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EASY SYNTHESIS OF 3,4-DIHYDROPYRIMIDIN-2-(1H)-ONE DERIVATIVES USING PHOSPHATE FERTILIZERS MAP, DAP, AND TSP AS EFFICIENT CATALYSTS

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Abstract: A simple, efficient, and green procedure has been developed for the synthesis of dihydropyrimidinones (Products of Biginelli) using phosphate fertilizers (mono-ammonium phosphate (MAP), di-ammonium phosphate (DAP) and triple super phosphate (TSP)) as catalyst. The one-step reaction involved the three compounds, which are registered aromatic aldehydes, dicarbonyl compounds and the urea/thiourea. This new method provides some advantages such as obtaining excellent yields (98%), as well as the short duration of the reaction, which may attain 2 minutes. These catalytic heterogeneous systems present also the advantage of being easily recycled.

Keywords: Heterogeneous catalysts; MAP; DAP; TSP; 3,4-dihydropyrimidin-2(1H)-ones; phosphate fertilizers.

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INTRODUCTION

The dihydropyrimidinone derivatives constitute a major family usually with therapeutic and pharmacological properties such as antiviral agents, antimitotic, anticarcinogenic, antihypertensive medications and especially, as modulators of calcium channels (1–4). The Biginelli reaction was described for the first time by the Italian chemist Pietro Biginelli 1893(5), where the reaction was carried out in one-step, putting together an aromatic aldehyde and urea with the ethyl acetoacetate in a strongly acidified ethanolic reflux. However, this method has some disadvantages, such as the severe conditions in which the reaction takes place and attains low yields. The use of catalysts in the condensation of Biginelli became necessary to improve the yields and the time of reaction. We note in recent years, significant efforts made in order to find new procedures to produce 3,4-dihydropyrimidin-2(1H)-one derivatives with good yields. The use of catalysts in the condensation of Biginelli became necessary to improve the yields and the time of reaction. We note in recent years, significant efforts which have been made to find new procedures to produce 3,4-dihydropyrimidin-2(1H)-one derivatives. These protocols use either Brønsted acids (6) metal catalysts such as sulfonic acid nanomagnetic (7) and the iron (III) tosylate (8), bis[(L)-prolinato-N,O]Zn-water (9), the 1-glycyl-3-methyl copper chloride imidazolium (II) (10), but the use of transition metals is toxic and dangerous. The aim of this work is to use a simple synthetic, green, and effective protocol for the synthesis of dihydropyrimidin-2(1H)-one and dihydropyrimidin-2(1H)-thione derivatives using three phosphate compounds as catalysts, in addition to traditional reagents of Biginelli reaction: urea or thiourea, ester β-ketones and aldehyde in ethanol. This method gave the expected products with good yields accompanied by a reduction in reaction time, compared to conventional conditions.

MATERIALS AND METHODS

All chemicals were purchased from Merck or Fluka Chemical Companies. The known products were identified by comparison of their melting points and spectral data with those reported in the literature. TLC using silica gel SIL G/UV 254 plates monitored the progress of the reactions. Melting points were recorded on a Kofler hot stage apparatus and are uncorrected.

General procedure of synthetic 3,4-dihydropyrimidin-2(1H)-one or thione derivatives 4. A mixture of aromatic aldehyde (1 mmol), 1.3-dicarbonyl compounds (1 mmol), urea or thiourea (1.5 mmol) was prepared. After that we added MAP (3 mol %) or DAP or TSP (1 mol %) as catalyst. The mixture was dissolved in 1 mL of absolute ethanol. The mixture was refluxed for appropriate time and the progress of the reaction was monitored by TLC. After

completion of the reaction the catalyst was recovered by filtration, the filtrate was evaporated and treated with acetonitrile and the solid was then washed with water. The product was purified by recrystallization with ethanol to give the pure 3,4-dihydropyrimidin-2(1H)-one derivatives **4a-k** and 3,4-dihydropyrimidin-2(1H)-thione derivatives **4l-o**.

All spectral data of synthesized products are described below and compare favorably to those reported in the literature. Melting points are reported in Table 4.

5-Acetyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one **4a**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.16 (s, 1H, NH), 7.78 (s, 1H, NH), 6.84-7.18 (m, 5H, ArH), 5.21 (s, 1H, CH), 2.35 (s, 3H, CH_3), 2.16 (s, 3H, CH_3). Anal. Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17%. Found C, 67.80; H, 6.15; N, 12.15%.

5-Acetyl-4-(4-chlorophenyl)-3,4-dihydro-6-methylpyrimidin-2(1H)-one **4b**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.17 (s, 1H, NH), 7.69 (s, 1H, NH), 7.17 (d, *J*= 8.2 Hz, 2H, ArH), 6.86 (d, *J*= 8.2 Hz, 2H, ArH), 5.10 (s, 1H, CH), 2.32 (s, 3H, CH_3), 2.10 (s, 3H, CH_3). Anal. Calcd for $C_{13}H_{13}ClN_2O_2$: C, 58.98; H, 4.95; N, 10.57; Cl, 13.38%. Found C, 85.97; H, 4.67; N, 10.55; Cl, 13.36%.

5-Acetyl-6-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one **4c**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.18 (s, 1H, NH), 8.20 (d, *J*= 8.4 Hz, 2H, ArH), 7.92 (s, 1H, NH), 7.50 (d, *J*= 8.4 Hz, 2H, ArH), 5.18 (s, 1H, CH), 2.31 (s, 3H, CH_3), 2.18 (s, 3H, CH_3). Anal. Calcd for $C_{13}H_{13}N_3O_4$: C, 56.72; H, 4.76; N, 15.27%. Found C, 56.70; H, 4.74; N, 15.28%.

5-Acetyl-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one **4d**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.35 (s, 1H, NH), 8.26 (d, *J*= 8.2 Hz, 2H, ArH), 7.99 (s, 1H, NH), 7.46 (d, *J*= 8.2 Hz, 2H, ArH), 5.31 (s, 1H, CH), 3.43 (s, 3H, OCH_3), 2.32 (s, 3H, CH_3), 2.09 (s, 3H, CH_3). Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.61; H, 6.20; N, 10.75%. Found C, 64.63; H, 6.22; N, 10.74%.

5-Ethoxycarbonyl-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one **4e**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.19 (s, 1H, NH), 8.16 (d, *J*= 8.1 Hz, 2H, ArH), 7.92 (s, 1H, NH), 7.58 (d, *J*= 8.1 Hz, 2H, ArH), 5.20 (s, 1H, CH), 3.97 (q, *J*= 7.0 Hz, 2H, OCH_2CH_3), 3.34

(s, 3H, OCH_3), 2.19 (s, 3H, CH_3), 1.07 (t, *J*= 7.0 Hz, 3H, OCH_2CH_3). Anal. Calcd for $C_{15}H_{18}N_2O_4$: C, 62.05; H, 6.25; N, 9.65%. Found C, 62.07; H, 6.23; N, 9.68%.

5-Ethoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one **4f**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.31 (s, 1H, NH), 7.87 (s, 1H, NH), 7.40 (d, *J*= 8.2 Hz, 2H, ArH), 7.21 (d, *J*= 8.2 Hz, 2H, ArH), 5.25 (s, 1H, CH), 3.92 (q, *J*= 7.0 Hz, 2H, OCH_2CH_3), 2.26 (s, 3H, CH_3), 1.06 (t, *J*= 7.0 Hz, 3H, OCH_2CH_3). Anal. Calcd for $C_{14}H_{15}N_3O_5$: C, 55.08; H, 4.92; N, 13.77%. Found: C, 55.14; H, 4.95; N, 13.69%.

5-Ethoxycarbonyl-4-(4-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one **4g**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.25 (s, 1H, NH), 7.78 (s, 1H, NH), 7.37 (d, *J*= 8.3 Hz, 2H, ArH), 7.23 (d, *J*= 8.3 Hz, 2H, ArH), 5.26 (s, 1H, CH), 3.95 (q, *J*= 7.0 Hz, 2H, OCH_2CH_3) 2.24 (s, 3H, CH_3), 1.10 (t, *J*= 7.0 Hz, 3H, OCH_2CH_3). Anal. Calcd for $C_{14}H_{15}ClN_2O_3$: C, 57.05; H, 5.13; N, 9.50, Cl, 12.03%. Found: C, 57.13; H, 5.09; N, 9.44, Cl, 12.04%.

5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one **4h**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.18 (s, 1H, NH), 7.85 (s, 1H, NH), 7.20-7.30 (m, 5H, ArH), 5.20 (s, 1H, CH), 3.98 (q, *J*= 7.2 Hz, 2H, OCH_2CH_3), 2.22 (s, 3H, CH_3), 1.08 (t, *J*= 7.2 Hz, 3H, OCH_2CH_3). Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.61; H, 6.20; N, 10.77%. Found: C, 64.63; H, 6.18; N, 10.80%.

5-Ethoxycarbonyl-6-methyl-4-(p-tolyl)-3,4-dihydropyrimidin-2(1H)-one **4i**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 8.98 (s, 1H, NH), 7.94 (s, 1H, NH), 7.21 (d, *J*= 8.1 Hz, 2H, ArH), 7.09 (d, *J*= 8. Hz, 2H, ArH), 5.17 (s, 1H, CH), 4.01 (q, *J*= 7.2 Hz, 2H, OCH_2CH_3), 2.35 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 1.10 (t, *J*= 7.2 Hz, 3H, OCH_2CH_3). Anal. Calcd for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.62; N, 10.21%. Found: C, 65.65; H, 6.60; N, 10.17%.

5-Ethoxycarbonyl-6-methyl-4-(4-N,N-dimethylaminophenyl)-3,4-dihydropyrimidin-2(1H)-one **4j**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.21 (s, 1H, NH), 7.78 (s, 1H, NH), 7.21-7.32 (m, 4H, ArH), 5.23 (s, 1H, CH), 3.94 (q, *J*= 7.3 Hz, 2H, OCH_2CH_3) 1.11 (t, *J*= 7.3 Hz, 3H, OCH_2CH_3), 2.60 (s, 6H, $N(CH_3)_2$), 2.24 (s, 3H, CH_3). Anal. Calcd for $C_{16}H_{21}N_3O_3$: C, 63.35; H, 6.99; N, 13.85%. Found C, 63.33; H, 6.96; N, 13.86%.

5-Ethoxycarbonyl-4-(2,4-dichlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one **4k**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 10.34 (s, 1H, NH), 9.66 (s, 1H, NH), 7.20-7.63 (m, 3H, ArH), 5.18 (s, 1H, CH), 4.09 (q, 2H, *J*= 7.2 Hz, OCH_2CH_3), 2.29 (s, 3H, CH_3), 1.12 (t, 3H, *J*= 7.2 Hz, OCH_2CH_3). Anal. Calcd for $C_{14}H_{14}Cl_2N_2O_3$: C, 51.08; H, 4.29; N, 8.51; Cl, 21.54%. Found C, 51.10; H, 4.32; N, 8.53; Cl, 21.52%.

5-Ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-thione **4l**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.16 (s, 1H, NH), 8.01 (s, 1H, NH), 7.46 (d, *J*= 8.1 Hz, 2H, ArH), 7.11 (d, *J*= 8.1 Hz, 2H, ArH), 5.10 (s, 1H, CH), 3.98 (q, *J*= 7.1 Hz, 2H, OCH_2CH_3), 3.35 (s, 3H, OCH_3), 2.25 (s, 3H, CH_3), 1.12 (t, *J*= 7.2 Hz, 3H, OCH_2CH_3). Anal. Calcd for $C_{15}H_{18}N_2O_3S$: C, 58.80; H, 5.92; N, 9.14, S, 10.47%. Found C, 58.82; H, 5.90; N, 9.16, S, 10.49%.

5-Ethoxycarbonyl-6-methyl-4-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1H)-thione **4m**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.25 (s, 1H, NH), 8.01 (s, 1H, NH), 7.37 (d, J= 8.3 Hz, 2H, ArH), 7.23 (d, J= 8.3 Hz, 2H, ArH), 5.18 (s, 1H, CH), 4.08 (q, *J*= 7.1 Hz, 2H, OCH_2CH_3), 2.26 (s, 3H, CH_3), 1.15 (t, *J*= 7.1 Hz, 3H, OCH_2CH_3). Anal. Calcd for $C_{14}H_{15}ClN_2O_2S$: C, 51.10; H, 8.87; N, 9.01, Cl, 11.41, S, 10.32%. Found: C, 51.08; H, 8.86; N, 9.04, Cl, 11.40, S, 10.30%.

5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-thione **4n**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.41 (s, 1H, NH), 8.28 (s, 1H, NH), 7.14-7.31 (m, 5H, ArH), 5.16 (s, 1H, CH), 4.12 (q, 2H, *J*= 7.2 Hz, OCH_2CH_3), 2.29 (s, 3H, CH_3), 1.11 (t, 3H, *J*= 7.2 Hz, OCH_2CH_3). Anal. Calcd for $C_{14}H_{16}N_2O_2S$: C, 60.85; H, 5.84; N, 10.14, S, 11.61%. Found: C, 60.84; H, 5.82; N, 10.15, S, 11.60%.

5-Ethoxycarbonyl-6-methyl-4-(p-tolyl)-3,4-dihydropyrimidin-2(1H)-thione **4o**: ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 9.32 (s, 1H, NH), 8.10 (s, 1H, NH), 7.30 (d, J= 8.1 Hz, 2H, ArH), 7.10 (d, J= 8.3 Hz, 2H, ArH), 5.20 (s, 1H, CH), 3.98 (q, *J*= 7.2 Hz, 2H, OCH_2CH_3), 2.35 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 1.10 (t, *J*= 7.2 Hz, 3H, OCH_2CH_3). Anal. Calcd for $C_{15}H_{18}N_2O_2S$: C, 62.04; H, 6.25; N, 9.65, S, 11.04%. Found: C, 62.01; H, 6.23; N, 9.61, S, 11.09%.

RESULTS AND DISCUSSION

The synthesis of 3,4-dihydropyrimidin-2(1H)-one and 3,4-dihydropyrimidin-2(1H)-thione derivatives is carried out according to the overall reaction below in the presence of catalysts phosphates (11) (MAP or DAP or TSP) (Figure 1).

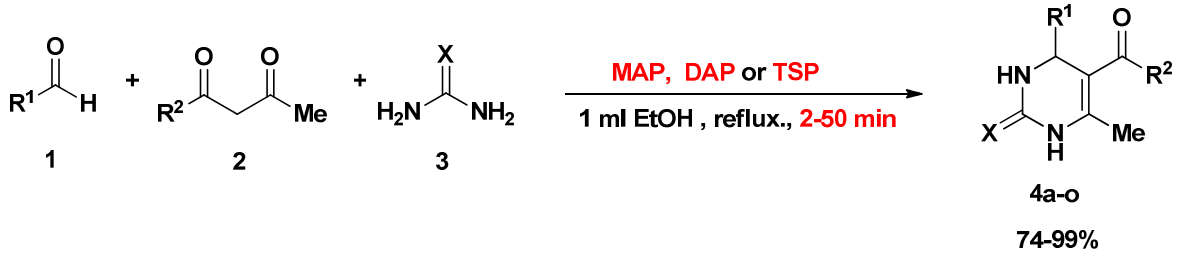

Figure 1. . Synthesis of the 3.4 -dihydropyrimidin-2-one derivatives in the presence of catalysts MAP or DAP or TSP.

To find the optimum conditions for the Biginelli reaction, we chose a reaction model on which we will study the influence of certain parameters that control the reaction, namely the solvent of the reaction, the volume of the solvent and the catalyst amount used. The condensation between benzaldehyde, ethyl acetoacetate and urea has been selected as a model of the reaction.

The 5-acetyl-6-methyl-4-phenyl-3,4-dihydropyrimidine-2-(1H)-one **4a** (R^1= C_6H_5, R^2= Me, X= O) has been prepared according to the reaction described in figure 1, in the presence of 5 mol% of MAP or DAP or TSP in 1 mL EtOH reflux, the yields and time of the reactions are shown in Table 1.

Table 1. Comparison between a few catalysts described in the literature and our catalysts.

Entry	Catalyst	Time	Yield %
1	nano-γ-Fe_2O_3-SO_3H	2 h	80 (7)
2	ASANPs	5.3 h	60 (12)
3	SBNPSA	3-4 h	90-95 (13)
4	MAP	7 min	87
5	DAP	17 min	98
6	TSP	7 min	92

According to the observed results, we note that the effectiveness of our three catalysts are higher than those of some catalysts described in the literature with respect to time and reaction yields. It should be noted that it is in heterogeneous catalysis in solid/liquid phase, the effect of the solvent is an essential factor. It can play a role as activating or inhibitor of the reaction. We studied the effect of the solvent on the reaction model chosen previously with different solvents, always in the presence of 5 mol% of the catalyst placed at reflux. The results are shown in Table 2 where the efficiency of the reaction in ethanol was higher compared to other solvents. Therefore, ethanol is the ideal solvent for this reaction.

Table 2. Influence of the solvent on the reaction of Biginelli[a].

Entry	Solvent (1 ml)	Time (min)			Yield%[b]		
		MAP	DAP	TAP	MAP	DAP	TSP
1	Ethanol	7	7	7	87	98	92
2	Methanol	11	7	7	57	97.7	88
3	Butanol	8	3	3	46	95	81
4	Isopropanol	23	4	4	53	86	80
5	DMF	8	4	4	48	89	89
6	Acetonitrile	14	11	11	54	78,7	86

[a] Reaction conditions: acetoacetate (**2a**) (1 mmol), benzaldehyde (**1a**) (1 mmol) and urea (**3a**) (1.5 mmol), catalyzed MAP or DAP or TSP under conditions at reflux.
[b] Isolated yield.

We have studied another factor, which is the volume of the solvent. To study the influence of this parameter we used ethanol; previously found to be the ideal solvent for this reaction (Table 2) by changing just the volume of the latter. The results summarized in Table 3 showed that the reaction yield does not exceed 58% in the absence of ethanol. Good yields were obtained when we used 1 mL of ethanol, but when the volume of ethanol is greater than 1 mL, it was noted that there is a lowering in the reaction yield. It may be explained by the formation of a film (layer) of ethanol into the surface of the catalyst disabling the interaction between the reactants and the catalyst, in addition to the dispersion of the substrates. Therefore, the optimal volume for carrying out this reaction is 1 mL.

Table 3. Influence of the solvent volume [a]

Entry	Volume of Ethanol	Time (min)			Yield %[b]		
		MAP	DAP	TSP	MAP	DAP	TSP
1	Solvent-free	3	2	4	58	74	89
2	1mL	7	7	7	87	98	92
3	2mL	30	50	21	86,3	90	90
4	3mL	55	110	40	85	60	85

[a] Reaction conditions: acetoacetate (**2a**) (1 mmol), benzaldehyde (**1a**) (1 mmol) and urea (**3a**) (1.5 mmol), catalyzed MAP or DAP or TSP under conditions at reflux.
[b] Isolated yield.

The effect of the amount of the catalysts was studied on the reaction of the synthesis of 3,4-dihydropyrimidin-2(1H)-one derivatives. To study the influence of this parameter on the

reaction, we have changed the amount of catalysts from 1 up to 10 mol%, the results are presented in Table 4. The good yields were obtained when we used the optimal weights (1 mol %) for the catalysts DAP or TSP, (3 mol %) for the catalyst MAP, we noted that when the amount of catalysts exceeds 4 mol%, the yields of reaction decreases.

One of the most significant features of the present article is the recyclability and reuse of the catalyst. The reuse of the catalyst was studied after the completion of the reaction performed under the optimized conditions. After the completion of the reaction, the catalyst was filtered hot and washed several times with ethyl acetate, then dried in the oven at 40°C. After these steps the catalyst was reused in other reactions. The experiment shows that our catalysts can be recycled five times without significant loss of catalytic activity (Figure 2).

Table 4. Optimization of amount of catalyst[a].

Entry	Amount of catalyst (mol %)	Time (min)			Yield %[b]		
		MAP	DAP	TSP	MAP	DAP	TSP
1	1	58	7	4	72	98	97
2	2	43	30	2	88	98	96
3	3	23	33	3	95	98	95
4	4	20	25	5	90	98	94
5	5	7	17	7	87	98	92
6	6	10	16	6	68	95	91
7	7	17	5	12	67	90	87
8	8	20	21	13	66	88	85
9	9	25	6	3	61	82	82
10	10	32	36	21	61	79	79

[a] Reaction conditions: acetoacetate (**2a**) (1 mmol), benzaldehyde (**1a**) (1 mmol) and urea (**3a**) (1.5 mmol), catalyzed MAP or DAP or TSP under conditions at reflux.
[b] Isolated yield.

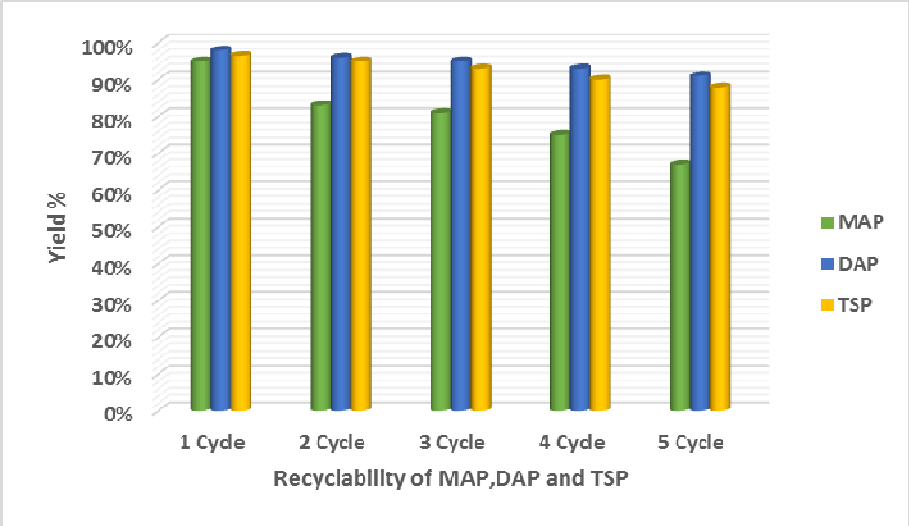

Figure 2. Recyclability of catalyst MAP, DAP and TSP in synthesis of 3.4-dihydropyrimidin-2(1H)-one.

After the optimization of the reaction conditions, we next thought to study the generality for the series of 3,4-dihydropyrimidin-2(1H)-one and 3,4-dihydropyrimidin-2(1H)-thione derivatives, using a wide range of various aryl-substituted aldehydes with different substituted β-ketoester (acetyl acetone or ethyl acetoacetate) and (urea or thiourea) under the optimal conditions. The results are presented in Table 5. As shown in this latter, the reaction of variety of substituted aromatic aldehydes with acetyl acetone and urea afforded the 3,4-dihydropyrimidin-2-one derivatives (entries **4a**-**4d**) at short time (2-25 min) in high yields (83-98%) and high purities. When using ethyl acetoacetate instead of acetyl acetone, the desired compounds were also obtained at significantly shortened times (2-50 min) and excellent yields (86-99%) (entries 4e-4k). Furthermore, the use of thiourea instead of urea the reaction provides the corresponding 3,4-dihydropyrimidin-2-thiones (**4l**-**4o**) with remarkable time-saving (2-9 min) and high-yielding process (74-98%).

CONCLUSION

In this work, we investigated a methodology for the synthesis of 3,4-dihydropyrimidin-2(1H)-one derivatives using phosphate fertilizers (MAP or DAP or TSP) as heterogeneous catalysts. We synthesized 3,4-dihydropyrimidin-2(1H)-one derivatives through a one step reaction using ethanol as a green solvent in short reaction times with high yields.

Table 5. Generalization of the synthesis of 3,4-dihydropyrimidin-2(1H)-one/thione **4** derivatives.

Compound no	R^1	R^2	X	Time (min)			Yield %[b]			Mp °C	
				MAP	DAP	TSP	MAP	DAP	TSP	Found	Reported
4a	C_6H_5	Me	O	7	7	4	98	95	96.5	210-212	208-219 (14)
4b	4-ClC_6H_4	Me	O	6	10	3	98	88	88	224-226	226-227 (14)
4c	4-$NO_2C_6H_4$	Me	O	3	2	2	91	90	89	236-238	238-240 (14)
4d	4-$MeOC_6H_4$	Me	O	20	25	10	84	83	97	190-191	191-193 (19)
4e	4-$MeOC_6H_4$	OEt	O	11	15	5	92	93	86	201-203	200-201 (13)
4f	4-$NO_2C_6H_4$	OEt	O	2	2	2	99	98	97	209-210	209-210 (13)
4g	4-ClC_6H_4	OEt	O	17	20	10	94	93	90	212-214	214-215 (13)
4h	C_6H_5	OEt	O	7	12	3	98	90	93	201-202	201-203 (13)
4i	4-MeC_6H_4	OEt	O	4	7	3	98	86	90	212-213	213-215 (16)
4j	4-$N(Me)_2C_6H_4$	OEt	O	35	50	20	92	91	92	231-233	228-230 (17)
4k	2,4-$(Cl)_2C_6H_3$	OEt	O	17	20	5	91	90	90	248-250	248-250 (13)
4l	4-$MeOC_6H_4$	OEt	S	7	5	3	97	98	92	138-140	140-141 (15)
4m	4-ClC_6H_4	OEt	S	3	5	2	98	96	97	192-194	193-195 (18)
4n	C_6H_5	OEt	S	4	9	5	74	94	91	208-209	209-210 (13)
4o	4-MeC_6H_4	OEt	S	3	3	2	90	88	93	214-215	214-215 (20)

[b] Isolated yield.

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