"SUSTAINABLE AND EFFICIENT SYNTHESIS OF 2-AMINO-4-ARYL-6-FERROCENYL PYRIMIDINES CATALYSED BY SODIUM ALKYLBENZENE SULFONATE IN AQUEOUS MEDIUM"

Mahesh B More[1], Mahesh P More[2], Omkar Kulkarni[3], Sandip Patil[4] and Parasnath Bele[5]*

Abstract:
The synthesis of ferrocene-functionalized heterocyclic compounds remains a dynamic area of research, yet documentation regarding the creation of ferrocene-functionalized 2-aminopyrimidines is conspicuously absent within existing literature. Addressing this gap, our study presents a pioneering approach to generate a novel class of compounds, specifically 2-amino-4-aryl-6-ferrocenyl pyrimidines, catalyzed by Sodium alkylbenzene sulfonate in an aqueous medium. Our methodology involves a base-induced condensation process, employing a diverse array of 3-aryl-1-ferrocenyl-2-propen-1-ones, commonly referred to as ferrocenyl chalcones, in conjunction with guanidine hydrochloride. The use of Sodium alkylbenzene sulfonate surfactant as a catalyst facilitates this synthesis, operating within an aqueous environment to ensure both sustainability and efficiency. This work not only expands the scope of ferrocene-based heterocyclic chemistry but also underscores the potential for further exploration and utilization of these newly synthesized compounds across various scientific domains. The demonstrated synthetic pathway, catalytic approach, and compound characterization herein provide a foundational framework for future investigations into ferrocene-functionalized 2-aminopyrimidines, stimulating continued research interest in this burgeoning field.

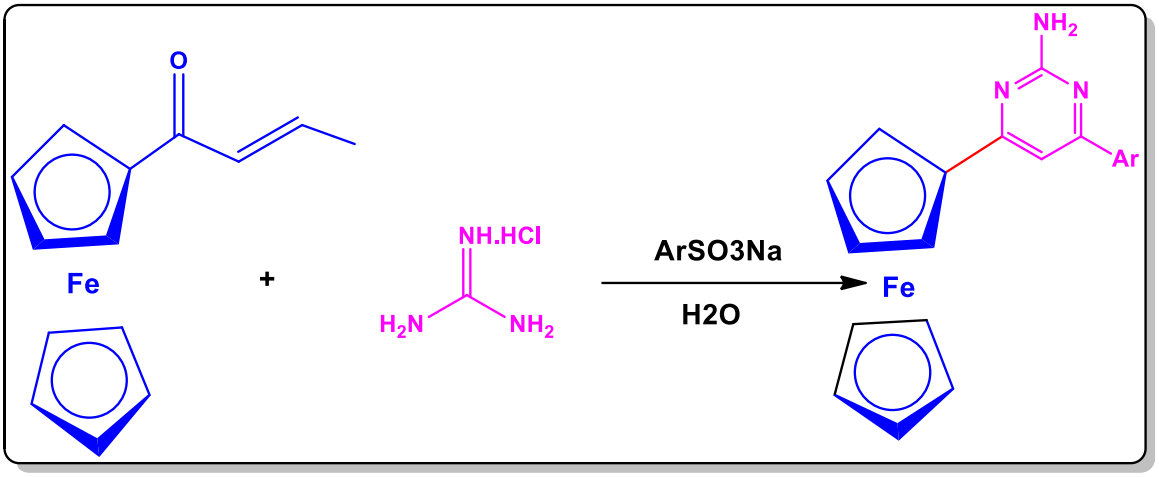
Key-words: 2-amino4-aryl-6-ferrocenyl pyrimidines, sodium alkylbenzene sulfonate medium, Aqueous Medium

[1,3,5*] Department of Chemistry, Mansarovar Global University, Sehore, (M.P.), India
[2] Department of Chemistry, Dr. A.P.J.Abdul Kalam University, Indore, (M.P.), India.
[4] Department of Chemistry, Shri Satya Sai University, Sehore (M.P.), India.

***Corresponding Author: -** Parasnath Bele,
* Mansarovar Global University, Sehore, (M.P.), India Email Id: Parasnathbele2013@gmail.com

DOI: 10.53555/ecb/2022.11.9.39

Graphical Abstract:

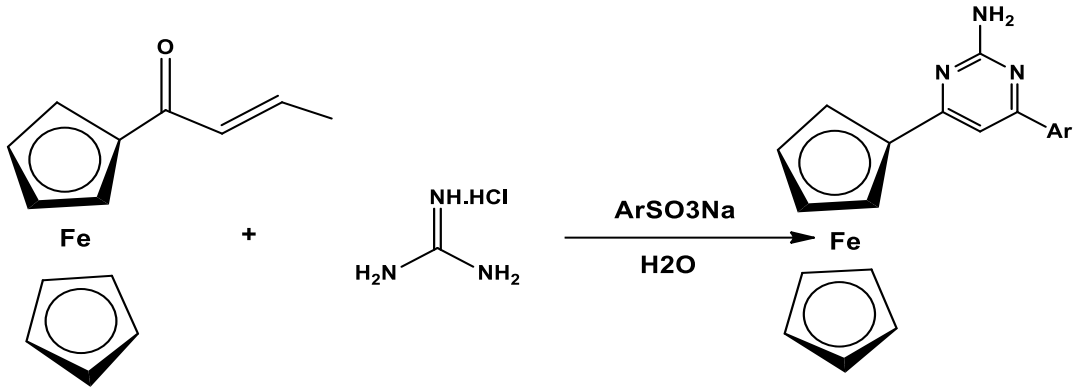


1.0Introduction:

The identification of ferrocene in 1951 sparked an extensive and fruitful interdisciplinary research endeavor. Since then, ferrocene and its derivatives have been thoroughly investigated for their diverse applications in fields like homogeneous catalysis, organic synthesis, supramolecular chemistry, biosensors, medicinal chemistry, and materials science. It is now firmly established that organic compounds containing ferrocene functionalities often exhibit unforeseen biological effects, attributed to distinct membrane permeability characteristics and unique metabolic behavior. The stability and non-toxic nature of the ferrocenyl group in both aqueous and aerobic environments make it an excellent candidate for drug design. Against this backdrop, the incorporation of ferrocene units into heterocyclic rings has emerged as a relevant avenue for research, aiming to broaden the potential applications of heterocyclic compounds. In recent years, there has been a notable increase in research activity focused on ferrocene-functionalized heterocyclic chemistry, indicating a growing interest in this field. The development of sustainable synthetic methodologies in organic chemistry represents a pivotal aspect of modern research, aiming to create environmentally benign processes while maintaining high efficiency and productivity. Among the diverse classes of organic compounds, pyrimidines hold significant importance due to their versatile applications in pharmaceuticals, agrochemicals, and materials science. The 2-amino-4-aryl-6-ferrocenyl pyrimidine scaffold presents a structurally intriguing moiety with emerging prominence in medicinal chemistry, offering potential pharmacological activities. However, the conventional synthetic routes often involve multiple steps, harsh reaction conditions, and the use of hazardous organic solvents, posing challenges from both environmental and synthetic efficiency perspectives. In this context, the utilization of aqueous media coupled with catalytic methodologies emerges as an attractive strategy for sustainable synthesis. Sodium alkylbenzene sulfonates, known for their surfactant properties and mild catalytic behavior, have shown promise in promoting various organic transformations under aqueous conditions. Their potential as catalysts for the synthesis of complex organic structures within an aqueous environment presents a promising avenue toward green and efficient synthetic protocols. This article aims to delineate a sustainable and efficient synthetic route for the construction of 2-amino-4-aryl-6-ferrocenyl pyrimidines catalyzed by sodium alkylbenzene sulfonate in an aqueous medium. The proposed methodology not only addresses the environmental concerns associated with traditional synthetic routes but also offers an expedited and practical approach towards accessing these valuable pyrimidine derivatives. The synthesis, characterization, and potential applications of these novel compounds will be discussed, emphasizing the significance of this methodology in the context of sustainable chemistry. Additionally, the mechanistic insights underlying the catalytic process will be explored, providing a deeper understanding of the reaction pathways involved. Overall, this study showcases a paradigm shift towards sustainable synthesis by harnessing the synergistic effects of aqueous media and mild catalysis, paving the way for the development of eco-friendly methodologies for the construction of pharmaceutically and biologically relevant pyrimidine derivatives.

2.0Result and Discussion:

For the synthesis of 2-amino-4-aryl-6-ferrocenyl pyrimidines, we adopted a common approach involving the base-catalyzed cyclocondensation of chalcones with guanidinium salts. Our strategy centered on reacting ferrocenyl chalcones with guanidine hydrochloride, using surfactant as the base in aqueous medium. Our initial step involved synthesizing a range of ferrocenyl chalcones by reacting acetyl ferrocene with various aryl aldehydes under basic conditions. Following this, we redirected our efforts toward producing aminopyrimidines from these chalcones. In a preliminary experiment, we combined 1-ferrocenyl-3-phenyl-2-propen-1-one (1 mmol), guanidine hydrochloride (1.5 mmol), Sodium alkylbenzene sulfonate (5 mmol), and 20 mL of water. This mixture underwent reflux, monitored via TLC. Upon completion, we poured the resulting mixture into 50 g of ice-cold water. Stirring led to the precipitation of the intended aminopyrimidines, which was filtered and dried. Further purification through column chromatography, using a petroleum ether and ethyl acetate mixture (8:2, v/v) as the eluent, resulted in the corresponding 2-amino-6-ferrocenyl-4-phenyl pyrimidine with a yield of 78%. The table 1.1 displays the yields of 2-amino-6-ferrocenyl-4-phenyl pyrimidine by different surfactants at varying reaction times and tempratute. The surfactants listed are sodium p-octylbenzene sulfonate (NaC8BS), sodium p-heptylbenzene sulfonate (NaC7BS), and sodium p-hexylbenzene sulfonate (NaC6BS). Sodium p-octylbenzene sulfonate (NaC8BS) was synthesized in 25 minutes with a yield of 78% at 70°C.Sodium p-heptylbenzene sulfonate (NaC7BS) took 50 minutes to synthesize, yielding 60% at 95°C and for Sodium p-hexylbenzene sulfonate (NaC6BS) required 120 minutes for synthesis and resulted in a yield of 55% at 110°C. Longer reaction times generally seem to have a negative impact on the yield of the synthesized surfactants with increasing temperature. NaC8BS, synthesized in the shortest time (25 minutes), exhibited the highest yield (78%), whereas NaC6BS, with the longest synthesis time (120 minutes), yielded the lowest (55%). There appears to be a trend of decreasing yield with increasing alkyl chain length in the surfactants, with NaC_8BS (octyl) having the highest yield, followed by NaC_7BS (heptyl), and then NaC_6BS (hexyl).This is because of long alky chain developed more micelle concentration were the maximum solubility of reactant achieved and it gives high yield of the product. These results suggest that shorter reaction times might be more favorable for achieving higher yields in the synthesis of 2-amino-6-ferrocenyl-4-phenyl pyrimidine, and there might be an optimum reaction time for synthesizing each surfactant with the highest yield. Additionally, the structure and length of the alkyl chain in the surfactant seem to influence the yield of the synthesis. We also screening different solvents and surfactant at various temperature and reaction conditions as shown in Table No.1.2 Encouraged by these promising results, we expanded our experiments to include reactions involving a series of 3-aryl-1-ferrocenyl-2-propen-1-ones (1 a-i) and guanidine hydrochloride (Scheme 1). The summarized findings from these experiments are detailed in Table 1.3."



Scheme-1: *Synthesis of 3,4- dihydropyrimidinone using Acacia concinna pods biocatalyst in aqueous medium*

In Table 4.1, it's evident that both the ferrocenyl chalcones containing substituted phenyl rings and those incorporating heterocyclic rings successfully underwent reactions with guanidine hydrochloride, resulting in the desired compounds. Across all cases, the reactions proceeded smoothly, yielding ferrocenyl-substituted 2-aminopyrimidines with moderate to good yields.

Table 1.1: *Screening of various Sodium alkylbenzene sulfonate for synthesis of 2- amino4-aryl-6-ferrocenyl pyrimidines:*

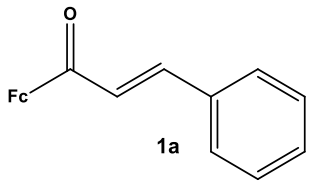
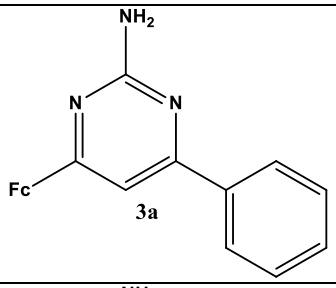
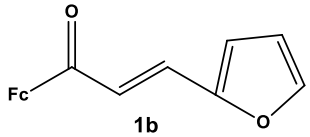
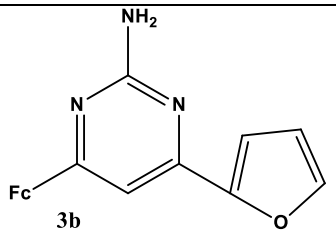
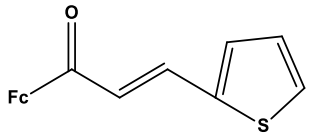
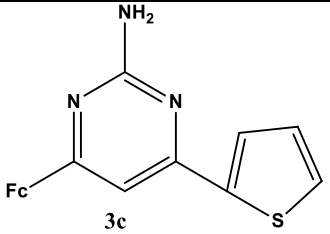
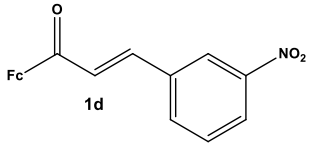
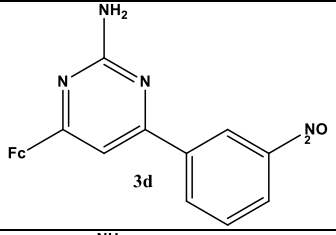
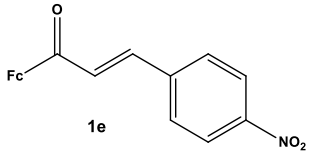
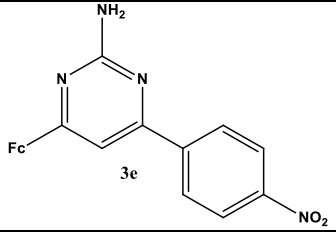
Entry	Surfactant	Temp., °C	Time (Min.)	Yield (%)[a]
1	Sodium *p*-octylbenzene sulfonate (NaC_8BS)	70	**25**	**78**
2	Sodium *p*-heptylbenzene sulfonate (NaC_7BS)	95	50	60
3	Sodium *p*-hexylbenzene sulfonate (NaC_6BS)	110	120	55

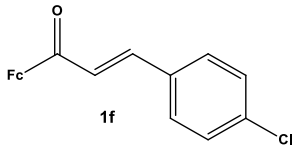
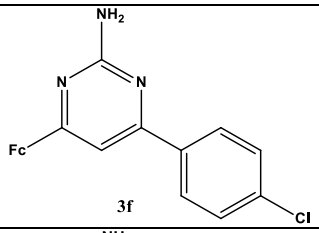
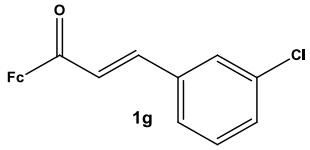
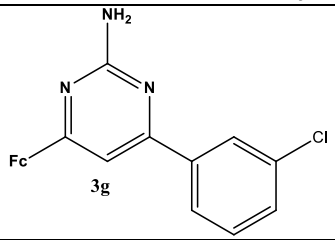
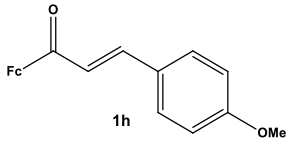
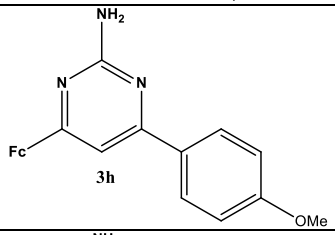
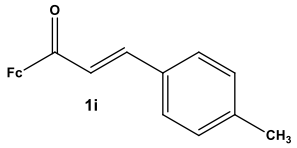
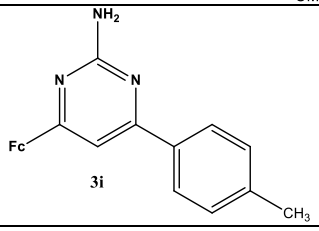
Reaction at various reaction conditions and isolated yield[a].

Table-1.2: *Screening of conditions for synthesis of 2amino4-aryl-6-ferrocenyl pyrimidines:*

Entry	Solvent/ Catalyst	Time	Yield	Temp.
1	Water	24hrs	trace	120°C
2	Ethanol	24hrs	trace	120°C
3	Water + Ethanol(1:1)	24hrs	trace	120°C
4	**Water + NaC_8BS**	**25 min**	**78%**	**70°C**
5	Water + NaC_7BS	50 min	60%	95°C
6	Water + NaC_6BS	120 min	55%	110°C

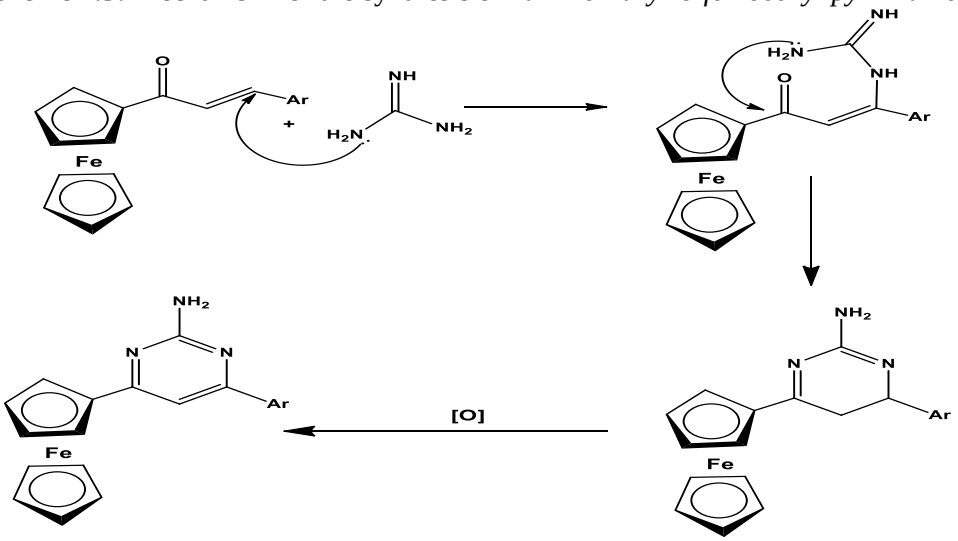
Table 1.3: *The various derivatives of 2-amino4-aryl-6-ferrocenyl pyrimidines catalyzed by Sodium alkylbenzene sulfonate in aqueous medium*

Entry	Ferrocenyl chalcone	Product[a]	Yield[b] %	Time (min)
1.	 1a	 3a	78	25
2.	 1b	 3b	72	32
3.		 3c	70	35
4.	 1d	 3d	75	30
5.	 1e	 3e	76	32

6.	 1f	 3f	66	40
7.	 1g	 3g	71	40
8.	 1h	 3h	64	45
9.	 1i	 3i	66	40

This organic transformation involves mechanism in which a nucleophilic attack on the activated double bond of the β-unsaturated carbonyl compound through a Michael addition. Subsequently, a series of steps, including ring closure, dehydration, and oxidation, occur, ultimately leading to the synthesis of 2-aminopyrimidines, as illustrated in Scheme 1.3.

Scheme 1.3: Mechanism for the synthesis of *2amino4-aryl-6-ferrocenyl pyrimidines*:



3.0Experimental Section:

General: The synthesis of 3-aryl-1-ferrocenyl-2-propen-1-ones (1a-i) followed established literature procedures, involving a base-catalyzed Claisen-Schmidt condensation of 1-acetyl ferrocene with various aldehydes. Uncorrected melting points were determined using an open capillary. Infrared (IR) spectra were recorded using a Perkin-Elmer Spectrum One FTIR spectrophotometer with KBr pellets. Proton nuclear magnetic resonance (^{1}H NMR) spectra were collected on a Varian instrument (300 MHz) with $CDCl_3$ as the solvent and TMS as the internal reference. Mass spectra were obtained using a Shimadzu QP2010 GCMS,

with an ion source temperature of 200 °C. All additional chemicals were obtained from local suppliers and used in their original state.

General Procedure:

After refluxing a mixture containing 3-aryl-1-ferrocenyl-2-propen-1-one (1 mmol), guanidine hydrochloride (1.5 mmol), sodium alkylbenzene sulfonate (5 mmol), and 20 mL of water for the specified duration (refer to Table 4.3), the reaction mixture was transferred to ice-cold water. The resulting solid was isolated through filtration, dried, and subsequently purified using column chromatography on silica gel with a mixture of ethyl acetate and petroleum ether.

Spectroscopic Data

2-Amino-6-ferrocenyl-4-phenyl pyrimidine (Table 1.3 Entry 3a): IR: 3455, 3355, 2924, 1630 cm-1. 1H NMR, 300 MHz, CDCl3:δ 4.09 (s, 5H), 4.47 (s, 2H), 4.96 (s, 2H), 5.09 (s, 2H), 7.06 (s, 1H), 7.23 (s, 3H), and 7.45 (s, 2H). MS: m/z 355 (M+).ES: C20H17N3Fe: C 67.62%, H 4.82%, N 11.82%. Observed: C 67.53%, H 4.86%, N 11.85%.

2-Amino-6-ferrocenyl-4-(furan-2-yl) pyrimidine (Table 1.3, Entry 3b): IR: 3323, 3187, 2923, 1645 cm-1.1H NMR, 300 MHz, CDCl3: δ 4.10 (s, 5H), 4.45 (s, 2H), 4.96 (s, 2H), 5.03 (s, 2H), 6.56 (s, 1H), 7.06 (s, 1H), 7.14 (d, J = 3.6 Hz, 1H), 7.58 (s, 1H).MS: m/z 345 (M+).ES: C18H15N3OFe: C 62.63%, H 4.37%, N 12.17%. Observed: C 62.48%, H 4.30%, N 12.05%.

2-Amino-6-ferrocenyl-4-(2-thienyl) pyrimidine (Table 1.3, Entry 3c): IR: 3395, 3304, 2925, 1621 cm-1.1H NMR, 300 MHz, CDCl3: δ 4.09 (s, 5H), 4.44
(s, 2H), 4.94 (s, 2H), 5.02 (s, 2H), 7.01 (s, 1H), 7.23 (d, 1H), 7.44 (d, 1H), 7.72
(d,1H).MS: m/z 361 (M+).ES: C18H15N3SFe are C 59.84%, H 4.18%, N 11.63%.
The observed values are C 59.80%, H 4.22%, N 11.57%.

2-Amino-6-ferrocenyl-4-(3-nitrophenyl) pyrimidine (Table 1.3, Entry 3d): IR 3324, 3193, 2924,1643 cm-1.1H NMR, 300 MHz, CDCl3: δ 4.11 (s, 5H), 4.50 (s, 2H), 4.98 (s, 2H), 5.10 (s, 2H), 7.13 (s, 1H), 7.65 (m, 1H), 8.32 (d, J = 7.9 Hz, 1H), 8.38 (d, J = 7.5 Hz, 1H), 8.87 (singlet, 1H).MS: m/z 400 (M+).ES: C20H16N4O2Fe are C 60.02%, H 4.02%, N 13.99%. The observed values are C 60.14%, H 4.08%, N 13.87%.

2-Amino-6-ferrocenyl-4 -(4-nitrophenyl) pyrimidine (Table1.3, Entry 3e): IR: 3391, 3198, 2923, 1625 cm-1. 1H NMR, 300 MHz, CDCl3: Chemical shifts at δ 4.10 (s, 5H), 4.48 (s, 2H), 4.98 (s, 2H), 5.09 (s, 2H), 7.23 (s, 1H), 8.32 (d, J = 6.4 Hz, 2H), 8.47 (d, J = 6.5 Hz, 2H). MS: m/z 389 (M+).ES: C20H16N4O2Fe are C 60.02%, H 4.02%, N 13.99%. The observed values are C 59.93%, H 4.10%, N 14.07%.

2-Amino-4-(3-chlorophenyl)-6-ferrocenyl pyrimidine (Table 1.3, Entry 3f): IR: 3324, 3193, 2924, 1643 cm-1.1H NMR, 300 MHz, CDCl3: δ 4.09 (s, 5H), 4.45 (s, 2H), 4.96 (s, 2H), 5.08 (s, 2H), and 7.04 to 8.01 (multiplet, Ar-H).MS: m/z 389 (M+).ES: C20H16N3Cl Fe are C 61.14%, H 4.13%, N 10.78%. The observed values are C 61.07%, H 4.06%, N 10.72%.

2-Amino-4-(4-chlorophenyl) -6-ferrocenylpyrimidine (Table 1.3, Entry 3g): IR: 3404, 3333, 2923,1645 cm-1. 1H NMR, 300 MHz, CDCl3: δ 4.09 (s, 5H), 4.46 (s, 2H), 4.95 (s, 2H), 5.04 (s, 2H), 7.06 (s, 1H), 7.45 (d, J = 6.2 Hz, 2H), and 7.96 (d, J = 6.7 Hz, 2H).MS: m/z 389 (M+). ES: C20H16N3ClFe are C 61.14%, H 4.13%, N 10.78%. The observed values are C 61.10%, H 4.18%, N 10.84%.

2-Amino-6-ferrocenyl-4-(4-methoxyphenyl)pyrimidine (Table1.3,Entry 3h): 1)IR 3323, 3280, 2924, and 1602 cm-1. 1H NMR, 300 MHz, CDCl3: δ 3.87 (s, 3H), 4.09 (st, 5H), 4.44 (s, 2H), 4.95 (s, 2H), 5.04 (s, 2H), 7.00 (d, J = 5 Hz, 2H), 7.08 (s, 1H), and 7.97 (d, J = 5 Hz, 2H).MS: m/z 385 (M+).ES: C21H19N3OFe are C 65.47%, H 4.97%, N 10.91%. The observed values are C 65.30%, H 4.90%, N 11.06%.

2-Amino-6-ferrocenyl-4-(4-methyphenyl) pyrimidine (Table 1.3 Entry 3i) : IR: 3308, 3179, 2923,1626 cm-1. 1H NMR, 300 MHz, CDCl3: δ 2.42 (s, 3H), 4.09 (s, 5H), 4.45 (s, 2H), 4.96 (s, 2H), 5.05 (s, 2H), 7.14 (s, 1H), 7.29 (d, J = 6.4 Hz, 2H), 7.89 (d, J = 6.8 Hz, 2H). MS: m/z 369 (M+).ES: C21H19N3Fe are C 68.31%, H 5.18%, N 11.37%. The observed values are C 68.39%, H 5.15%, N 1

4.0Conclusion:

The successful synthesis of a new series of 2-amino-4-aryl-6-ferrocenyl pyrimidines has been achieved with high yields. This accomplishment was realized through a base-induced cyclo-condensation method involving 3-aryl-1-ferrocenyl-2-propen-1-ones, commonly referred to as ferrocenyl chalcones, and guanidine

hydrochloride. The catalysis by sodium alkylbenzene sulfonate, employed as a surfactant, facilitated this reaction in an aqueous medium. Critical aspects of the synthesized compounds have been rigorously addressed and verified. The molecular formulas were initially established using CHN microanalysis, ensuring accuracy in the elemental composition. Subsequent confirmation through mass spectroscopy reinforced the validity of these formulas. Overall, this comprehensive approach of synthesis and subsequent characterization, employing a range of analytical techniques, confirms the successful preparation of the targeted series of 2-amino-4-aryl-6-ferrocenyl pyrimidines. The utilization of base-induced cyclo-condensation in an aqueous medium, alongside the catalytic role of sodium alkylbenzene sulfonate, underscores the efficiency and potential applicability of this synthetic method in accessing novel compounds with significant chemical and possibly biological relevance.

5.0Acknowledgments:
Authors are thankfull to Department of Chemistry, Mansarovar Global University, Sehore, (M.P.), India for providing necessary facilities.

6.0Disclosure statement
The authors declare no potential conflict of interest.

7.0 References:

1. a) K. Undheim, T. Benneche, in Comprehensive Heterocyclic Chemistry II, *Vol. 6* (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven, A. McKillop), Pergamon, Oxford, **1996**, p. 93; b) I. M. Lagoja, Chem. Biodiversity, **2005**, *2*, 1; c) J. P. Michael, Nat. Prod. Rep., **2005**, *22*, 627; d) J. A. Joule, K. Mills, in Heterocyclic Chemistry, 4th ed. Blackwell, Cambridge, **2000**, p. 194; e) A.W.Erian, Chem. Rev., **1993**, *93*, 1991.
2. A. M. Joffe, J. D. Farley, D. Linden, G. Goldsand, Am. J. Med., 1989,87, 332.
3. E. Petersen, D. R. Schmidt, Expert Rev. Anti-Infect. Ther., **2003**, *1*,175.
4. E. Nadal, E. Olavarria, Int. J. Clin. Pract., **2004**, *58*, 511.
5. J. L. Blum, Oncologist, **2001**, *6*, 56.
6. a) S. Köytepe, A. Pasahan, E. Ekinci, T. Seçkin, Eur. Polym. J., **2005**, *41*, 121; b) R. Gompper, H-J. Mair, K. Polborn, Synthesis, **1997**, 696;c) T. Kanbara, T. Kushida, N. Saito, I. Kuwajima, K. Kubota, T. Yamamoto, Chem. Lett., **1992**,583.
7. a) G. Brugnatelli, Giornale di fisica, chimica, et storia Naturale (Pavia) decada seconda, **1818**, *1*, 117.
8. E. Frankland, H. Kolbe, Justus Liebigs Ann. Chem., **1848**, *65*, 269
9. H. Mathur, M. S. K. Zai, P. Khandelwal, N. Kumari, V. P. Verma, and D. K. Yadav, Chem. Heterocycl. Compd., vol. 54, no. 3, 2018, pp. 375–378.
10. D. J. Brown, B. T. England, J. Chem. Soc. C, **1971**, 425.
11. V. P. Mamaev, A. L. Vais, Chem. of Heterocyclic Compd., **1975**, *11*, 1322.
12. El-Rayyes, Journal of Heterocyclic Chemistry, 1982, 415-419.
13. Jung Pyo Kwak, Pham Duy Quang Dao,Chan Sik Cho. European Journal of Chem., **2020,** 3468-3474.
14. A. Alberola, L. F. Antolin, A. M. González, M. A. Laguna, F. J.Pulido, Heterocycles, **1987**, *25*, 393.
15. N. Zanatta, M. D. F. M. Cortelini, M. J. S. Carpes, H. G. Bonacorso, M. A. P. Martins, J. Heterocyclic Chem., **1997**, *34*, 509.
16. S. P. Singh, H. Batra, R. Naithani, O. Prakash, Indian J. Heterocyclic Chem., **1999**, *9*, 73.
17. P. Forgo, I. Vincze, Steroids, **2002**, *67*, 749.
18. R.V. Hangarge, M. S. Shingare, Indian J. Heterocyclic Chem., **2002**, *11*, 323.
19. Sarosh Iqbal, Nimra Naveed Shaikh, Khalid Mohammed Khan, Shumaila Kiran , Sehrish Naz , Zaheer Ul-Haq , Shahnaz Perveen and M. Iqbal Choudhary *Molecules*, vol. 27, Art. no. 22. **Jan. 2022**,7786
20. Z. Xu, H. Chen, G.-J. Deng, and H. Huang, *Org. Biomol. Chem.*, vol. 19, no. 40, **2021**, pp. 8706–8710.
21. M. Zhao, J. Cai, and X. Zhao, *Org. Chem. Front*, vol. **2019,**4, pp. 426–431.
22. T. Balasankar, S. Nagarajan, Heterocyclic Commun., **2004**. *10*, 451.
23. S. Chandrasekaran, S. Nagarajan, Il Faramco, **2005**, *60*, 279.
24. S. S. Rindhe, P.N. Mandhare, L. R. Patil, R. A. Mane, Indian J. Heterocyclic Chem., **2005**, *15*, 133.
25. D. Kidemet, I. Elenkov, V. Prgomet, Synlett, **2005**, 2531.
26. S. Buscemi, A. Pace, A. P. Piccionello, N. Vivona, M. Pani, Tetrahedron, **2006**. *62*, 1158.
27. N. Ingarsal, G. Saravanana, P. Amutha, S. Nagarajan, Eur. J. Med.Chem., **2007**, *42*, 517.
28. B. Zhang *et al.*, *Nat. Commun.*, vol. 13, **2022**, no. 1, p. 3365.
29. T. V. Hughes, S. L. Emanuel, A. K. Beck, S. K. Wetter, P. J.Connolly, P. Karnachi, M.

Reuman, J. Seraj, A. R. Fuentes-Pesquera,R. H. Gruninger, S. A. Middleton, R Lin, J. M. Davis, D. F. C. Moffat, Biorg. Med. Chem. Lett., **2007**, *17*, 3266.
30. P. Benderittera, J. X. de Araújo Júnior, M. Schmitt,J.–J.Bourguignon, Tetrahedron, **2007**, *63*, 12465.
31. A. Srinivas, A. Nagraj, S. Reddy, Journal of Heterocyclic Chem.,**2008**, *45*, 1121.
32. Duygu Bayramoglu , Gulbin Kurtay , Mustafa Gull., Synthetic communications., **2020,** 649–658.
33. S. Goswami, S. Jana, A. Hazra, H. -K. Fun, S. Chantrapromma , Supramol. Chem., **2008**, *20*, 495.
34. R.J. Altenbach, R. M. Adair, B. M. Bettencourt, L. A. Black, S. R. Fix-Stenzel, S. M. Gopalakrishnan, G. C. Hsieh, H. Liu, K. C. Marsh,M. J. McPherson, I. Milicic, T. R. Miller, T. A. Vortherms, U. Warrior, J. M. Wetter, N. Wishart, D. G. Witte, P. Honore, T. A. Esbenshade, A. A. Hancock, J. D. Brioni, M. D. Cowart, J. Med. Chem., **2008**, *51*, 6571.
35. J. Coboa, M. Noguerasa, J. N. Lowb, R.Rodrígueza, Tetrahedron Lett., **2008**, *49*, 7271
36. F. Chioma, Anthony C. Ekennia, Collins U. Ibeji, Sunday N. Okafor, Damian C. Onwudiwe, Aderoju A. Osowole, Oguejiofo T. Ujam , *J. Mol. Struct.*, vol. 1163, 2018, pp. 455–464.
37. B. Zhang *et al. Nat. Commun.*, vol. 13, no. 1, **2022** ,p. 3365.
38. T. J. Kealy, P. L. Pauson, Nature, **1951**, *168*, 1039.
39. S. A. Miller, J. A. Tebboth, J. F. Tremaine, J. Chem. Soc., **1952**, 632.
40. T. J. Colacot, Chem. Rev., **2003**, *103*, 3101; (b)A. E. Kaifer, J. deMendoza, S. A. Miller, J. A. Tebboth, J. F. Tremaine, J. Chem. Soc., **1952**, 632.Comprehensiv Supramolecular Chemistry *Vol.1*, (Oxford) Elsevier, **1996**, 701.
41. T. Yao, G. A. Rechnitz, Biosensors, **1987**, *3*, 307.
42. P. Kopf-Maier, H. Kopf, Chem. Rev., **1987**, *87*, 1137.
43. C. Biot, L. Delhaes, C. M. N'Diaye, L. A. Maciejewski, D. Camus, D.Dive, Bioorg. Med. Chem., **1999**, *7*, 2843.
44. R. Epton, G. Marr, G. K. Rogers, J. Organomet. Chem., **1976**, *10*,C42.
45. H. Zhu, H. Lin, H. Guo, L. Yu , Mat. Sci. Eng. B, **2007**, *138*, 101.
46. J. Fang, Z. Jin, Z. Li, W. Liu, J. Organomet. Chem., **2003**, *674*.
47. N. Fu, Y. Yuan, M. Pang, J. Wang, C. J. Peppe, J. Organomet, Chem., **2003**, *672*, 52.
48. D. Braga, D. Addario, M. Polito, Organometallics, **2004**, *23*, 2810.