalytic method for synthesis of a series of novel 4-substituted pyrazolyl-3,4-dihydropyrimidin-2(1H)-(thio)ones using 5-chloro/phenoxyl-3-methyl-1-phenyl-4-formylpyrazole instead of conventional aldehydes, employing $Mg(ClO_4)_2$ as an efficient and reusable catalyst in ultrasound irradiation compared with the conventional refluxing method. It is an important supplement to the existing methods for the synthesis of dihydroprimidiones and their thio-derivatives.

References

[1] B. Jauk, F. Belaj, C.O. Kappe, J. Chem. Soc., Perkin Trans. 1 (1999) 307.

[2] (a) B.C. Ranu, A. Hajra, U. Jana, J. Org. Chem. 65 (2000) 6270;
(b) Y. Ma, C. Qian, L. Wang, M. Yang, J. Org. Chem. 65 (2000) 3864;
(c) K. Ramalinga, P. Vijayalakshmi, T.N. Kaimal, Synlett (2001) 863.

[3] (a) J. Lu, Y.J. Bai, Z.J. Wang, B.Q. Yang, H.R. Ma, Tetrahedron Lett. 41 (2000) 9075;
(b) C.O. Kappe, Tetrahedron 49 (1993) 6937.

[4] P. Biginelli, Gazz. Chim. Ital. 23 (1893) 360.

[5] C.O. Kappe, Eur. J. Med. Chem. 35 (2000) 1043.

[6] (a) K. Singh, J. Singh, P.K. Deb, H. Singh, Tetrahedron 55 (1999) 12873;
(b) A. Dondoni, A. Massi, E. Minghini, S. Sabbatini, V.J. Bertolasi, Org. Chem. 68 (2003) 6172.

[7] I. Cepanec, M. Litvić, A. Bartolinčić, M. Lovrić, Tetrahedron 61 (2005) 4275.

[8] H.E. Badaoui, F. Bazi, R. Tahir, H.B. Lazrek, S. Sebti, Catal. Commun. 6 (2005) 455.

[9] G. Jenner, Tetrahedron Lett. 45 (2004) 6195.

[10] G. Sabitha, G.S.K.K. Reddy, K.B. Reddy, J.S. Yadav, Tetrahedron Lett. 44 (2003) 6497.

[11] (a) N.Y. Fu, Y.F. Yuan, M.L. Pang, J.T. Wang, C. Peppe, J. Organomet. Chem. 672 (2003) 52;
(b) M.A.P. Martins, M.V.M. Teixeira, W. Cunico, E. Scapin, R. Mayer, C.M.P. Pereira, N. Zanatta, H.G. Bonacorso, C. Peppe, Y.F. Yuan, Tetrahedron Lett. 45 (2004) 8991.

[12] A. Shaabani, A. Bazgir, F. Teimouri, Tetrahedron Lett. 44 (2003) 857.

[13] C.V. Reddy, M. Mahesh, P.V.K. Raju, T.R. Babu, V.V.N. Reddy, Tetrahedron Lett. 43 (2002) 2657.

[14] S.J. Tu, F. Fang, C.B. Miao, H. Jiang, Y.J. Feng, D.Q. Shi, X.S. Wang, Tetrahedron Lett. 44 (2003) 6153.

[15] K.A. Kumar, M. Kasthuraiah, C.S. Reddy, C.D. Reddy, Tetrahedron Lett. 42 (2001) 7873.

[16] P. Salehi, M. Dabiri, M.A. Zolfigol, M.A.B. Fard, Tetrahedron Lett. 44 (2003) 2889.

[17] J.S. Yadav, B.V.S. Reddy, R. Srinivas, C. Venugopal, T. Ramalingam, Synthesis (2001) 1341.

[18] W.K. Su, J.J. Li, Z.G. Zheng, Y.C. Shen, Tetrahedron Lett. 46 (2005) 6037.

[19] R. Ghosh, S. Maiti, A. Chakraborty, J. Mol. Catal. A Chem. 217 (2004) 47.

[20] M.A. Chari, K. Syamasundar, J. Mol. Catal. A Chem. 221 (2004) 137.

[21] J.T. Li, J.F. Han, J.H. Yang, T.S. Li, Ultrason. Sonochem. 10 (2003) 119.

[22] J.J. Peng, Y.Q. Deng, Tetrahedron Lett. 42 (2001) 5917.

[23] A. Dondoni, A. Massi, Tetrahedron Lett. 42 (2001) 7975.

[24] R.V. Yarapathi, S. Kurva, S. Tammishetti, Catal. Commun. 5 (2004) 511.

[25] (a) H.A. Stefani, C.M.P. Pereira, R.B. Almeida, R.C. Braga, K.P. Guzen, R. Cella, Tetrahedron Lett. 46 (2005) 6833;
(b) Z.L. Shen, S.J. Ji, S.Y. Wang, X.F. Zeng, Tetrahedron 61 (2005) 10552.

[26] (a) J. Regan, S. Breitfelder, P. Cirillo, T. Gilmore, A.G. Graham, E. Hickey, B. Klaus, J. Madwed, M. Moriak, N. Moss, C. Pargellis, S. Pav, A. Proto, A. Swinamer, L. Tang, C. Torcellini, J. Med. Chem. 45 (2002) 2994;
(b) P. Pevarello, M.G. Brasca, R. Amici, P. Orsini, G. Traquandi, L. Corti, C. Piutti, P. Sansonna, M. Villa, B.S. Pierce, M. Pulici, P. Giordano, K. Martina, E.L. Fritzen, R.A. Nugent, E. Casale, A. Cameron, M. Ciomei, F. Roletto, A. Isacchi, G. Fogliatto, E. Pesenti, W. Pastori, A. Marsiglio, K.L. Leach, P.M. Clare, F. Fiorentini, M. Varasi, A. Vulpetti, M.A. Warpehoski, J. Med. Chem. 47 (2004) 3367.