Chemical Papers
https://doi.org/10.1007/s11696-020-01327-7

ORIGINAL PAPER

# Synthesis of 3,4-dihydropyrimidin-2(1H)-ones catalyzed by poly(ferric 2-acrylamido-2-methylpropanesulfonate)

**Zhihao Zhao**[1] · **Hongguang Dai**[1] · **Lan Shi**[1]

Received: 28 May 2020 / Accepted: 17 August 2020

## Abstract

Poly(ferric 2-acrylamido-2-methylpropanesulfonate) (PFAMPS) was prepared via the reaction of poly(2-acrylamido-2-methylpropanesulfonic acid) and $Fe(OH)_3$. PFAMPS was used as a heterogeneous catalyst for the Biginelli reaction of aldehyde, ethyl acetoacetate, and urea to synthesize 3,4-dihydropyrimidin-2(1H)-ones with yields of 70–87%. PFAMPS can be recycled six times without significant loss in catalytic activity. For comparison, ferric lignosulfonate (FLSA), ferric cellulose sulfonate (FCSA), ferric starch sulfonate (FSSA), and ferric 732 cation exchange resin (FACER) were used as catalysts of the Biginelli reaction. It was shown that the catalytic activities of recycled FLSA, FCSA, FSSA, and FACER significantly decreased after two reactions. $Fe^{3+}$ in the polymer sulfonates acted as the catalyst for the Biginelli reaction. PFAMPS was the chelate, where the action between $Fe^{3+}$ and the poly(2-acrylamido-2-methylpropanesulfonate) matrix was strong, and $Fe^{3+}$ lost little from the PFAMPS. However, significant $Fe^{3+}$ loss was observed in the FLSA, FCSA, FSSA and FACER polymer matrices after reuse.

**Keywords** Biginelli reaction · Catalyst · Poly(ferric 2-acrylamido-2-methylpropanesulfonate) · Synthesis

## Introduction

3,4-Dihydropyrimidin-2(1H)-ones exhibit biological and pharmacological activities, and are widely used as calcium channel antagonists, anti-bacterial, anti-hypertensive, and anti-inflammatory agents (Tayebee and Ghadamgahi 2017). In 1893, Pietro Biginelli (1893) first reported the synthesis of 3,4-dihydropyrimidin-2(1H)-one (DHPM) by a simple one-pot condensation reaction of aromatic aldehydes, β-ketoesters and urea under strongly acidic conditions (Tayebee and Ghadamgahi 2017). In recent decades, a number of catalysts for the Biginelli reaction were studied by researchers, such as calix[8]arene sulfonic acid (An et al. 2016), phthalic acid (Mohamadpour et al. 2018), zirconium(IV) 4-sulphophenylethyliminobismethylphosphonate (Yang et al. 2011), gallium(III) triflate (Li et al. 2010), $Co(NO_3)_2$ (Nasr-Esfahani et al. 2014), iron(III) tosylate (Starcevich et al. 2013), 3-[(3-(trimethoxysilyl)propyl)thio]propane-1-oxy-sulfonic acid (Jetti et al. 2017), mesoporous $NH_4H_2PO_4$/MCM-41 (Tayebee and Ghadamgahi 2017), phosphotungstic acid grafted zeolite imidazolate (Tayebee et al. 2019), $Fe_3O_4$@meglumine sulfonic acid (Moradi and Tadayon 2018), sulfated graphene and graphene oxide (Vessally et al. 2017), ionic liquid 1,3-disulfonic acid benzimidazolium chloride (Abbasi 2016), Pb/Cu (Mathur et al. 2018), $Fe^{+3}$-montmorillonite K10 (Fekri et al. 2017), Co@imine-$Na^+$-MMT (Khorshidi et al. 2017), metal-supported nanocatalyst Fe–Cu/ZSM-5 (Safa et al. 2015), KF-modified clay (Bentahar et al. 2019), aluminium-planted mesoporous silica (Murata et al. 2010), $FeCl_3$-supported nanopore silica (Ahn et al. 2008), and polycarbosilanes containing Cu(II) (Mangala and Sreekumar 2019). Some catalysts are expensive, toxic, and non-recyclable. Although some recyclable solid organic and inorganic acids were invented as catalysts for the Biginelli reaction, there are still many drawbacks. Silica solid acids as catalysts for the Biginelli reaction have been studied, but the Brunauer–Emmett–Teller (BET) surface greatly influences catalytic activity, and the process for preparing porous silica catalysts is complex (Cheng et al. 2014). The catalytic activity of some recycled catalysts decreases significantly (Moradi and Tadayon 2018). It is necessary to study the reason why the catalytic activity decreases with increasing numbers of catalytic cycles. Typically, there are

✉ Hongguang Dai
imaudm@imau.edu.cn

[1] College of Science, Inner Mongolia Agricultural University, Hohhot 010018, People's Republic of China

still some drawbacks for the reported catalysts, and it has become necessary to explore new catalysts for the Biginelli reaction.

Iron ions are nontoxic Lewis acids, and used extensively as catalysts. Generally, iron salts as catalysts are difficult to be recycled, so ionic iron compounds must be supported on inorganic materials or polymers for catalysis (Shi et al. 2018). However, significant iron ion losses occur with increasing numbers of recycle loops, and catalytic effects decrease. There are amido and sulfonic groups in poly(2-acrylamido-2-methylpropanesulfonic acid) (PAMPS), which can be used as the chelant of the metal ions (Zhang et al. 2007). PAMPS is extensively used as a superabsorbent, electrolyte for batteries (Cui and Tang 2012), a catalyst (Yin et al. 2014), or catalyst supporter (Asadi et al. 2017). In this manuscript, PAMPS was prepared by free-radical polymerization using 2-acrylamido-2-methylpropanesulfonic acid as the monomer and N,N'-methylenebisacrylamide as the crosslinking agent. Poly(ferric 2-acrylamido-2-methylpropanesulfonate) (PFAMPS) was obtained by the reaction of PAMPS and ferric hydroxide. 3,4-Dihydropyrimidin-2(1H)-ones were synthesized by the Biginelli reaction catalyzed by PFAMPS, which is recyclable. For comparison, ferric lignosulfonate (FLSA), ferric cellulose sulfonate (FCSA), ferric starch sulfonate (FSSA), and ferric 732 cation exchange resin (FACER) were used as catalysts for the Biginelli reaction.

## Experimental

### Chemicals and measurements

Analytical grades of 2-acrylamido-2-methylpropane sulfonic acid (AMPS), N,N'-methylenebisacrylamide (MBA), ammonium persulfate, aromatic aldehyde, ethyl acetoacetate, urea, starch, cellulose, 732 cation exchange resin and sodium lignosulfonate were commercially purchased from Tianjin Chemical Reagent Ltd.

Fourier-transform infrared (FT-IR) spectra of PFAMPS were acquired with a Spectrum 65 Infrared spectrum scanner (PerkinElmer, USA) in reflection mode.

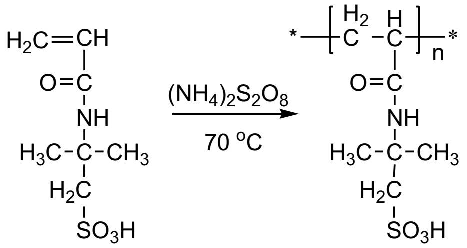
$^1$H NMR spectra were determined by a BioSpin GmbH 600 M NMR spectrometer (Bruker, Switzerland) with TMS as the internal standard and DMSO as the solvent.

### Synthesis of PAMPS and PFAMPS

According to a reported method (Cui and Tang 2012), PAMPS was synthesized by free-radical polymerization. First, 10 g monomer AMPS and crosslinking agent MBA (as shown in Table 1), were dissolved in 90 mL of $H_2O$, the solution was deoxygenated by bubbling pure nitrogen for 0.5 h, and the polymerization reaction was thermally induced at 70 °C using 0.03 g ammonium persulfate as the free-radical initiator. After 6 h, PAMPS gel was obtained. The PAMPS gel was soaked in distilled water and filtered to remove impurities. Finally, PAMPS was dried in an oven at 70 °C until the weight was unchanged. PAMPS was ground and sieved to obtain 0.25–1 mm particles. The reaction equation is shown in Scheme 1.

**Table 1** Preparation of PAMPS

| Entry | PAMPS | AMPS/g | MBA/g | $(NH_4)_2S_2O_8$/g |
|---|---|---|---|---|
| 1 | PAMPS5M | 10 | 0.5 | 0.03 |
| 2 | PAMPS10M | 10 | 1 | 0.03 |
| 3 | PAMPS15M | 10 | 1.5 | 0.03 |
| 4 | PAMPS20M | 10 | 2 | 0.03 |
| 5 | PAMPS25M | 10 | 2.5 | 0.03 |



**Scheme 1.** Synthesis of PAMPS

### Synthesis of poly(ferric 2-acrylamido-2-methylpropanesulfonate) (PFAMPS)

PAMPS5M and stoichiometric $Fe(OH)_3$ in ethanol were stirred for 8 h at 50 °C and then filtered. Acetic acid was added to the mixtures to neutralize the unreacted $Fe(OH)_3$, and then PFAMPS was filtered and rinsed with ethanol. PFAMPS was dried at 70 °C until the weight was unchanged.

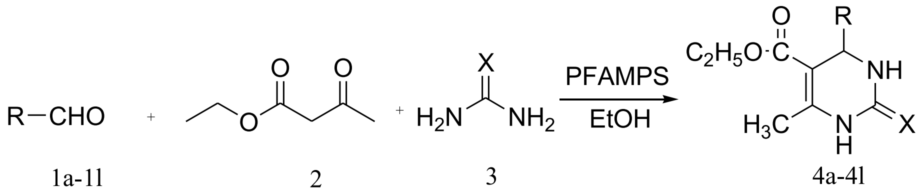
### Synthesis of other polymer sulfonic acids and ferric polymer sulfonate

Cellulose sulfonic acid (CSA) and starch sulfonic acid (SSA) were synthesized according to Vekariya and Patel 2015. Lignosulfonic acid (LSA) and acidic 732 cation exchange resin (ACER) were prepared according to Dai et al. 2018. FLSA, FCSA, FSSA, and FACER were synthesized in a similar way as PFAMPS.

### Synthesis of 3,4-dihydropyrimidin-2(1H)-ones

Aldehyde (5 mmol), urea (or thiourea) (7.5 mmol), ethyl acetoacetate (5 mmol, 650 mg), and the catalyst in ethanol (5 mL) were heated under reflux (Scheme 2). The catalyst

**Scheme 2.** Synthesis of 3,4-dihydropyrimidin-2(1H)-ones



was separated from the solution by filtering. The catalyst was washed with hot ethanol (5 mL × 2), the hot ethanol solution was combined with the mixtures, and the solvent was evaporated under reduced pressure. The solid was recrystallized from ethanol to give a pure product. The catalyst was dried at 70 °C for reuse.

*5-ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-one (4b)* Crystalline solid, m.p.: 205–208 °C; $^1$H NMR (600 MHz, DMSO) δ 9.15 (s, 1H), 7.66 (s, 1H), 7.15–7.14 (m, 2H), 6.89–6.87 (m, 2H), 5.09 (d, $J=3.0$ Hz, 1H), 3.98 (q, $J=7.2$ Hz, 2H), 3.72 (s, 3H), 2.24 (s, 3H), 1.11 (t, $J=7.2$ Hz, 3H).

*5-ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-thione (4j)* Crystalline solid, m.p.: 150–152 °C; $^1$H NMR (600 MHz, DMSO) δ 10.29 (s, 1H), 9.60 (s, 1H), 7.14–7.12 (m, 2H), 6.92–6.89 (m, 2H), 5.12 (d, $J=6$ Hz, 1H), 4.01 (q, $J=7.2$ Hz, 2H), 3.73 (s, 3H), 2.29 (s, 3H), 1.11 (t, $J=7.2$ Hz, 3H).

### Determination of $H^+$ *density of the catalyst*

$H^+$ density of the catalyst was determined using acid–base back titration. Approximately 30 mg of the catalyst was soaked in 10 mL water, and 0.1 mol/L NaOH solution (10.00 mL) was added to react with the samples for 12 h for neutralization. An excess amount of sodium hydroxide was then titrated against hydrochloric acid (0.1 mol/L). The $H^+$ density of the catalyst was calculated using the equation below:

$$H^+\text{density} = \left(V_\text{b} - V_\text{a}\right) \times c/w \quad (1)$$

where $V_\text{b}$ is the volume of HCl used for the back titration in the absence of the sample, $V_\text{a}$ is the volume of HCl used in the presence of the sample, $C$ is the concentration of HCl, and $w$ is the weight of dried sample used in the titration. The experiments were carried out in triplicate, and an average value was obtained.

### Determination of $Fe^{3+}$ *density of the catalyst*

The $Fe^{3+}$ density of the catalyst was determined using EDTA back titration (Khalifa and Ismail 1969). 30 mg of the catalyst was reacted with 15 mL EDTA standard solution for 12 h. The pH of the solution was adjusted to six using ammonia and acetic acid. Then, 10 mL ammonia and ammonium acetate buffer solution were added, and four drops of xylenol orange were added as the indicator. The solution was titrated with standard zinc solution to purple red as the end point. The $Fe^{3+}$ density of the catalyst was calculated using the equation below:

$$\text{Fe}^{3+}\text{density} = \frac{15 \times \text{c}_1 - \text{c}_2\text{v}_2}{\text{w}} \quad (2)$$

where $c_1$ is the concentration of EDTA, $c_2$ is the concentration of $Zn^{2+}$, $v_2$ is the volume of $Zn^{2+}$ solution, and $w$ is the weight of dried catalyst used in the titration.

## Results and discussion

### FT-IR

As shown in Fig. 1, of the FT-IR of PAMPS5M, the peak at 1639 cm$^{-1}$ is ascribed to the C = O stretching vibration. The peak at 2922 cm$^{-1}$ is ascribed to saturated C–H stretching. The peaks of O–H and N–H are all shown to be greater than 3000 cm$^{-1}$. Peaks' wavenumbers of 1216 and 1039 cm$^{-1}$ are characteristic peaks of -$SO_3$H.

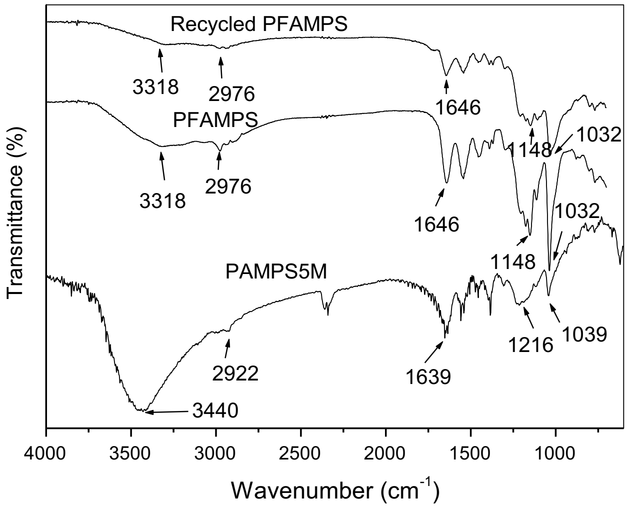


**Fig. 1** FT-IR of PAMPS and PFAMPS

Compared with the FT-IR of PAMPS5M, the peak at 3318 cm$^{-1}$ of PFAMPS, ascribed to N–H stretching, is weaker, because $–SO_3H$ was displaced by $(–SO_3)_3Fe$. The peak at 2976 cm$^{-1}$ is ascribed to saturated C–H stretching, the peak at 1646 cm$^{-1}$ is ascribed to C$=$O stretching, and the peaks at 1032 and 1148 cm$^{-1}$ are indicative of the presence of $–SO_3^{-}$.

The FT-IR of recycled PFAMPS is similar to that of virgin PFAMPS, which confirms that the structure of PFAMPS does not change after reaction catalysis. Therefore, the catalytic effect of recycled PAMPS does not significantly decrease.

## The influence of catalysts on the yield of 4a

The influence of catalysts containing sulfonic groups on the yield of 4a was examined. As shown in Table 2, the Biginelli reaction of benzaldehyde (1a), ethyl acetoacetate, and urea without catalyst yielded 4a less than 5%. The H$^+$ densities of PAMPS5M, p-TsOH·$H_2O$, sulfamic acid, LSA, CSA, SSA, and ACER were 4.51, 5.26, 10.30, 2.20, 5.17, 4.39, and 0.82 mmol/g, respectively. They were each used as catalysts to synthesize 4a. To compare the catalytic effects of different catalysts, appropriate amounts of each catalyst were added to give the same H$^+$ contents. The yields of 4a catalyzed by PAMPS5M, p-TsOH·$H_2O$, sulfamic acid, LSA, CSA, SSA, and ACER were 95, 93, 91, 80, 90, 87, and 83%, respectively. As shown, the catalytic effect of PAMPS5M was the best. The experiments also showed that p-TsOH·$H_2O$ and sulfamic acid cannot be recycled as catalysts. ACER is a traditional catalyst widely used in industry, and the amount of ACER is 5.5 times that of PAMPS5M. The yield of 4a catalyzed by ACER is lower than that of 4a catalyzed by PAMPS5M.

**Table 2** Effects of various sulfonic acid-type catalysts on 4a

| Entry | Catalyst | H$^+$ density of catalyst/ mmol·g$^{-1}$ | Amount of catalyst/ mg | Reaction time /h | Yield/% |
|---|---|---|---|---|---|
| 1 | Catalyst free | – | 0 | 5 | $<5$ |
| 2 | PAMPS5M | 4.51 | 100 | 5 | 95 |
| 3 | PAMPS10M | 4.01 | 100 | 5 | 90 |
| 4 | PAMPS15M | 3.97 | 100 | 5 | 88 |
| 5 | PAMPS20M | 3.86 | 100 | 5 | 83 |
| 6 | PAMSP25M | 3.62 | 100 | 5 | 83 |
| 7 | p-TsOH·$H_2O$ | 5.26 | 85 | 5 | 93 |
| 8 | Sulfamic acid | 10.30 | 45 | 5 | 91 |
| 9 | LSA | 2.20 | 240 | 5 | 80 |
| 10 | CSA | 5.17 | 100 | 5 | 90 |
| 11 | SSA | 4.39 | 100 | 5 | 87 |
| 12 | ACER | 0.82 | 550 | 5 | 83 |

The influence of PAMPS with different crosslinking degrees on the reaction was studied. PAMPS5M, PAMPS10M, PAMPS15M, PAMPS20M, and PAMPS25M were used as catalysts for the reaction, where the yields of 4a were 95, 90, 88, 83, and 83%, respectively. With increasing crosslinking degrees of PAMPS, the H$^+$ content and the yields of 4a decreased. There was not a sulfonic group in the crosslinking reagent MBA, so the H$^+$ content of PAMPS decreased with increasing crosslinking degrees.

As shown in Table 3, with increased PAMPS5M amounts and reaction times, the yields of 4a increased. PAMPS could catalyze the Biginelli reaction to synthesize 3,4-dihydropyrimidin-2(1H)-ones, where ionized H$^+$ from PAMPS acted as a catalyst. Additionally, protonic acid could act as an acid, and Lewis acids could act catalysts. Lewis acidic Fe$^{3+}$ is widely used as a catalyst and is nontoxic, but inorganic ferric salts, for example $FeCl_3$, used as catalysts are generally unable to be recycled. Fe$^{3+}$ could be supported on inorganic materials or polymers, and recycled after reaction catalysis, but Fe$^{3+}$ can be easily lost after recycling for some supported Fe$^{3+}$ catalysts and the catalytic effects of recycled catalysts decrease. The reason may be that the action between Fe$^{3+}$ and matrix is weak. There are amido and sulfonic groups in PAMPS that can be used as chelants for metal ions (Wang et al. 2009). PAMPS reacts with $Fe(OH)_3$ to give PFAMPS, and the action between Fe$^{3+}$ and the polymer matrix is strong. Fe$^{3+}$ was not easily lost in the PAMPS matrix. In the manuscript, PAMPS5M was chosen to react with $Fe(OH)_3$ to prepare PFAMPS, which was subsequently used as a catalyst for the Biginelli reaction. As shown in Table 3, when the amounts of PFAMPS catalyzing the reaction for 5 h were 60, 80, and 100 mg, the yields of 4a were 76, 85, and 87%, respectively. As the amount of PFAMPS increased, the yield of 4a increased.

For comparison, other sulfonic acid-type polymers, such as LSA, CSA, SSA, and ACER, were reacted with

**Table 3** Optimization of reaction conditions

| Entry | Catalyst | Amount of catalyst/mg | Reaction time/h | Yield of 4a/% |
|---|---|---|---|---|
| 1 | PAMPS5M | 100 | 5 | 95 |
| 2 | PAMPS5M | 80 | 5 | 89 |
| 3 | PAMPS5M | 60 | 5 | 80 |
| 4 | PAMPS5M | 100 | 4 | 94 |
| 5 | PAMPS5M | 100 | 3 | 90 |
| 6 | PAMPS5M | 100 | 2 | 81 |
| 7 | PFAMPS | 100 | 5 | 87 |
| 8 | PFAMPS | 80 | 5 | 85 |
| 9 | PFAMPS | 60 | 5 | 76 |
| 10 | PFAMPS | 80 | 4 | 86 |
| 11 | PFAMPS | 80 | 3 | 73 |

**Table 4** $Fe^{3+}$ density of polymer-supported $Fe^{3+}$

| Entry | Catalyst | $Fe^{3+}$ density / $mmol \cdot g^{-1}$ | $Fe^{3+}$ density of recycled catalyst / $mmol \cdot g^{-1}$ |
|---|---|---|---|
| 1 | PFAMPS | 1.37 | 1.23 |
| 2 | FLSA | 0.57 | 0.24 |
| 3 | FACER | 0.20 | 0.041 |
| 4 | FCSA | 1.39 | 0.62 |
| 5 | FSSA | 1.41 | – |

**Table 5** The influence of polymer-supported $Fe^{3+}$ on the yield of 4a

| Entry | Catalyst | Amount of catalyst/mg | Yield of 4a /% | | |
|---|---|---|---|---|---|
| | | | 1 cycle | 2 cycle | 3 cycle |
| 1 | PFAMPS | 100 | 87 | 86 | 86 |
| 2 | FLSA | 240 | 80 | 73 | 67 |
| 3 | FACER | 700 | 85 | 77 | 69 |
| 4 | FCSA | 100 | 80 | 67 | – |
| 5 | FSSA | 100 | 83 | – | – |

$Fe(OH)_3$ to prepare corresponding ferric sulfonate of polymers, FLSA, FCSA, FSSA, and FACER. Their $Fe^{3+}$ densities were determined and shown in Table 4. For comparison, when PFAMPS, FLSA, FACER, FCSA, and FSSA were used as catalysts, respectively, their $Fe^{3+}$ amounts were the same. As shown in Table 5, the yields of 4a were 87, 80, 85, 80, and 83%, respectively. Among the catalysts, the catalytic effect of PFAMPS was the best. Additionally, the reusability of catalyst was examined, as shown in Table 5, and with increased number of cycles, the catalytic effects of PFAMPS did not decrease, while the catalytic effects of other catalysts significantly decreased. PFAMPS is able to be recycled six times as a catalyst, and the yields of 4a after each successive cycle were 87, 86, 86, 86, 84, and 84%, respectively. As shown in Table 4, after recycling, little $Fe^{3+}$ was lost from PFAMPS, but significant losses of $Fe^{3+}$ were observed from FLSA, FACER, FCSA, and FSSA, where the ionized $Fe^{3+}$ from the polymer matrix acted as the catalyst for the Biginelli reaction. There are sulfonic groups in FLSA, FACER, FCSA, and FSSA, but there are sulfonic groups and amido groups in PFAMPS. A complex was formed between $Fe^{3+}$ and the sulfonic and amido groups in PFAMPS, and the complex was stable (Zhang et al. 2007). Complexes between $Fe^{3+}$ and LSA, ACER, CSA, and SSA were also formed, but the stabilities of the complexes were inferior to that of PFAMPS.

As shown in Table 6, the catalytic efficiency of PFAMPS was compared with other catalysts in the synthesis of 4a. PFAMPS catalytic system reacted faster compared with other catalysts.

As shown in Table 7, the Biginelli reaction catalyzed by PFAMPS gave 3,4-dihydropyrimidin-2(1H)-ones in good yields. According to Fekri et al. 2017, Lewis acids can act as catalysts in the Biginelli reaction, and the $Fe^{3+}$ ionized from PFAMPS acted as the catalyst. The reaction mechanism is shown in Scheme 3 (Khorshidi et al. 2017). The reaction proceeded through acylimine formation between aldehyde and urea in the presence of $Fe^{3+}$. Subsequently, enolate of ethyl acetoacetate was added to the acylimine, and then cyclodehydration occurred to afford 3,4-dihydropyrimidin-2(1H)-ones (Fekri et al. 2017).

## Conclusion

PFAMPS was prepared and used as the catalyst for the Biginelli reaction to synthesize 3,4-dihydropyrimidin-2(1H)-ones in good yields. PFAMPS can be reused without significant decreases in catalytic effect. For comparison, ferric lignosulfonate, ferric cellulose sulfonate, ferric starch sulfonate, and ferric 732 cation exchange resin were used as catalysts of the Biginelli reaction. Each of these catalysts can be reused, but their catalytic effects significantly decrease after reuse and $Fe^{3+}$ was significantly lost from the polymer matrix after reuse. A chelate of $Fe^{3+}$ and poly(2-acrylamido-2-methylpropanesulfonate) matrix was formed, where the action between $Fe^{3+}$ and

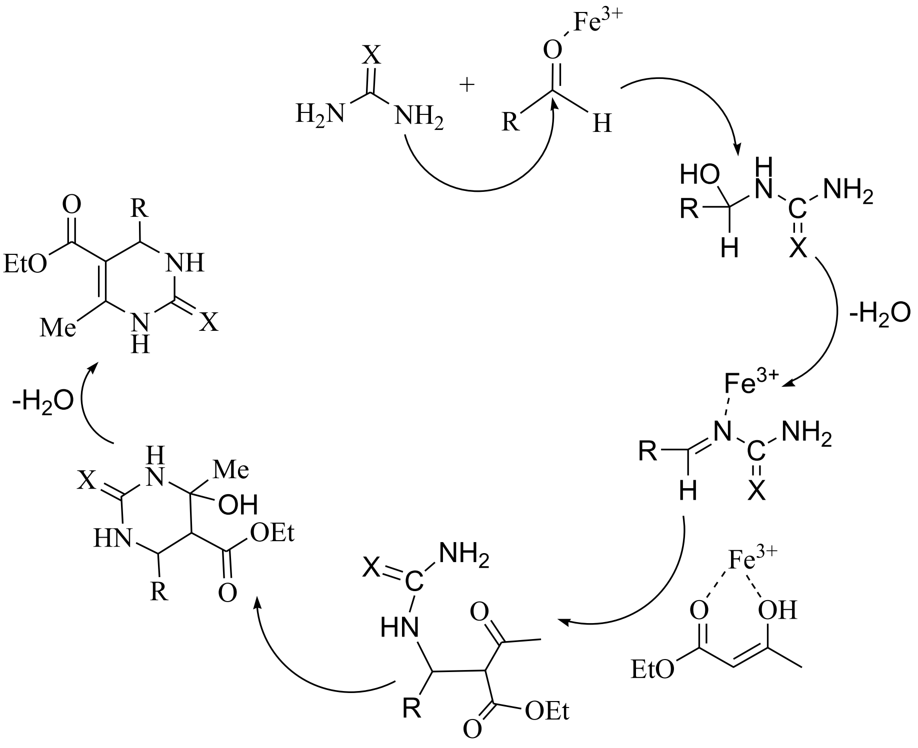
**Table 6** Comparison of the efficiency of PFAMPS with that of other reported catalysts in the synthesis of 4a

| Entry | Catalyst | Conditions | Reaction time/h | Yield/% |
|---|---|---|---|---|
| 1 | $Fe_3O_4$@mesoporous SBA-15 (Mondal et al. 2012) | EtOH/60 °C | 6 | 85 |
| 2 | Al-M41 (Murata et al. 2010) | Octane/115 °C | 10 | 94 |
| 3 | $[Al(H_2O)_6](BF_4)_3$ (Litvic et al. 2010) | $CH_3CN$/Reflux | 20 | 81 |
| 4 | $NH_4H_2PO_4$/MCM-41 (Tayebee and Ghadamgahi 2017) | Solvent free/100 °C | 6 | 72 |
| 5 | Nano ZnO (Tamaddon and Moradi 2013) | Solvent free/60 °C | 10 | 95 |
| 6 | PFAMPS (This work) | EtOH/Reflux | 5 | 87 |

**Table 7** Synthesis of 3,4-dihydropyrimidin-2(1H)-ones/thiones catalyzed by PFAMPS[a]

| Entry | R | X | Yield /% | m.p./℃ | |
|---|---|---|---|---|---|
| | | | | Found | Reported |
| 4a | $C_6H_5$ | O | 87 | 201–203 | 200–202 (Mohamadpour et al. 2018) |
| 4b | $4\text{-}CH_3OC_6H_4$ | O | 82 | 205–208 | 200–202 (Tayebee and Ghadamgahi 2017) |
| 4c | $4\text{-}NO_2C_6H_4$ | O | 76 | 208–210 | 207–209 (Moradi and Tadayon 2018) |
| 4d | $4\text{-}ClC_6H_4$ | O | 80 | 210–211 | 210–213 (Vessally et al. 2017) |
| 4e | $4\text{-}FC_6H_4$ | O | 79 | 175–177 | 176–178 (Mohamadpour et al. 2018) |
| 4f | $2\text{-}NO_2C_6H_4$ | O | 74 | 203–205 | 204–206 (Kuraitheerthakumaran et al. 2016) |
| 4g | $2\text{-}ClC_6H_4$ | O | 80 | 221–223 | 220–222 (Tayebee and Ghadamgahi 2017) |
| 4h | $4\text{-}CH_3C_6H_4$ | O | 81 | 215–217 | 215–217 (Vessally et al. 2017) |
| 4i | $C_6H_5$ | S | 83 | 208–209 | 208–210 (Jetti et al. 2017) |
| 4j | $4\text{-}CH_3OC_6H_4$ | S | 80 | 150–152 | 154–156 (Jetti et al. 2017) |
| 4k | $4\text{-}ClC_6H_4$ | S | 70 | 188–190 | 188–189 (Fekri et al. 2017) |
| 4l | $2\text{-}NO_2C_6H_4$ | S | 75 | 197–199 | 196–198 (Kuraitheerthakumaran et al. 2016) |

[a] Aldehyde (5 mmol), urea (or thiourea) (7.5 mmol), ethyl acetoacetate (5 mmol), and 100 mg PFAMPS in ethanol (5 ml) were heated under reflux for 5 h



**Scheme 3.** Reaction mechanism of the Biginelli reaction catalyzed by PFAMPS

poly(2-acrylamido-2-methylpropanesulfonate) matrix in PFAMPS was strong, and little $Fe^{3+}$ was lost from PFAMPS after reuse.

**Acknowledgements** The work was supported by National Natural Science Foundation of China (21607085) and the Inner Mongolia Agricultural University Research Initiation Funds for Doctor (BJ09-38).

## Compliance with ethical standards

**Conflict of interest** On behalf of all authors, the corresponding author states that there is no conflict of interest.

## References

Abbasi M (2016) 1,3-Disulfonic acid benzimidazolium chloride as an efficient and recyclable ionic liquid catalyst for the synthesis of

3,4-dihydropyrimidine-2-(1H)-ones/thiones. Res Chem Intermed 42(4):3303–3314. https://doi.org/10.1007/s11164-015-2211-2

Ahn BJ, Gang MS, Chae K, Oh Y, Shin J, Chang W (2008) A microwave-assisted synthesis of 3,4-dihydro-pyrimidin-2-(1H)-ones catalyzed by $FeCl_3$-supported nanopore silica under solvent-free conditions. J Ind Eng Chem 14(3):401–405. https://doi.org/10.1016/j.jiec.2008.01.008

An L, Han L, Wang Z et al (2016) Calix[8]arene sulfonic acid catalyzed three-component reaction for convenient synthesis of 3,4-dihydropyrimidin-2(1H)-ones/thiones under ultrasonic irradiation. Biol Pharm Bull 39(2):267–271. https://doi.org/10.1248/bpb.b15-00681

Asadi S, Sedghi R, Heravi MM (2017) Pd nanoparticles immobilized on supported magnetic GO@PAMPS as an auspicious catalyst for Suzuki-Miyaura coupling reaction. CataL Lett 147(8):2045–2056. https://doi.org/10.1007/s10562-017-2089-2

Bentahar S, Taleb MA, Sabour A et al (2019) Potassium fluoride-modified clay as a reusable heterogeneous catalyst for one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones. Russ J Org Chem 55(9):1423–1431. https://doi.org/10.1134/s1070428019090240

Biginelli P (1893) Synthesis of 3,4-dihydropyrimidin-2(1H)-ones. Gazz Chim Ital 23:360–413

Cheng Y, Zhou Y, Zhang J, Fei X, Ma T, Liang X (2014) Synthesis of a novel solid acid with both sulfonic and carbonyl acid groups and its catalytic activities in acetalization. Chinese J Chem Eng 22(3):312–317. https://doi.org/10.1016/s1004-9541(14)60048-3

Cui WW, Tang DY (2012) Electrospun Poly(lithium 2-acrylamido-2-methylpropanesulfonic acid) fiber-based polymer electrolytes for lithium-ion batteries. J Appl Polym Sci 126(2):510–518. https://doi.org/10.1002/app.36804

Dai HG, Liu XH, Wang LR, Shi L (2018) Synthesis of N-substituted pyrroles using lignosulfonic acid as biomass-based catalyst. Huaxue Tongbao 81(10):929–933. https://doi.org/10.14159/j.cnki.0441-3776.2018.10.016

Fekri LZ, Nikpassand M, Movaghari M (2017) $Fe^{+3}$-Montmorillonite K10: as an effective and reusable catalyst for the synthesis of 3,4-dihydropyrimidin-2(1H)-ones and –thiones. Bull Chem Soc Ethiop 31(2):313–321. https://doi.org/10.4314/bcse.v31i2.12

Jetti SR, Verma D, Jain S (2017) 3-[(3-(Trimethoxysilyl)propyl)thio]propane-1-oxy-sulfonic acid: an efficient recyclable heterogeneous catalyst for the synthesis of 3,4-dihydropyrimidin-2(1H)-ones/thiones. Arab J Chem 10:S3184–S3189. https://doi.org/10.1016/j.arabjc.2013.12.012

Khalifa H, Ismail IA (1969) Application of back titration of EDTA with mercury(II) to the analysis of ilmenite. Microchem J 14(3):464–470. https://doi.org/10.1016/0026-265x(69)90074-5

Khorshidi A, Tabatabaeian K, Azizi H, Aghaei-Hashjin M, Abbaspour-Gilandeh E (2017) Efficient one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones catalyzed by a new heterogeneous catalyst based on Co-functionalized $Na^+$-montmorillonite. RSC Adv 7(29):17732–17740. https://doi.org/10.1039/c7ra00794a

Kuraitheerthakumaran A, Pazhamalai S, Gopalakrishnan M (2016) Microwave-assisted multicomponent reaction for the synthesis of 3,4-dihydropyrimidin-2(1H)-ones and their corresponding 2(1H)-thiones using lanthanum oxide as a catalyst under solvent-free conditions. Arab J Chem 9:S461–S465. https://doi.org/10.1016/j.arabjc.2011.06.005

Li D, Mao H, An L, Zhao Z, Zou J (2010) Gallium(III) iodide-catalyzed Biginelli-type reaction under solvent-free conditions: efficient synthesis of dihydropyrimidine-2(1H)-one derivatives. Chinese J Chem 28(10):2025–2032. https://doi.org/10.1002/cjoc.201090338

Litvic M, Vecenaj I, Ladisic ZM, Lovric M, Vinkovic V, Filipan- Litvic M (2010) First application of hexaaquaaluminium(III) tetrafluoroborate as a mild, recyclable, non-hygroscopic acid catalyst in organic synthesis: a simple and efficient protocol for the multigram scale synthesis of 3,4-dihydropyrimidinones by Biginelli reaction. Tetrahedron 66:3463–3471. https://doi.org/10.1016/j.tet.2010.03.024

Mangala K, Sreekumar K (2019) Study of polycarbosilane-supported copper(II) as a heterogeneous catalyst. Polym Bull 77:153. https://doi.org/10.1007/s00289-019-02741-y

Mathur H, Zai MSK, Khandelwal P, Kumari N, Verma VP, Yadav DK (2018) Pd/Cu-assisted C-S activation and N–H insertion: highly versatile synthesis of 2-aminopyrimidines from 3,4-dihydropyrimidine-2(1H)-thiones. Chem Heterocycl Com 54(3):375–378. https://doi.org/10.1007/s10593-018-2276-0

Mohamadpour F, Lashkari M, Maghsoodlou MT, Heydari R (2018) Phthalic acid: a green, biodegradable and environmentally benign nature di-functional Brønsted acid catalyst for the one-pot synthesis of 3, 4-dihydropyrimidin-2-(1H)-one derivatives and substituted Dihydro-2-oxypyrroles. J Chil Chem Soc 63(1):3811–3818. https://doi.org/10.4067/s0717-97072018000103811

Mondal J, Sen T, Bhaumik A (2012) $Fe_3O_4$@mesoporous SBA-15: a robust and magnetically recoverable catalyst for one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones via the Biginelli reaction. Dalton Trans 41:6173–6181. https://doi.org/10.1039/c2dt30106g

Moradi L, Tadayon M (2018) Green synthesis of 3,4-dihydropyrimidinones using nano $Fe_3O_4$@meglumine sulfonic acid as a new efficient solid acid catalyst under microwave irradiation. J Saudi Chem Soc 22(1):66–75. https://doi.org/10.1016/j.jscs.2017.07.004

Murata H, Ishitani H, Iwamoto M (2010) Synthesis of Biginelli dihydropyrimidinone derivatives with various substituents on aluminium-planted mesoporous silica catalyst. Org Biomol Chem 8(5):1202–1211. https://doi.org/10.1039/b920821f

Nasr-Esfahani M, Montazerozohori M, Aghel-Mirrezaee M, Kashi H (2014) Efficient and green catalytic synthesis of dihydropyrimidinone (thione) derivatives using Cobalt nitrate in solvent-free conditions. J Chil Chem Soc 59(1):2311–2314. https://doi.org/10.4067/s0717-97072014000100015

Safa KD, Esmaili M, Allahvirdinesbat M (2015) Aqua-mediated one-pot synthesis of Biginelli dihydropyrimidinone/thiones (DHPMs), hantzsch dihydropyridines (DHPs), and polysubstituted pyridines sonocatalyzed by metal-supported nanocatalysts. J Iran Chem Soc 13(2):267–277. https://doi.org/10.1007/s13738-015-0734-5

Shi XL, Chen Y, Hu Q, Wang F, Duan P (2018) An efficient, recyclable and large-scalable fiber-supported Fe(III) catalytic system on a simple fixed-bed reactor verified in the Biginelli reactions. J Ind Eng Chem 60:333–340. https://doi.org/10.1016/j.jiec.2017.11.019

Starcevich JT, Laughlin TJ, Mohan RS (2013) Iron(III) tosylate catalyzed synthesis of 3,4-dihydropyrimidin-2(1H)-ones/thiones via the Biginelli reaction. Tetrahedron Lett 54(8):983–985. https://doi.org/10.1016/j.tetlet.2012.12.032

Tamaddon F, Moradi S (2013) Controllable selectivity in Biginelli and Hantzsch reactions using nano ZnO as a structure base catalyst. J Mol Catal A Chem 370:117–122. https://doi.org/10.1016/j.molcata.2012.12.005

Tayebee R, Ghadamgahi M (2017) Solvent free one-pot multi-component synthesis of 3,4-dihydropyrimidin-2(1-H)-ones catalyzed by mesoporous $NH_4H_2PO_4$/MCM-41 as an environmentally friendly, cheap, and effective catalyst. Arab J Chem 10:S757–S764. https://doi.org/10.1155/2014/761209

Tayebee R, Abdizadeh MF, Erfaninia N, Amiri A, Baghayeri M, Kakhki RM, Maleki B, Esmaili E (2019) Phosphotungstic acid grafted zeolite imidazolate framework as an effective heterogeneous nanocatalyst for the one-pot solvent-free synthesis of 3,4-dihydropyrimidinones. Appl Organomet Chem 33(8):e4959. https://doi.org/10.1002/aoc.4959

Vekariya RH, Patel HD (2015) Cellulose sulfuric acid (CSA) and starch sulfuric acid (SSA) as solid and heterogeneous catalysts in green organic synthesis: recent advances. Arkivoc 1:136. https://doi.org/10.3998/ark.5550190.p008.975

Vessally E, Hassanpour A, Hosseinzadeh-Khanmiri R, Babazadeh M, Abolhasani J (2017) Green and recyclable sulfonated graphene and graphene oxide nanosheet catalysts for the syntheses of 3,4-dihydropyrimidinones. Monatsh Chem 148(2):321–326. https://doi.org/10.1007/s00706-016-1762-2

Wang HJ, Kang J, Liu HJ, Qu JH (2009) Preparation of organically functionalized silica gel as adsorbent for copper ion adsorption. J Environ Sci-China 21(11):1473–1479. https://doi.org/10.1016/s1001-0742(08)62442-0

Yang XB, Fu XK, Huang Y, Zeng RQ (2011) Zirconium(IV)4-sulphophenylethyliminobismethylphosphonate as an efficient and reusable catalyst for one-pot synthesis of 3,4-dihydropyrimidones under solvent-free conditions. Chem Pap 65(6):829–834. https://doi.org/10.2478/s11696-011-0091-5

Yin XB, Ding WB, Shen X, Yan YF, Chen L (2014) Application of poly(2-acrylamido-2-methylpropanesulfonic acid) hydrogel in the catalyzing esterification reaction. Funct Mater 15:15065–15069

Zhang L, Yu C, Zhao W, Hua Z, Chen H, Li L, Shi J (2007) Preparation of multi-amine-grafted mesoporous silicas and their application to heavy metal ions adsorption. J Non-Cryst Solids 353(44):4055–4061. https://doi.org/10.1016/j.jnoncrysol.2007.06.018