Asian Journal of Chemistry; Vol. 36, No. 10 (2024), 2307-2310

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2024.32303

Synthesis, Characterization and Antifungal Studies of Novel Substituted Benzaldehyde Derivatives of 2-Amino-6-ferrocenyl-4-phenylpyrimidine

AJITKUMAR VIJAY INGLE* and SHRIMANT VHANNAPPA RATHOD

Department of Chemistry, Bhavan's Hazarimal Somani College, Mumbai-400007, India

*Corresponding author: E-mail: inglevajit@gmail.com

Received: 12 July 2024; *Accepted*: 21 August 2024; *Published online*: 30 September 2024; AJC-21761

A series of novel 2-amino-6-ferrocenyl-4-phenylpyrimidine (AFPP) derivatives (**6a-j**) have been synthesized by coupling AFPP with thioglycolic acid and various substituted benzaldehydes (**a-j**) using standard 1,3-dicyclohexylcarbodiimide (DCC) protocol. The synthesized compounds were characterized by FTIR, ^{13}C NMR, ^{1}H NMR and MS techniques. The synthesized compounds **6a-j** were evaluated for antifungal activities against *Candida albicans* MTCC 183. Comparing compounds **6a-j** to standard amphotericin B, it was found that the synthesized compounds showed excellent activity.

Keywords: 2-Amino-6-ferrocenyl-4-phenylpyrimidine, Substituted benzaldehydes, Antifungal activity, Molecular docking study.

INTRODUCTION

Numerous ferrocene derivatives have been synthesized since then they are discovered to possess a multitude of vital uses across numerous domains and most importantly in medicinal chemistry [1]. Due to their unusual metabolism and diverse membrane penetration properties, ferrocene-functionalized organic compounds often demonstrate a wide range of biological activities [2-4]. Ferrocene is favoured for new drug creation due to its ease of substitution, ring stability and significant changes in the biological activities. Ferrocene heterocycles have emerged as a key route for bioactive chemicals since the ferrocenyl moiety when combined with the heterocyclic structure may boost their biological activities or provide novel therapeutic benefits [5-10].

Ferrocenyl pyrimidine derivatives also has wide applications in medical field and has emerged with analgesic, anti-inflammatory [11], antibacterial [12,13], antifungal [14-16], antiplasmodial [17], anticancer [18], antimalarial [19], antitubercular [20-22], antiproliferative [23], anti-amoebic [24] properties. In this work, a series of novel 2-amino-6-ferrocenyl-4-phenylpyrimidine (AFPP) derivatives (**6a-j**) have been synthesized by coupling with thioglycolic acid and various substituted benzaldehydes (**5a-j**). The structures of compounds were confirmed using spectroscopic techniques and evaluated for the antifungal activity.

EXPERIMENTAL

The AR grade chemicals and solvents in this work were procured from the various commercial sources and used without further purification. The characterization of the compounds for its physical parameters and spectral analysis was recorded for IR on Perkin-Elmer FTIR spectrophotometer, ^{1}H NMR on Bruker 300 MHz NMR spectrophotometer and & ^{13}C NMR on Bruker AVANCE NEO 500 MHz NMR spectrophotometer was used. The mass spectra was measured on Thermo Finnigan-TSQ Quarter Ultra (Triple Quad) instrument. The melting points were measured in an open capillary and are uncorrected.

General procedure of synthesis: Aqueous NaOH (1.2 mol) was gradually added at 5-10 ºC to a solution of acetyl ferrocene (1 mol) and benzaldehyde in 100 mL of ethanol and at room temperature, while stirring the solution for 4-6 h. The progress of reaction was monitored using TLC using petroleum ether and ethyl acetate as mobile phase. Dilute HCl was used to neutralize the reaction mixture. The resultant solid was washed several times with water after filtration, dried and recrystallized with methanol yielding a red solid compound **3**.

Product **3** obtained in stage 1 (1 mol) was dissolved in ethanol and then added gradually in a solution containing Na_2CO_3 (1.2 mol) and guanidine hydrochloride (1.2 mol) at 25-30 ºC and stirred for 4-6 h at 50-60 ºC. Using ethyl acetate

and petroleum ether as mobile phase, the progress of the reaction was monitored using TLC. After the solid formation, the mixture was added on ice and the solid produced was filtered, washed with water, dried and purified with 10% hexane/ethyl acetate *via* column chromatography to obtain red solid compound **4**.

Finally, dicyclohexylcarbodiimide (DCC) (1 mol) was mixed in ice-cold solution of compound **4** (1 mol) in dry DCM with substituted aldehydes **5a-j** (1 mol). After 5 min, 1 mol of thioglycolic acid was added at 0 ºC while stirring the solution continuously for 24-48 h. TLC was used to monitor the progress the reaction. Drying of the reaction mixture was carried out using anhydrous Na_2SO_4 after the completion of product formation then being washed with 10% $NaHCO_3$, brine solution, 5% citric acid and water. The final compounds were obtained by chromatography column packed with silica gel and eluted using methyl acetate-petroleum ether, the excess of solvent was removed under reduced pressure and the obtained mass was further solidified after being treated with petroleum ether to yield the final compounds **6a-j** (**Scheme-I**).

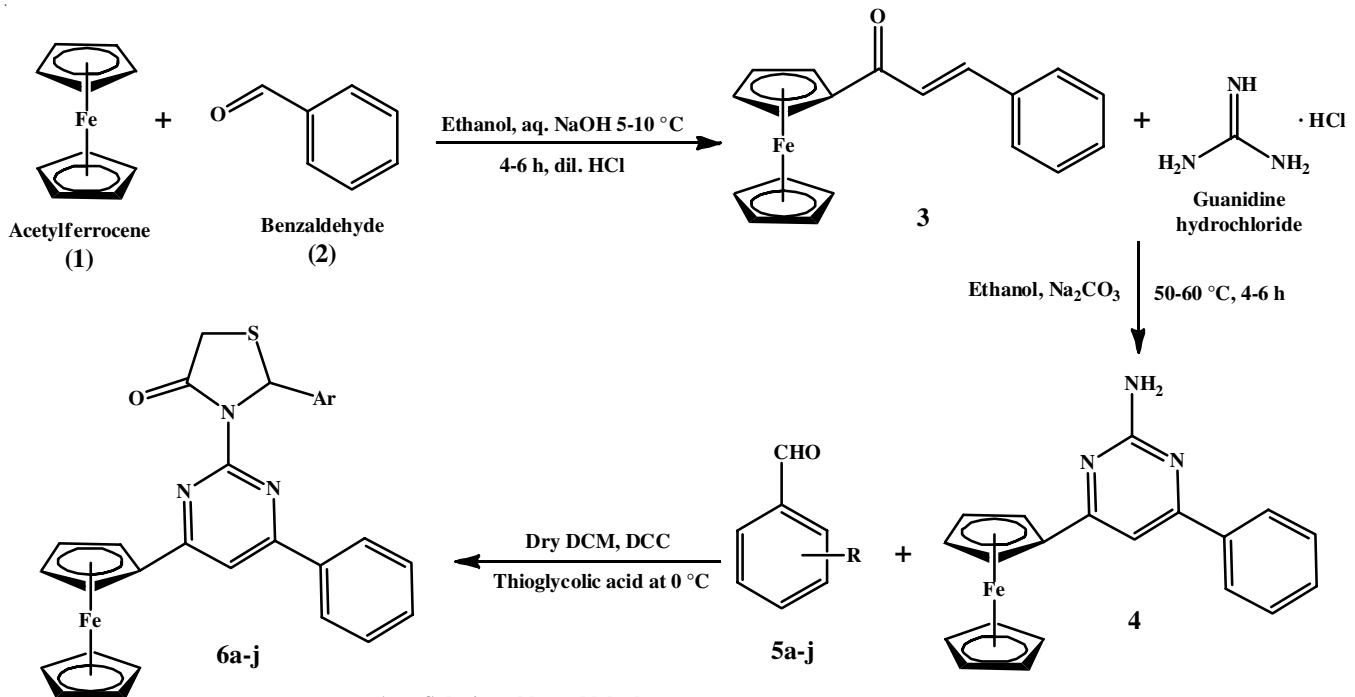
Compound 3: Yield: 78%, m.p.: 111-113 ºC. IR (KBr, ν_{max}, cm^{-1}): 2946 (Ar-H), 1708 (C=O), 1594 (C=C); ^{1}H NMR ($CDCl_3$/DMSO, 400 MHz, δ ppm): 7.80 (d, *J* = 15.6 Hz, 1H), 7.64-7.67 (m, 2H), 7.40-7.46 (m, 3H), 7.13 (d, *J* = 16.0 Hz, 1H), 4.91 (dd, *J* = 1.6 & 2.4 Hz, 2H), 4.59 (t, *J* = 2.0 Hz, 2H), 4.21 (s, 5H); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 169.7, 130.6, 128.5, 128.3, 126.8, 124.2, 123.6, 79.4, 70.5, 69.6, 67.8. MS (APCI): *m/z* 317.2.

Compound 4: Yield: 73%, m.p.: 142-144 ºC. IR (KBr, ν_{max}, cm^{-1}): 3453, 3288 (-NH_2), 2958 (Ar-H), 1598 (C=N), 1572 (C=C), 1384 (C-N), ; ^{1}H NMR ($CDCl_3$/DMSO, 400 MHz, δ ppm): 8.01-8.04 (m, 2H), 7.49-7.51 (m, 3H), 7.13 (s, 1H), 5.12 (s, 2H), 4.98 (t, *J* = 2.0 Hz, 3H), 4.47 (t, *J* = 2.0 Hz, 3H), 4.11 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 130.6, 128.5, 128.2, 126.8, 124.2, 123.6, 113.0, 112.6, 79.4, 70.5, 69.6, 67.9. MS (APCI): *m/z* 356.1.

2-Phenyl-3-(2′-(4′-ferrocenyl-6′-phenylpyrimidinyl)-thiazolidin-4-one (6a): Colour: Light brown solid, Yield: 72%, m.p.: 210-212 ºC. IR (KBr, ν_{max}, cm^{-1}): 2927 (Ar-H), 1735 (C=O), 1577 (C=N), 1534 (C=C), 1372 (C-N); ^{1}H NMR ($CDCl_3$/DMSO, 400 MHz, δ ppm): 8.25-8.28 (m, 2H), 7.89 (s, 1H), 7.49-7.57 (m, 5H), 7.34 (t, *J* = 10.1 Hz, 2H), 7.24 (d, *J* = 9.7 Hz, 1H), 6.85 (s, 1H), 5.21 (d, *J* = 1.6 Hz, 1H), 5.10 (d, *J* = 1.6 Hz, 1H), 4.55 (d, *J* = 3.0 Hz, 2H), 4.14 (s, 1H), 3.96 (s, 1H), 3.85 (s, 5H). ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 169.9, 169.5, 163.3, 156.7, 153.1, 142.9, 135.9, 131.1, 128.8, 127.3, 110.7, 108.3, 106.8, 79.7, 71.3, 69.8, 68.3, 56.1, 33.1. MS (APCI): *m/z* 518.

2-(2″-Methoxyphenyl)-3-(2′-(4′-ferrocenyl-6′-phenyl-pyrimidinyl)thiazolidin-4-one (6b): Colour: dark brown solid, yield: 76%, m.p.: 95-97 ºC. IR (KBr, ν_{max}, cm^{-1}): 2928 (Ar-H), 1716 (C=O), 1577 (C=N), 1530 (C=C), 1370 (C-N), 1245 (C-O); ^{1}H NMR ($CDCl_3$/DMSO, 400 MHz, δ ppm): 8.13-8.16 (m, 2H), 7.52 (t, *J* = 4.2 Hz, 3H), 7.40 (s, 2H), 7.24-7.33 (m, 2H), 7.12 (s, 2H), 6.87-7.00 (m, 3H), 4.87 (t, *J* = 2.4 Hz, 3H), 4.47 (s, 3H), 3.93-4.12 (m, 2H), 3.85-3.91 (m, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 170.2, 169.7, 156.8, 137.4, 136.4, 136.0, 131.1, 130.1, 129.4, 128.9, 128.5, 126.8, 120.6, 79.6, 71.3, 70.3, 69.6, 68.2, 67.8, 62.9, 57.1, 33.0. MS (APCI): *m/z* 548.5.

2-(3″-Methoxyphenyl)-3-(2′-(4′-ferrocenyl-6′-phenyl-pyrimidinyl)thiazolidin-4-one (6c): Colour: dark brown solid, yield: 78%, m.p.: 92-94 ºC. IR (KBr, ν_{max}, cm^{-1}): 2930 (Ar-H), 1720 (C=O), 1635 (C=N), 1577 (C=C), 1371 (C-N), 1244



Ar = Substituted benzaldehyde
R = H (6a); 2-OCH_3 (6b); 3-OCH_3 (6c); 4-OCH_3 (6d); 2-CF_3 (6e); 3-CF_3 (6f); 4-CF_3 (6g); 2-Cl (6h); 3-Cl (6i); 4-Cl (6j)

Scheme-I

(C-O); ^{1}H NMR ($CDCl_3$/DMSO, 400 MHz, δ ppm): 8.13-8.16 (m, 2H), 7.52 (t, *J* = 4.4 Hz, 3H), 7.40 (s, 3H), 7.13 (s, 3H), 6.89-7.00 (m, 2H), 4.86-4.89 (m, 3H), 4.47 (s, 1H), 4.12 (s, 3H), 3.96-4.07 (m, 2H), 3.79-3.89 (m, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 170.2, 169.9, 156.8, 156.0, 136.4, 136.0, 131.1, 129.3, 128.9, 128.5, 126.8, 124.7, 120.4, 79.6, 71.3, 70.2, 69.6, 68.2, 67.8, 61.1, 55.8, 33.0. MS (APCI): *m/z* 548.5.

2-(4″-Methoxyphenyl)-3-(2′-(4′-ferrocenyl-6′-phenylpyrimidinyl)thiazolidin-4-one (6d): Colour: dark brown solid, yield: 68%, m.p.: 96-98 ºC. IR (KBr, ν_{max}, cm^{-1}): 2929 (Ar-H), 1707 (C=O), 1627 (C=N), 1578 (C=C), 1363 (C-N), 1244 (C-O); ^{1}H NMR ($CDCl_3$/DMSO, 400 MHz, δ ppm): 8.27 (d, *J* = 5.3 Hz, 2H), 7.89 (s, 1H), 7.57 (s, 3H), 7.44 (d, *J* = 11.0 Hz, 2H), 6.87 (d, *J* = 11.2 Hz, 2H), 6.78 (s, 1H), 5.59 (d, *J* = 10.3 Hz, 2H), 5.23 (s, 2H), 5.12 (s, 1H), 4.56 (s, 3H), 4.08 (dd, *J* = 8.5 & 12.6 Hz, 3H), 3.95 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 170.2, 169.7, 157.9, 142.8, 137.6, 136.0, 130.2, 128.5, 126.7, 121.7, 116.4, 79.5, 71.3, 70.3, 69.6, 68.2, 67.8, 62.4, 57.5, 33.3. MS (APCI): *m/z* 548.6.

2-(2″-Trifluoromethoxyphenyl)-3-(2′-(4′-ferrocenyl-6′-phenylpyrimidinyl)thiazolidin-4-one (6e): Colour: reddish brown solid, yield: 78%, m.p.: 115-117 ºC. IR (KBr, ν_{max}, cm^{-1}): 2935 (Ar-H), 1713 (C=O).1632 (C=N), 1583 (C=C), 1352 (C-N), 1120 (C-F); ^{1}H NMR ($CDCl_3$/DMSO, 400 MHz, δ ppm): 8.09-8.14 (m, 2H), 7.77 (d, *J* = 9.9 Hz, 1H), 7.65 (d, *J* = 10.9 Hz, 1H), 7.49-7.54 (m, 4H), 7.40 (dd, *J* = 9.0 & 10.1 Hz, 2H), 7.12 (s, 1H), 4.89-4.92 (m, 2H), 4.49 (t, *J* = 2.5 Hz, 2H), 4.03 (d, *J* = 1.4 Hz, 1H), 3.91 (s, 1H), 3.86 (s, 5H); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 170.4, 169.8, 163.0, 156.6, 135.9, 131.2, 130.1, 128.8, 128.5, 127.3, 126.8, 126.4, 125.7, 108.3, 102.0, 79.5, 71.4, 70.3, 69.7, 68.2, 61.6, 33.0. MS (APCI): *m/z* 586.4.

2-(3″-Trifluoromethoxyphenyl)-3-(2′-(4′-ferrocenyl-6′-phenylpyrimidinyl)thiazolidin-4-one (6f): Colour: reddish brown solid, yield: 80%, m.p.: 96-98 ºC. IR (KBr, ν_{max}, cm^{-1}): 2928 (Ar-H), 1717 (C=O), 1632 (C=N), 1577 (C=C), 1404 (C-N), 1117 (C-F); ^{1}H NMR ($CDCl_3$/DMSO, 400 MHz, δ ppm): 8.25 (dd, *J* = 4.1 & 6.2 Hz, 2H), 7.92 (s, 1H), 7.83 (d, *J* = 10.8 Hz, 1H), 7.61-7.69 (m, 2H), 7.47-7.57 (m, 3H), 7.00 (s, 1H), 5.18 (s, 1H), 4.99 (s, 1H), 4.55 (s, 2H), 4.38 (s, 1H), 4.11 (s, 1H), 3.99 (d, *J* = 14.4 Hz, 1H), 3.81 (s, 5H); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 170.0, 169.6, 163.0, 156.9, 133.7, 131.2, 129.5, 129.0, 128.8, 128.1, 127.1, 126.8, 126.0, 125.4, 123.0, 121.3, 79.5, 71.1, 69.3, 68.0, 64.6, 33.5. MS (APCI): *m/z* 586.5.

2-(4″-Trifluoromethoxyphenyl)-3-(2′-(4′-ferrocenyl-6′-phenylpyrimidinyl)thiazolidin-4-one (6g): Colour: reddish brown solid, yield: 78%, m.p.: 116-118 ºC. IR (KBr, ν_{max}, cm^{-1}): 2930 (Ar-H), 1711 (C=O), 1605 (C=N), 1588 (C=C), 1351 (C-N), 1128 (C-F); ^{1}H NMR ($CDCl_3$/DMSO, 400 MHz, δ ppm): 8.07-8.10 (m, 2H), 7.60-7.66 (m, 2H), 7.53 (dd, *J* = 3.4 & 5.0 Hz, 4H), 7.42 (s, 1H), 6.82 (s, 1H), 4.90 (d, *J* = 1.5 Hz, 1H), 4.84 (d, *J* = 1.6 Hz, 1H), 4.51 (dd, *J* = 1.8 & 3.4 Hz, 2H), 4.25 (s, 1H), 4.06 (s, 1H), 3.90 (s, 1H), 3.70 (s, 5H); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 170.5, 169.6, 148.2, 147.7, 141.6, 137.1, 134.9, 130.9, 128.5, 124.0, 123.1, 122.1, 79.5, 71.3. 70.3, 69.8, 68.2, 67.8, 62.4, 34.1. MS (APCI): *m/z* 586.4.

2-(2″-Chlorophenyl)-3-(2′-(4′-ferrocenyl-6′-phenylpyrimidinyl)thiazolidin-4-one (6h): Colour: orange red solid, yield: 72%, m.p.: 56-58 ºC. IR (KBr, ν_{max}, cm^{-1}): 2927 (Ar-H), 1577 (C=N), 1536 (C=C), 1735 (C=O), 1372 (C-N), 831 (C-Cl). ^{1}H NMR ($CDCl_3$/DMSO, 400 MHz, δ ppm): 8.17 (s, 2H), 7.54 (s, 2H), 7.41 (s, 3H), 7.20-7.25 (m, 3H), 4.94 (s, 3H), 4.85 (s, 1H), 4.49 (s, 2H), 4.06 (s, 1H), 3.88 (s, 5H). ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 170.2, 169.9, 163.4, 156.9, 136.4, 131.1, 129.3, 128.9, 128.5, 127.2, 126.3 124.5, 120.2, 79.8, 71.3, 70.3, 69.3, 68.1, 67.8, 61.3, 33.0. MS (APCI): *m/z* 552.9.

2-(3″-Chlorophenyl)-3-(2′-(4′-ferrocenyl-6′-phenylpyrimidinyl)thiazolidin-4-one (6i): Colour: orange red solid, yield: 74%, m.p.: 114-116 ºC. IR (KBr, ν_{max}, cm^{-1}): 2928 (Ar-H), 1715 (C=O), 1575 (C=N), 1537 (C=C), 1366 (C-N), 832 (C-Cl); ^{1}H NMR ($CDCl_3$/DMSO, 400 MHz, δ ppm): 8.28 (s, 2H), 7.91 (s, 1H), 7.59 (d, *J* = 16.0 Hz, 2H), 7.32-7.45 (m, 2H), 6.85 (s, 1H), 5.21 (s, 1H), 5.09 (s, 1H), 4.56 (s, 2H), 4.37 (s, 1H), 4.11 (s, 3H), 3.95 (s, 1H), 3.86 (s, 5H); ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 170.0, 169.8, 163.4, 156.7, 153.3, 143.0, 136.0, 131.3, 128.7, 127.2, 121.6, 120.3, 118.2, 108.1, 79.8, 71.3, 69.8, 68.3, 68.2, 62.0, 33.1. MS (APCI): *m/z* 552.8.

2-(4″-Chlorophenyl)-3-(2′-(4′-ferrocenyl-6′-phenylpyrimidinyl)thiazolidin-4-one (6j): Colour: orange red solid, yield: 76%, m.p.: 134-136 ºC. IR (KBr, ν_{max}, cm^{-1}): 2930 (Ar-H), 1711 (C=O), 1632 (C=N), 1584 (C=C), 1362 (C-N), 816 (C-Cl); ^{1}H NMR ($CDCl_3$/DMSO, 400 MHz, δ ppm): 8.28 (d, *J* = 5.0 Hz, 2H), 7.91 (s, 1H), 7.55 (dd, *J* = 4.8 & 11.1 Hz, 5H), 7.42 (d, *J* = 11.1 Hz, 2H), 6.85 (s, 1H), 5.21 (s, 1H), 5.07 (s, 1H), 4.56 (s, 2H), 4.09 (s, 1H), 3.96 (s, 1H), 3.86 (s, 5H). ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 170.1, 169.8, 163.3, 156.7, 140.7, 135.9, 132.9, 132.4, 131.1, 128.8, 127.8, 127.3, 108.4, 79.5, 71.4, 69.8, 68.2, 61.7, 33.1. MS (APCI): *m/z* 552.7.

Antifungal activity: *Candida albicans* MTCC 183 cultures were passed on three sterile nutrient agar slants followed by incubation at 37 ºC at 24 h. On incubation, in each slant 5 mL sterile saline (0.85% NaCl solution) was added and entire culture suspension was pooled in sterile side arm flask. Using sterile saline and spectrophotometer (540 nm), the optical density of each culture was adjusted 0.1 (approximately 10^6 cells/mL) and used for antimicrobial susceptibility test (AST).

The concentration of compound under study was adjusted to 25 µg/mL using DMSO. Agar well diffusion method was used for AST. Sterile melted Muller-Hinton agar (20 mL) was filled with 1 mL of each culture and the mixture was carefully stirred to prevent bubbles from forming. After thoroughly mixing, it was transferred onto sterile petri dishes with a diameter of 10 cm and left to solidify. Agar wells were made on solidified Muller-Hinton agar plates using ethanol and flame sterilized cork borer (8 mm diameter) and loaded with 100 µL DMSO solution containing compounds under study (25 µg/mL) followed by their incubation at 37 ºC for 24 h. Amphotericin B at a concentration of 25 µg/mL was employed as positive control, while dimethyl sulfoxide (DMSO) served as negative control in the experiment. Diameter of well borer was 8 mm. After incubation, the zones of inhibition (ZOI) (mm) were measured. The

experiments was performed in triplicates and mean ZOI value has been reported.

RESULTS AND DISCUSSION

The synthesis route of ferrocene heterocyclic derivatives (**6a-j**) is outlined in **Scheme-I**. As it is reported, the synthesis of compounds (**6a-j**) was synthesized with acetyl ferrocene and subsituted benzaldehyde with the help of guanidine hydrochloride, DCC, thioglycolic acid in dry MDC at 0 ºC. All the synthesized compounds provided satisfactory IR, ^{1}H, ^{13}C NMR and MS spectral data with the assigned structures.

The results of antifungal activities of synthesized ferrocene heterocyclic derivatives (**6a-j**) are summarized in Table-1. It is observed that all the compounds displayed excellent antifungal against *Candida albicans* MTCC 183 as compared to the standard Amphotericin B.

TABLE-1
MEAN ZOI VALUES (mm) OF COMPOUNDS **6a-j** AND STANDARD AGAINST FUNGI *Candida albicans* MTCC 183

Compd. No.	Mean zone of inhibition (mm)	Compd. No.	Mean zone of inhibition (mm)
6a	9	**6g**	19
6b	10	**6h**	18
6c	11	**6i**	13
6d	11	**6j**	12
6e	18	Amphotericin B	21
6f	19	DMSO	24

Conclusion

A series of novel 2-amino-6-ferrocenyl-4-phenylpyrimidine (AFPP) derivatives (**6a-j**) was synthesized by coupling with thioglycolic acid and various substituted benzaldehydes (**5a-j**). The structures of compounds were confirmed using spectroscopic techniques. The antifungal activities of the novel structures were evaluated and compounds **6d-j** showed good to moderate antifungal activity.

ACKNOWLEDGEMENTS

The authors are grateful to The Head, Chemistry Research Laboratory, Bhavan's Hazarimal Somani College, Mumbai, India for providing the basic research facilities. Thanks are also due to The Director, Institute of Science, Mumbai, India for providing the antifungal activity.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. M. Patra and G. Gasser, *Nat. Rev. Chem.*, **1**, 66 (2017); https://doi.org/10.1038/s41570-017-0066
2. U. Rauf, G. Shabir, S. Bukhari, F. Albericio and A. Saeed, *Molecules*, **28**, 5765 (2023); https://doi.org/10.3390/molecules28155765
3. F.A. Larik, A. Saeed, T.A. Fattah, U. Muqadar and P.A. Channar, *Appl. Organomet. Chem.*, **31**, 3664 (2017); https://doi.org/10.1002/aoc.3664
4. M. Patra and G. Gasser, *Nat. Rev. Chem.*, **1**, 0066 (2017); https://doi.org/10.1038/s41570-017-0066
5. N. Fu, Y. Yuan, M. Pang, J. Wang and C. Peppe, *J. Organomet. Chem.*, **672**, 52 (2003); https://doi.org/10.1016/S0022-328X(03)00139-6
6. T. Mochida, F. Shimizu, H. Shimizu, K. Okazawa, F. Sato and D. Kuwahara, *J. Organomet. Chem.*, **692**, 1834 (2007); https://doi.org/10.1016/j.jorganchem.2006.11.011
7. W. Zhou, S. Ji and Z. Shen, *J. Organomet. Chem.*, **691**, 1356 (2006); https://doi.org/10.1016/j.jorganchem.2005.09.046
8. M. Joksovic, Z. Ratkovic, M. Vukicevic and R.D. Vukicevic, *Synlett*, **16**, 2581 (2006); https://doi.org/10.1055/s-2006-950436
9. D. Braga, D. D'Addari, M. Polito and F. Grepioni, *Organometallics*, **23**, 2810 (2004); https://doi.org/10.1021/om049958j
10. B.S. Ludwig, J.D.G. Correia and F.E. Kühn, *Coord. Chem. Rev.*, **396**, 22 (2019); https://doi.org/10.1016/j.ccr.2019.06.004
11. Z.M. Nofal, H.H. Fahmy, E.S. Zarea and W. El-Eraky, *Acta Poloniae Pharmaceutica*, *Drug Res.*, **68**, 507 (2011).
12. S.A. Khan, A.M. Asiri, M.E.M. Zayed, H. Parveen, F.M.S. Aqlan and K. Sharma, *J. Heterocycl. Chem.*, **56**, 312 (2019); https://doi.org/10.1002/jhet.3381
13. R. Gul, M.K. Rauf, A. Badshah, S.S. Azam, M.N. Tahir and A. Khan, *Eur. J. Med. Chem.*, **85**, 438 (2014); https://doi.org/10.1016/j.ejmech.2014.07.109
14. A.M. Jancic, J.S. Katanic Stankovic, N. Sreckovic, V. Mihailovic, D.I. Komatina and D. Stevanovic, *J. Organomet. Chem.*, **967**, 122335 (2022); https://doi.org/10.1016/j.jorganchem.2022.122335
15. L. Chen, H. Duan, X. Zhang, Q. Zhang, H. Huang, J. Zhao, B. Chen, C. Hua and X. Gou, *J. Heterocycl. Chem.*, **55**, 1978 (2018); https://doi.org/10.1002/jhet.3238
16. Y. Lin, H. Betts, S. Keller, K. Cariou and G. Gasser, *Chem. Soc. Rev.*, **50**, 10346 (2021); https://doi.org/10.1039/D0CS00945H
17. R. Chopra, C. de Kock, P. Smith, K. Chibale and K. Singh, *Eur. J. Med. Chem.*, **100**, 1 (2015); https://doi.org/10.1016/j.ejmech.2015.05.043
18. Y. Guo, S.-Q. Wang, Z.-Q. Ding, J. Zhou and B.-F. Ruan, *J. Organomet. Chem.*, **851**, 150 (2017); https://doi.org/10.1016/j.jorganchem.2017.09.032
19. S. Peter and B.A. Aderibigbe, *Molecules*, **24**, 3604 (2019); https://doi.org/10.3390/molecules24193604
20. A.R. Trivedi, V.R. Bhuva, B.H. Dholariya, D.K. Dodiya, V.B. Kataria and V.H. Shah, *Bioorg. Med. Chem. Lett.*, **20**, 6100 (2010); https://doi.org/10.1016/j.bmcl.2010.08.046
21. P. Liu, Y. Yang, Y. Tang, T. Yang, Z. Sang, Z. Liu, T. Zhang and Y. Luo, *Eur. J. Med. Chem.*, **163**, 169 (2019); https://doi.org/10.1016/j.ejmech.2018.11.054
22. C.B. Scarim, R.L. de Farias, A.V. de Godoy Netto, C.M. Chin, J.L. dos Santos and F.R. Pavan, *Eur. J. Med. Chem.*, **214**, 113166 (2021); https://doi.org/10.1016/j.ejmech.2021.113166
23. E.V. Filho, J.W.S. Pina, M.K. Antoniazi, L.B. Loureiro, M.A. Ribeiro, C.B. Pinheiro, C.J. Guimarães, F.C.E. de Oliveira, C. Pessoa, A.G. Taranto and S.J. Greco, *J. Bioorg. Med. Chem. Lett.*, **48**, 128240 (2021); https://doi.org/10.1016/j.bmcl.2021.128240
24. H. Parveen, F. Hayat, A. Salahuddin and A. Azam, *Eur. J. Med. Chem.*, **45**, 3497 (2010); https://doi.org/10.1016/j.ejmech.2010.04.023