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Synthesis of pyrimidines by $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles

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Abstract: $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles have been used as an effective catalyst for the preparation of pyrimidines by three-component reactions of 1,3-dimethylbarbituric acid, aromatic aldehydes and 4-methyl aniline or 4-methoxy aniline under reflux condition in ethanol. $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles have been characterized by scanning electronic microscopy (SEM), powder X-ray diffraction (XRD), vibrating sample magnetometer (VSM), thermal gravimetric analysis (TGA), energy dispersive X-ray (EDS), dynamic light scattering (DLS) and FT-IR spectroscopy. This method provides several advantages including, the reusability of the catalyst, low catalyst loading, atom economy, short reaction times and high yields of products.

Keywords: Pyrimidines; Fe_3O_4 nanoparticles; heterogeneous catalyst; one-pot.

1 Introduction

Pyrimidines have many biological properties including anticancer (Singh et al., 2009), anti-diabetic (Barakat et al., 2015), antioxidant (Barakat et al., 2016), antibacterial, anti-fungal (Dhorajiya et al., 2014), and anticonvulsant (Andrews et al., 1979). The discovery impressive ways for the preparation of pyrimidines is a serious challenge (Maleki and Paydar, 2016; Shaabani et al., 2010; Maleki and Aghaei, 2017). The synthesis of pyrimidine derivatives have been developed by InCl_3 (Sharma et al., 2015), $\text{H}_3\text{PW}_{12}\text{O}_{40}$ (Panahi et al., 2013), K_2CO_3

(Azzam and Pasha, 2012), p-toluene sulfonic acid (Rahmati and Khalesi, 2012), $[\text{Bmim}]\text{PF}_6$ (Shirvan et al., 2012). Each of these procedures may have its own advantages but also suffer from such apparent drawbacks as prolonged reaction times, complicated work-up, low yield, or hazardous reaction conditions. Despite the availability of these ways, there remains enough choice for a capable and reusable catalyst with high catalytic activity for the preparation of pyrimidines. Multicomponent reactions (MCRs) enhance the efficiency by combining several operational steps without isolation of intermediates or changing the reaction conditions (Maleki, 2013; Maleki et al., 2018a; Shaabani et al., 2007, 2009). Ideally, introducing neat processes and utilizing eco-friendly and green catalysts which can be simply recycled at the end of reactions has obtained great attention in recent years (Maleki, 2018). Magnetic nanoparticles (MNPs) have been utilized as a robust catalyst with a very significant feature of straightforward separation by external magnet bar (Chen et al., 2015; Elsayed et al., 2018; Fakheri-Vayeghan et al., 2018; Maleki et al., 2018b; Safaei-Ghomi et al., 2018). Magnetic materials have appeared as a useful group of heterogeneous catalysts owing to their various usages in synthesis and catalysis (Huang et al., 2016; Maleki, 2012, 2014; Shin et al., 2015; Tietze et al., 2015). The surface of magnetic nanoparticles can be functionalized by surface modifications to provide the attachment of a variety of eligible functionalities (Deatsch and Evans, 2014; Maleki and Firouzi-Haji, 2018; Zhang et al., 2012; Zheng et al., 2009). Herein, we report the use of nano- $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline as an effective catalyst for the synthesis of pyrimidines by three-component reactions of 1,3-dimethylbarbituric acid, aromatic aldehydes and 4-methyl aniline or 4-methoxy aniline under reflux condition in ethanol (Scheme 1).

2 Results and discussion

The process of the preparation $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles is shown in Scheme 2.

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Scheme 1: Synthesis of pyrimidines using $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles.

Scheme 2: Schematic illustration of the preparation $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles.

XRD pattern of Fe_3O_4 and $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles is indicated in Figure 1. The pattern agrees with the reported pattern for Fe_3O_4 (JCPDS No. 75-1609). The crystallite size of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline was calculated by the Debye–Scherer equation is about 46–50 nm, in good agreement with the result gained by SEM.

The particle size and morphology of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline was indicated by SEM. The statistic of results from

SEM images exhibit that the average size of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline is about 45–50 nm (Figure 2).

Figure 3 displays FT-IR spectra of Fe_3O_4 , $\text{Fe}_3\text{O}_4@\text{SiO}_2$ and $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles. The FT-IR spectra of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ and $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles show the vibrations of Fe–O at 570–588 cm^{-1} . The band at about 1050 cm^{-1} belongs to Si–O stretching vibrations. The peaks that appear at 1042, 1131 and 3320 cm^{-1} are related

Figure 1: The XRD pattern of (a) Fe_3O_4 and (b) $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles.

Figure 2: SEM image of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles.

to the stretching of C–O, C–N and N–H bonds. A peak appears at about 1720 cm^{-1} due to the stretching of the C=O group in L-proline.

The magnetic properties of Fe_3O_4 , $\text{Fe}_3\text{O}_4@\text{SiO}_2$ and $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline were determined using VSM (Figure 4). The amount of saturation magnetization for Fe_3O_4 , $\text{Fe}_3\text{O}_4@\text{SiO}_2$ and $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline is 59.2, 41.3 and 14.5 emu/g. These results demonstrate that the magnetization property decreases by coating and functionalization.

TGA indicates the thermal stability of the $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline. These nanoparticles display appropriate thermal stability without a significant decrease in weight (Figure 5). The weight loss at temperatures below 200°C is

Figure 3: FT-IR spectra of (a) Fe_3O_4 (b) $\text{Fe}_3\text{O}_4@\text{SiO}_2$ and (c) $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles.

Figure 4: The VSM curve of: (a) Fe_3O_4 (b) $\text{Fe}_3\text{O}_4@\text{SiO}_2$ and (c) $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles.

Figure 5: TGA curve of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles.

owing to the removal of physically adsorbed solvent. The curve indicates a weight loss about 12.7% from 250°C to 600°C, resulting from the decomposition of the organic spacer grafting to the nanoparticles surface.

An EDS spectrum of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline (Figure 6) displays that the elemental compositions are carbon, silicon, oxygen, iron and nitrogen.

In order to investigate the size distribution of nanocatalysts, DLS (dynamic light scattering) measurements of the nanoparticles were showed in Figure 7. The size distribution is centered at a value of 49.2 nm. The dispersion for DLS analysis (1.25 g nanocatalyst at 25 mL ethanol) was prepared using an ultrasonic bath (50 W) for 20 min.

Initially, we had optimized different reaction parameters for the preparation of pyrimidines by three-component reactions of 1,3-dimethylbarbituric acid, 4-chlorobenzaldehyde and 4-methoxy aniline as a model reaction. The model reactions were performed using CAN, L-proline, Et_3N , Fe_3O_4 , $\text{Fe}_3\text{O}_4@\text{SiO}_2$ and $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-

proline nanoparticles. Several reactions were investigated using diverse solvents such as ethanol, water, acetonitrile and dimethylformamide. The best results were achieved in EtOH and we found that the reaction gave satisfying results using $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline which gave good yields of products (Table 1).

The above results indicate the present catalytic way is extendable to a wide diversity of substrates to create pyrimidines. Investigations of the reaction scope showed that diverse aromatic aldehydes can be utilized in this method (Table 2). Turnover frequency (TOF) for this catalytic system is listed in Table 2.

The reusability of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles was investigated for the reaction of 1,3-dimethylbarbituric acid, 4-chlorobenzaldehyde and 4-methoxy aniline. After completion of the reaction, the nanocatalyst was separated using an external magnet. The recovered magnetite nanoparticles were washed several times with ethanol and then dried at room temperature. Figure 8 shows that the nanocatalyst could be reused for six times with a minimal loss of activity.

FT-IR analysis before and after reuse of the $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles is shown in Figure 9. The nanoparticles remained unchanged before and after reaction. We suppose that, this is also the possible reason for the extreme stability of the $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles presented herein. The extreme stability of the $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles is mainspring of the continuous and high catalytic activity.

The proposed mechanism for the reaction is shown in Scheme 3. Initially, 1,3-dimethylbarbituric acid is reacted with aldehyde to form intermediate (I) via condensation reaction. Intermediate (I), in the presence of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline, is condensed with aniline derivatives to form intermediate (II). The migration of the hydrogen atom will provide the final product. It is assumed that catalytically active site of catalyst is contains SiO_2 that acts as a Lewis acid and L-proline ($-\text{NH}-$) that acts as a Lewis basic. This proposed mechanism has also been supported by the literature (Fekri et al., 2019; Keshavarz et al., 2018; Safaei-Ghomi et al., 2017).

3 Conclusions

In conclusion, we have developed an effective method for the synthesis of pyrimidines using $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline. The method offers several advantages containing high yields, cleaner reaction profiles, shorter reaction times, easy availability, reusability of the catalyst and low catalyst loading.

Figure 6: EDS spectrum of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles.

Figure 7: DLS of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles.

Table 1: Optimization of reaction conditions using different catalysts.^a

Entry	Solvent (reflux)	Catalyst	Time (min)	Yield (%) ^b
1	EtOH	-----	500	trace
2	EtOH	CAN (4 mol%)	400	22
3	EtOH	Et_3N (10 mol%)	300	35
4	EtOH	L-proline (10 mol%)	150	55
5	EtOH	Fe_3O_4 NP (50 mg)	200	25
6	EtOH	Nano- $\text{Fe}_3\text{O}_4@\text{SiO}_2$ (20 mol%)	200	33
7	H_2O	Nano- $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline (8 mg)	120	62
8	DMF	Nano- $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline (8 mg)	120	70
9	CH_3CN	Nano- $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline (8 mg)	120	85
10	EtOH	Nano- $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline (6 mg)	120	90
11	EtOH	Nano- $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline (8 mg)	120	92
12	EtOH	Nano- $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline (10 mg)	120	92

^a1,3-dimethylbarbituric acid (1 mmol), 4-chlorobenzaldehyde (1 mmol) and 4-methoxy aniline (1 mmol); ^bIsolated yield**Table 2:** Synthesis of pyrimidines by nano- $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline (8 mg) under reflux condition.

Entry	R (Aldehyde)	R' (Aniline)	Product	Time (min)	Yield ^a (%)	M.p. (°C)	TOF (min ⁻¹)
1	2- NO_2	4- CH_3	4a	150	88	183-185	0.56
2	4- SCH_3	4- OCH_3	4b	150	84	190-192	0.52
3	4-Cl	4- OCH_3	4c	120	92	240-242	0.77
4	3- NO_2	4- CH_3	4d	130	88	188-190	0.68
5	4- NO_2	4- OCH_3	4e	120	93	237-239	0.78
6	2,4-di-Cl	4- CH_3	4f	120	90	198-200	0.75
7	4-F	4- OCH_3	4g	120	89	222-224	0.73
8	4- CH_3	4- CH_3	4h	120	82	205-207	0.66

^aIsolated yield **Figure 8:** Reusability of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles as catalyst for the synthesis of **4c**. **Figure 9:** FT-IR analysis before and after reuse of the $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanoparticles.

Experimental

Preparation of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline nanocatalyst

Firstly, nano- $\text{Fe}_3\text{O}_4@\text{SiO}_2$ (1 g) were dispersed in dry ethanol (10mL) using an ultrasonic bath for 30 min.

Subsequently, L-proline (0.6 g) and H_2SO_4 (1 mL) were added to the solution of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ (1 g) and heated under reflux conditions. Then, the mixture was stirred for a further 12 h to allow for the completion of the reaction. The resulting magnetic nanoparticles were separated by external magnet and washed with ethanol and water

Scheme 3: Proposed reaction pathway for the synthesis of pyrimidines by nano- $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline.

before being dried in an oven at 60°C to give $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline as a light brown powder.

General procedure for the preparation of pyrimidines

A mixture of 1,3-dimethylbarbituric acid (1 mmol), aromatic aldehydes (1 mmol) and 4-methyl aniline or 4-methoxy aniline (1 mmol) and $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -L-proline (8 mg) were heated in EtOH (10 mL) under reflux conditions. The completion of the mixture was monitored by TLC and the catalyst was separated from reaction before work up by an external magnet field. The precipitate was washed with EtOH to afford the pure product.

Spectral data of products

5-((2-amino-5-methylphenyl)(2-nitrophenyl)methyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (4a): Yellow solid; m. p. 183°C - 185°C , – IR (KBr): $\nu = 3323, 3318, 2922, 1689, 1550, 1350\text{ cm}^{-1}$. – ^1H NMR (400 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 2.99 (s, 3H, CH_3), 3.33 (s, 6H, 2 CH_3), 5.33 (d, $J = 8.8\text{ Hz}$, 1H, CH), 5.47 (d, $J = 8.8\text{ Hz}$, 1H, CH), 6.99-7.47 (m, 7H, ArH), 9.18 (s, 2H, NH_2). – ^{13}C NMR (100 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 25.15, 31.76, 32.19, 43.73, 54.14, 121.20, 121.21, 125.15, 129.07, 129.11, 136.80, 136.82, 139.08, 142.20, 148.19, 154.19, 170.01. – Analysis for $\text{C}_{20}\text{H}_{20}\text{N}_4\text{O}_5$: calcd. C, 60.60; H, 5.09; N, 14.13, Found C, 60.52; H, 5.03; N, 14.05%.

5-((2-amino-5-methoxyphenyl)(4-(methylthio)phenyl)methyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (4b): Yellow solid; m. p. 190°C - 192°C , – IR (KBr): $\nu = 3414, 2917, 1680, 1490, 1442, 816\text{ cm}^{-1}$. – ^1H NMR (400 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 2.04 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 2.81 (s, 6H, 2 CH_3), 4.93 (d, $J = 9.2\text{ Hz}$, 1H, CH), 5.10 (d, $J = 9.2\text{ Hz}$, 1H, CH), 6.31-7.23 (m, 9H, ArH and NH_2). – ^{13}C NMR (100 MHz,

$[\text{D}_6]$ DMSO): δ (ppm) = 22.12, 27.90, 28.54, 50.51, 59.12, 64.58, 121.98, 124.92, 125.85, 126.05, 127.54, 127.92, 128.08, 135.05, 138.12, 139.83, 142.53, 148.77, 164.63, 169.61. – Analysis for $\text{C}_{21}\text{H}_{23}\text{N}_3\text{O}_4\text{S}$: calcd. C, 61.00; H, 5.61; N, 10.16; S, 7.75, Found C, 61.09; H, 5.75; N, 10.19; S, 7.82%.

5-((2-amino-5-methoxyphenyl)(4-chlorophenyl)methyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H, 5H)-trione (4c): Yellow solid; m. p. 240°C - 242°C , – IR (KBr): $\nu = 3343, 2925, 1667, 1493, 528\text{ cm}^{-1}$. – ^1H NMR (400 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 2.80 (s, 6H, 2 CH_3), 2.96 (s, 3H, CH_3), 4.80 (d, $J = 10.2\text{ Hz}$, 1H, CH), 5.12 (d, $J = 10.2\text{ Hz}$, 1H, CH), 6.49-7.43 (m, 9H, ArH and NH_2). – ^{13}C NMR (100 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 27.15, 28.14, 44.00, 51.50, 59.15, 111.49, 117.32, 120.31, 129.84, 130.01, 135.51, 138.42, 139.50, 145.01, 153.30, 157.49, 161.96. – Analysis for $\text{C}_{20}\text{H}_{20}\text{ClN}_3\text{O}_4$: calcd. C, 59.78; H, 5.02; N, 10.46, Found C, 59.82; H, 5.15; N, 10.58%.

5-((2-amino-5-methylphenyl)(3-nitrophenyl)methyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (4d): Yellow solid; m. p. 188°C - 190°C , – IR (KBr): $\nu = 3405, 2916, 1681, 1532, 1350, 1112\text{ cm}^{-1}$. – ^1H NMR (400 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 2.06 (s, 3H, CH_3), 2.75 (s, 3H, CH_3), 2.77 (s, 3H, CH_3), 5.06 (d, $J = 8.8\text{ Hz}$, 1H, CH), 5.33 (d, $J = 8.8\text{ Hz}$, 1H, CH), 6.31-8.26 (m, 9H, ArH and NH_2). – ^{13}C NMR (100 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 20.78, 27.98, 28.66, 49.32, 64.11, 122.02, 123.51, 124.77, 125.15, 128.07, 130.44, 130.77, 134.56, 138.86, 139.55, 142.78, 142.20, 153.01, 168.81. – Analysis for $\text{C}_{20}\text{H}_{20}\text{N}_4\text{O}_5$: calcd. C, 60.60; H, 5.09; N, 14.13, Found C, 60.75; H, 5.19; N, 14.25%.

5-((2-amino-5-methoxyphenyl)(4-nitrophenyl)methyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H, 5H)-trione (4e): Yellow solid; m. p. 237°C - 239°C , – IR (KBr): $\nu = 3473, 3073, 2955, 1667, 1524, 1349\text{ cm}^{-1}$. – ^1H NMR (400 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 2.79 (s, 6H, 2 CH_3), 3.51 (s, 3H, CH_3), 4.99 (d, $J = 8.2\text{ Hz}$, 1H, CH), 5.36 (d, $J = 8.2\text{ Hz}$, 1H, CH), 6.70-8.25 (m, 9H, ArH and NH_2). – ^{13}C NMR (100 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 28.01, 28.69, 50.06, 55.69, 59.15, 113.50, 113.63, 116.23, 122.30, 123.99, 129.14, 132.01, 132.09,

145.53, 147.51, 148.22, 148.41, 151.50, 168.74. – Analysis for $\text{C}_{20}\text{H}_{20}\text{N}_4\text{O}_6$: calcd. C, 58.25; H, 4.89; N, 13.59, Found C, 58.35; H, 4.95; N, 13.68%.

5-((2-amino-5-methylphenyl)(2,4-dichlorophenyl)methyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H, 5H)-trione (4f): Yellow solid; m. p. 198°C–200°C, – IR (KBr): $\nu = 3294$, 3203, 3067, 2921, 1683, 1474 cm^{-1} . – ^1H NMR (400 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 2.11 (s, 3H, CH_3), 3.72 (s, 3H, CH_3), 2.88 (s, 3H, 2 CH_3), 4.90 (d, $J = 10.8$ Hz, 1H, CH), 4.94 (d, $J = 10.8$ Hz, 1H, CH), 6.34–7.94 (m, 7H, ArH), 9.02 (s, 2H, NH_2). – ^{13}C NMR (100 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 20.23, 30.34, 40.53, 40.55, 52.95, 115.63, 124.86, 124.91, 125.22, 128.48, 129.77, 134.42, 135.05, 138.51, 138.51, 139.45, 145.06, 149.96, 158.46, 171.98. – Analysis for $\text{C}_{20}\text{H}_{19}\text{Cl}_2\text{N}_3\text{O}_3$: calcd. C, 57.15; H, 4.56; N, 10.00, Found C, 57.05; H, 4.42; N, 10.15%.

5-((2-amino-5-methoxyphenyl)(4-fluorophenyl)methyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H, 5H)-trione (4g): Yellow solid; m. p. 222°C–224°C, – IR (KBr): $\nu = 3376$, 1686, 1524, 1464, 473 cm^{-1} . – ^1H NMR (400 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 2.80 (s, 3H, CH_3), 2.82 (s, 3H, CH_3), 3.51 (s, 3H, CH_3), 5.04 (d, $J = 10.8$ Hz, 1H, CH), 5.36 (d, $J = 10.8$ Hz, 1H, CH), 6.70–8.25 (m, 9H, ArH and NH_2). – ^{13}C NMR (100 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 28.05, 28.69, 50.66, 55.69, 59.15, 113.15, 113.63, 116.23, 122.30, 123.96, 129.14, 132.01, 132.09, 145.53, 147.51, 148.32, 149.41, 151.50, 168.74. – Analysis for $\text{C}_{20}\text{H}_{20}\text{FN}_3\text{O}_4$: calcd. C, 62.33; H, 5.23; N, 10.90, Found C, 62.45; H, 5.35; N, 10.98%.

5-((2-amino-5-methylphenyl)(p-tolyl)methyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (4h): Yellow solid; m. p. 205°C–207°C, – IR (KBr): $\nu = 3376$, 1686, 1524, 1464, 473 cm^{-1} . – ^1H NMR (400 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 2.82 (s, 3H, CH_3), 2.84 (s, 3H, CH_3), 2.92 (s, 6H, CH_3), 4.95 (d, $J = 10.2$ Hz, 1H, CH), 5.04 (d, $J = 10.2$ Hz, 1H, CH), 6.72–7.50 (m, 9H, ArH and NH_2). – ^{13}C NMR (100 MHz, $[\text{D}_6]$ DMSO): δ (ppm) = 22.20, 25.03, 28.67, 51.66, 58.60, 60.15, 115.18, 116.73, 117.20, 122.32, 123.95, 129.14, 132.01, 132.09, 145.53, 147.51, 148.32, 149.41, 151.50, 168.74. – Analysis for $\text{C}_{21}\text{H}_{23}\text{N}_3\text{O}_3$: calcd. C, 69.02; H, 6.34; N, 11.50; Found C, 69.15; H, 6.42; N, 11.65%.

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