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Synthesis and Characterization of (Thieno[2,3-D]Pyrimidin-4-Yl) Hydrazine Tethered with Quinoline Derivatives and Their Antimicrobial Activity

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ABSTRACT

In an effort to develop biologically active molecules, a series of novel thieno[2,3-d]pyrimidine derivatives tethered with 2-chloroquinoline-3-carbaldehyde through an amino linkage were synthesized and characterized using appropriate spectroscopic techniques. The synthetic methodology exhibited several notable advantages, including a reduced number of reaction steps, high product yields, mild reaction conditions, and elimination of additional purification procedures. The synthesized compounds were screened for their in vitro antimicrobial activity against selected microbial strains. Biological evaluation revealed that several derivatives displayed moderate to good antimicrobial potency, indicating the potential of these heterocyclic scaffolds as good antimicrobial agents.

Keywords: Thieno[2,3-d]pyrimidin, Quinoline, Antimicrobial activity.

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1. INTRODUCTION

Thieno[2,3-d]pyrimidines represent an important class of fused heterocyclic systems that have attracted considerable attention due to their various biological activities [1-3]. Pyrimidine-based compounds are commonly used to synthesize fused-ring molecules because of their easy chemical modification and important biological activities [4,5]. The addition of another ring to the pyrimidine nucleus often improves the biological activity of the compound, making structural modification an important approach in drug design. Different synthetic methods have been reported for the preparation of thieno[2,3-d]pyrimidine derivatives, and research interest in these compounds has increased continuously. During the last two decades, several fused pyrimidine derivatives such as thienopyrimidines, triazolothienopyrimidines, pyrazolopyrimi-dines, quinazolines, purines, furopyrimidines, and pyrrolopyrimidines have been widely studied because of their promising pharmaceutical applications [6,7].

Schiff bases derived from 2-chloroquinoline have also gained significant attention because of their broad range of biological and pharmacological activities [8-10]. Quinoline derivatives are known to exhibit various biological properties such as antimicrobial [11-12], antimalarial [13-14], anticancer [15], anti-inflammatory [16], anti-tuberculosis [17], and antioxidant activities [18]. Furthermore, these compounds have been identified as potential inhibitors of important biological targets including tyrosine kinase [19], DNA gyrase [20], and DNA topoisomerase enzymes [21], demonstrating their importance in medicinal chemistry and drug development. Quinoline-based compounds are also widely used for the synthesis of novel hybrid molecules by combining them with other biologically active scaffolds. Among these, the 5-phenylthieno[2,3-d]pyrimidine scaffold has been reported to possess significant biological activities, including antitumor, antimicrobial, antipyretic, anti-inflammatory, and antiproliferative effects [22].

In the present research work, 4-hydrazineyl-thieno[2,3-d]pyrimidine was employed as a key intermediate for the synthesis of a novel thieno[2,3-d]pyrimidine derivative. The structures of the synthesized compounds were confirmed by spectroscopic analyses, including IR, mass spectrometry, and ^{1}H and ^{13}C NMR techniques. Furthermore, all prepared derivatives were screened for their antimicrobial activities.

2. EXPERIMENTAL

All chemicals and reagents were obtained from commercial sources and utilized as received without any additional purification. The progress of the reactions was monitored by analytical thin-layer chromatography (TLC) using pre-coated silica gel plates (G60, F254). Visualization of the spots was carried out under ultraviolet light as well as by exposure to iodine vapors. Melting points were measured using the open capillary method with a melting point apparatus and are reported without correction. Fourier-transform infrared (FT-IR) spectra were recorded on a Shimadzu FT-IR-8400 instrument and expressed in cm^{-1}. Nuclear magnetic resonance (NMR) spectra were obtained using a Bruker Advance 500 MHz spectrometer. The ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were recorded in DMSO-d_6 with tetramethylsilane (TMS) employed as the internal reference.

Synthesis of 2-(1-Phenylethylidene)malononitrile (1). A mixture of acetophenone (10 mmol), malononitrile (11 mmol), ammonium acetate (10 mmol), and glacial acetic acid (10 mmol) in toluene (80 mL) was heated at 110 °C for 2-4 h. A Dean-Stark apparatus was used to continuously remove the water formed during the reaction. Reaction progress was monitored by thin-layer chromatography (TLC). After completion, the solvent was removed by vacuum evaporate, and the reaction mixture was allowed to cool to room temperature.

The resulting solid was collected by filtration, washed with distilled water, and dried. Recrystallization from ethanol afforded compound (**1**) as a solid (Yield: 92%, M.P.: 94-96 °C).

Synthesis of 2-Amino-4-phenylthiophene-3-carbonitrile (2). Compound **(1)** (10 mmol) and elemental sulfur (13 mmol) was suspended in THF (30 mL) and heated to 35 °C. A solution of sodium bicarbonate (3.2 g) in water (30 mL) was added dropwise over 1 h. The reaction mixture was stirred at 35 °C for an additional 35 min. After completion of the reaction, the mixture was transferred to a separatory funnel, and the organic layer was separated. The aqueous layer was extracted with ethyl acetate. After removal the solvent, the compound was recrystallized from ethanol to afford 2-amino-4-phenylthiophene-3-carbonitrile **(2)** as a solid (Yield: 88%, M.P.: 123 °C).

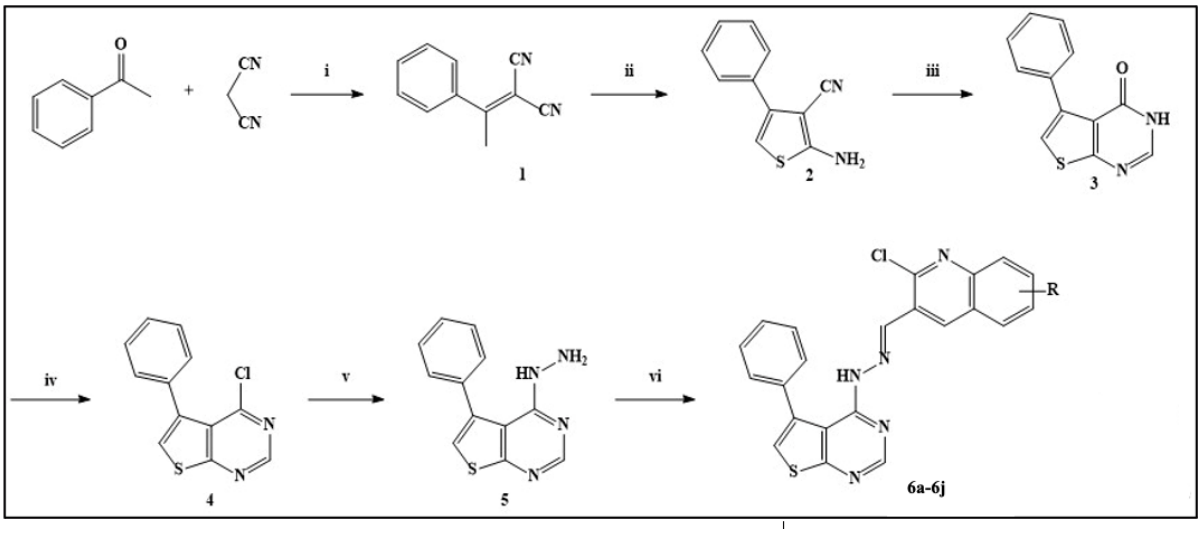
Synthesis of 5-Phenylthieno[2,3-d]pyrimidin-4(3H)-one (3). 2-Amino-4-phenylthiophene-3-carbonitrile (**2)** (20 mmol) was refluxed in formic acid (20 mL) for 16-18 h. After cooling to room temperature, water (40 mL) was added to the reaction mixture, resulting in the formation of a precipitate. The solid was filtered, washed with cold water followed by hexane, and dried to afford compound (**3)** as a solid (yield : 86%; M.P.: 205-208 °C).

Synthesis of 4-Chloro-5-phenylthieno[2,3-d]pyrimidine (4). A mixture of 5-phenylthieno[2,3-d]pyrimidin-4(3H)-one (**3**) (2 mmol) and phosphorus oxychloride ($POCl_3$, 80 mL) was heated at 80 °C for 2.5 h with stirring. The progress of the reaction was monitored by thin-layer chromatography. Upon completion, the reaction mixture was carefully poured onto crushed ice and neutralized with aqueous sodium bicarbonate solution. The resulting precipitate was collected by vacuum filtration, washed thoroughly with cold water, and dried to afford 4-chloro-5-phenylthieno[2,3-d]pyrimidine (**4**) as a white solid (yield: 93.67%; M.P.: 125-127 °C).

Synthesis of 4-hydrazineyl-5-phenylthieno[2,3-d]pyrimidine (5). A mixture of 4-chloro-5-phenylthieno[2,3-d]pyrimidine (1 mmol) and 80% hydrazine hydrate (1 mmol) in methanol (40 mL) was refluxed for 1 h. Thereafter, an additional amount of hydrazine hydrate was introduced, and the reaction mixture was further refluxed for another 1 h. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was allowed to cool to room temperature and kept refrigerated overnight. The separated yellow precipitate was filtered, washed with cold 40% methanol in water and dried to afford 4-hydrazineyl-5-phenylthieno[2,3-d]pyrimidine **(5)** as an off-white solid compound. (Yield: 92%, M.P.: 148-150 °C)

General Procedure for the Synthesis of 2-Chloroquinoline-3-carbaldehyde Derivatives.
A precooled solution of N,N-dimethylformamide (DMF) (1 mmol) at 0-5 °C was treated dropwise with phosphorus oxychloride ($POCl_3$) (1 mmol) under continuous stirring. After stirring for 30 min, N-phenylacetamide derivatives (1 mmol) was added portion-wise, and the reaction mixture was refluxed at 80-90 °C for 15-16 h. Upon completion of the reaction, the mixture was poured into ice-cold water and stirred for 30-40 min. The obtained solid was filtered, washed successively with saturated $NaHCO_3$ solution and water, dried, and recrystallized from ethyl acetate or acetonitrile to afford the corresponding 2-chloroquinoline-3-carbaldehydes.

Synthesis of substituted 2-chloro-3-[(1E)-(2-{5-phenylthieno[2,3-d]pyrimidin-4-yl}-hydrazin-1-ylidene)methyl]quinoline derivatives (6a-6j). A mixture of various 2-chloroquinoline-3-carbaldehyde derivatives (1 mmol) and 4-hydrazineyl-5-phenylthieno [2,3-d]pyrimidine (**5**) (1 mmol) in methanol was treated with a few drops of glacial acetic acid and refluxed for 3 h. The progress of the reaction was monitored by TLC using ethyl acetate:n-hexane (2:1) as the mobile phase. After completion of the reaction, the resulting precipitate was filtered, washed with methanol, and recrystallized from a suitable solvent to afford the corresponding novel Schiff bases **(6a-6j)** as yellow solids. **(Scheme 1)** and characteristic data is represented in **Table 1**.

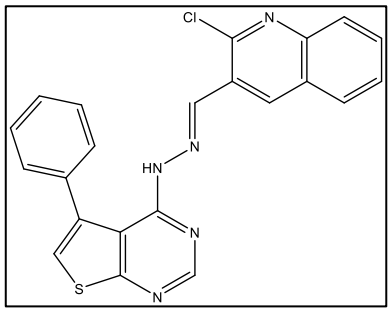


Scheme 1. Ammonium acetate, acetic acid, reflux, toluene, 1-2 h; (II) S8, NaHCO3, THF, 35 °C, 30 min; (III) HCOOH, reflux, 18 h; (IV) $POCl_3$, 90 °C, 2-4 h; (V) Hydrazine Hydrate, methanol, reflux 1 h (VI) Quinoline carbaldehydes derivatives, acetic acid, methanol, reflux, 3 h

Table 1. Characteristics physical data of Schiff base derivatives (6a-6j).

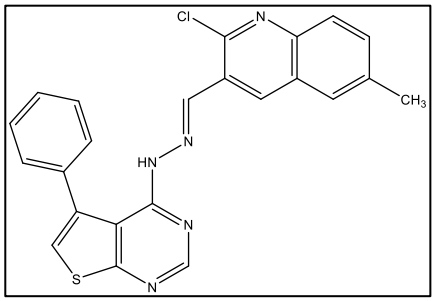
Entry	Compound Code	R	M.P. (°C)	Yield (%)
01	6a	H	206-208	94
02	6b	6-CH_3	210-212	91
03	6c	7-Cl	220-222	74
04	6d	6-OCH_3	216-218	81
05	6e	6-Cl	218-220	68
06	6f	6-F	231-233	66
07	6g	8-OCH_3	213-215	77
08	6h	8-CH_3	208-210	89
09	6i	6,8-CH_3	212-214	60
10	6j	6-Br	241-243	68

2-chloro-3-[(1E)-(2-{5-phenylthieno[2,3-d]pyrimidin-4-yl}hydrazin-1-ylidene)methyl]quinoline (6a)



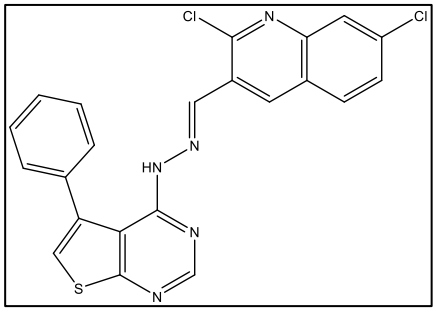
Yield: 94%, yellow solid, M.P.: 206-208 °C; **IR (KBr, cm⁻¹):** 3368, 3329, 3072, 2922, 2169, 2041, 1930, 1663, 1584, 1493, 1450, 1375, 1291, 1208, 1143, 1057, 1018, 974, 942, 911, 827, 774, 738, 653, 625, 598, 556, and 507 cm⁻¹; MS(ESI): 415.90 m/z [M^+].

2-chloro-6-methyl-3-[(1E)-(2-{5-phenylthieno[2,3-d]pyrimidin-4-yl}hydrazin-1-ylidene)methyl]quinoline (6b)



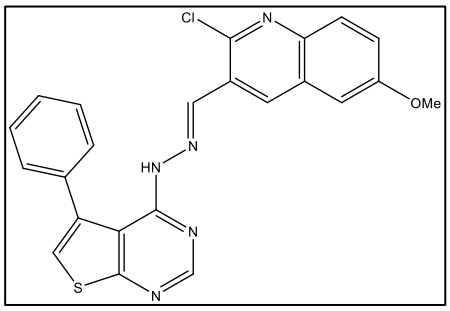
Yield: 91%, light yellow solid, M.P.:210-212 °C ; IR (KBr, cm⁻¹): 3813, 3355, 3296, 3072, 2920, 2855, 2160, 2070, 1931, 1887, 1827, 1737, 1666, 1619, 1584, 1536, 1494, 1448, 1404, 1367, 1329, 1250, 1189, 1132, 1104, 1057, 1010, 976, 941, 893, 815, 768, 7717, 653, 621, 591, 560, 520 cm⁻¹; MS(ESI):429.93m/z[M^+].

2,7-dichloro-3-[(1E)-(2-{5-phenylthieno[2,3-d]pyrimidin-4-yl}hydrazin-1-ylidene)methyl]quinoline (6c)



Yield: 74%, yellow solid, M.P.:220-222 °C; IR (KBr, cm⁻¹): 3651, 3361, 3296, 3072, 2920, 2858, 2163, 2048, 1940, 1805, 1736, 1665, 1584, 1507, 1451, 1428, 1395, 1326, 1295, 1228, 1189, 1136, 1070, 1004, 957, 892, 867, 768, 740, 683, 620, 591, 555 cm⁻¹; ^{1}H NMR (400 MHz, DMSO) δ 12.23 (s, 1H), 11.39 (s, 1H), 9.28 (s, 1H), 8.65 (d, *J* = 8.2 Hz, 1H), 8.29 (d, *J* = 8.8 Hz, 1H), 8.13 (d, *J* = 9.1 Hz, 2H), 8.08 – 7.96 (m, 4H), 7.99 – 7.76 (m, 1H), 7.76 – 7.67 (m, 2H), 7.60 – 7.34 (m, 7H), 7.10 (t, *J* = 7.6 Hz, 2H), 6.95 (dt, *J* = 19.8, 7.5 Hz, 1H); MS(ESI): 450.34 m/z [M^+].

2-chloro-6-methoxy-3-[(1E)-(2-{5-phenylthieno[2,3-d]pyrimidin-4-yl}hydrazin-1-ylidene)methyl]quinoline (6d)



Yield: 81%, yellow solid, M.P.:216-218 °C; IR (KBr, cm⁻¹): 3359, 3288, 3059, 2974, 2920, 2162, 2075, 1949, 1674, 1586, 1497, 1457, 1339, 1239, 1167, 1057, 1018, 974, 910, 844, 774, 704, 653, 600, 561, 507; ^{1}H NMR (400 MHz, DMSO) δ 12.23 (s, 1H), 11.39 (s, 1H), 9.28 (s, 1H), 8.65 (d, *J* = 8.2 Hz, 1H), 8.29 (d, *J* = 8.8 Hz, 1H), 8.13 (d, *J* = 9.1 Hz, 2H), 8.08 – 7.96 (m, 4H), 7.99 – 7.76 (m, 1H), 7.76 – 7.67 (m, 2H), 7.60 – 7.34 (m, 7H), 7.10 (t, *J* = 7.6 Hz, 2H), 6.95 (dt, *J* = 19.8, 7.5 Hz, 1H); MS (ESI): 445.93 m/z [M^+].

3. ANTIMICROBIAL ACTIVITY

The in vitro antimicrobial potential of the synthesized compounds was evaluated using the microbroth dilution method. Antibacterial activity was assessed against *Escherichia coli* and *Pseudomonas aeruginosa* (Gram-negative), as well as *Staphylococcus aureus* and *Bacillus subtilis* (Gram-positive) strains. Antifungal activity was examined against *Aspergillus niger* and *Aspergillus flavus*. Mueller–Hinton broth was employed as the nutrient medium for bacterial cultures, whereas Sabouraud dextrose broth was used for fungal growth. The inoculum density for each test organism was standardized to approximately 1×10^8 CFU/mL based on turbidity measurements. Stock solutions of the test compounds and reference drugs were prepared at a concentration of 2000 µg/mL. Primary screening was carried out using serial dilutions to obtain concentrations of 1000, 500, 250, and 125 µg/mL. Compounds exhibiting significant activity in the initial screening were further evaluated in a secondary assay at concentrations of 200, 100, 50, 25, 12.5, and 6.25 µg/mL. All inoculated wells were incubated at 37 °C for 24 h under appropriate conditions, and microbial growth was assessed based on turbidity observations.

4. RESULTS AND DISCUSSION

The synthetic route commenced with the preparation of 2-(1-phenylethylidene)malononitrile **(1)** via a Knoevenagel condensation reaction [23,24]. This intermediate was subsequently subjected to a Gewald reaction with sulfur in the presence of sodium bicarbonate in a THF–water system to yield 2-amino-4-phenylthiophene-3-carbonitrile **(2)** [25,26]. Further transformation of compound (2) through intermolecular cyclization under reflux in formic acid afforded 5-phenylthieno[2,3-d]pyrimidin-4(3H)-one **(3)** [27]. Finally, compound **(3)** was treated with phosphorus oxychloride ($POCl_3$) under heating conditions to produce 4-chloro-5-phenylthieno[2,3-d]pyrimidine **(4)** [28]. Compound **(4)** then reacted with Hydrazine in the presence of methanol in reflux condition to afforded 4-hydrazineyl-5-phenylthieno[2,3-d]pyrimidine **(5)** [29]. In the next reaction, compound **(5)** reacted with various derivatives of 2-chloroquinoline refluxed with Methanol and few drops of Acetic acid, to afford desired compounds **(6a-6j)** [30]. The synthetic pathway for the preparation of the target compounds is illustrated in **Scheme 1**.

The optimization studies revealed that both solvent and catalyst significantly influenced the reaction efficiency and product yield. Among the various reaction conditions examined, methanol in the presence of acetic acid proved to be the most effective system, affording the desired product in an excellent yield of 92% within 3 h. Therefore, methanol/acetic acid was identified as the optimum reaction condition for the synthesis of the titled compounds due to its higher yield, shorter reaction time, and operational simplicity. **(Table 2)**

Table 2. Optimization of Reaction Conditions for Synthesized Compounds.

Entry	Solvent	Catalyst	Time (h)	Yield (%)
1	Methanol	Hydrochloric Acid	6	42
2	Butanol	Sulphuric Acid	4.5	61
3	Diethyl ether	Nitric Acid	6	36
4	Acetone	$FeCl_3$	6	54
5	DMF	Sulphuric Acid	4.5	61
6	Methanol	Acetic Acid	3	92

7	IPA	Acetic Acid	6	79
8	DCM	Acetic Acid	6	74
9	Butanol	$FeCl_3$	12	58
10	Methanol	$FeCl_3$	12	52

5. BIOLOGICAL EVALUATION

The synthesized compounds **(6a-6j)** were screened for antimicrobial activity against selected bacterial and fungal strains using the MIC method. **(Table-3)** Compounds show moderate to good antimicrobial activity. Among the tested compounds, **6b** and **6e** exhibited the most effective antibacterial activity, particularly against *Enterobacter aerogenes* and *Pseudomonas aeruginosa*, with lower MIC values. Compounds **6a**, **6d**, **6e**, and **6i** showed moderate antifungal activity against *Candida albicans* and *Aspergillus niger*. Overall, the results indicate that the synthesized thieno[2,3-d]pyrimidine derivatives possess moderate antimicrobial potential.

Table 3. Antibacterial and Antifungal Activities.

Compounds	**Antifungal MIC (µg/mL)**		**Antibacterial MIC (µg/mL)**			
	C. albicans MTCC183	*A. niger* MTCC282	*E.aerogenes* MTCC2823	*P.aeruginosa* MTCC3541	*S.aureus* MTCC737	*S.pyogenus* MTCC1925
Ampicillin	-	-	-	-	100	100
Streptomycin	-	-	50	50	-	-
Nystatin	100	100	-	-	-	-
6a	250	250	500	500	500	500
6b	500	500	125	125	250	250
6c	500	500	250	250	500	500
6d	250	250	1000	1000	500	500
6e	250	250	250	250	125	125
6f	500	500	1000	1000	250	250
6g	1000	1000	1000	1000	500	500
6h	500	500	250	250	250	250
6i	250	250	500	500	500	500
6j	500	500	250	250	250	250

6. CONCLUSION

In conclusion, a series of novel thieno[2,3-d]pyrimidine derivatives containing a 2-chloroquinoline moiety were successfully synthesized and characterized through conventional synthetic methods. The structures of the synthesized compounds were confirmed using various spectroscopic techniques. The antimicrobial evaluation revealed that several derivatives exhibited moderate to good antibacterial and antifungal activities when compared with standard drugs. Among them, some compounds demonstrated promising inhibitory activity against the tested microbial strains, indicating that these scaffolds may serve as potential candidates for further antimicrobial studies.

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CONFLICT OF INTEREST

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

References

[1] Puthran, D.; Poojary, B.; Purushotham, N.; Harikrishna, N.; Nayak, S. G.; Kamat, V. ; Heliyon **2019**, 5, e02233. https://doi.org/10.1016/j.heliyon.2019.e02233

[2] Elmetwally, S. A.; Saied, K. F.; Eissa, I. H.; Elkaeed, E. B. Bioorg. Chem. **2019**, 88, 102944. https://doi.org/10.1016/j.bioorg.2019.102944

[3] Zaidi, S. L.; Agarwal, S. M.; Chavalitshewinkoon-Petmitr, P.; Ahmad, K.; Suksangpleng, T.; Avecilla, F.; Azam, A. RSC Adv. **2016**, 6, 90371–90381. https://doi.org/10.1039/C6RA15181G

[4] Jabli, D.; Dridi, K.; El Efrit, M. L. Lett. Org. Chem. **2014**, 11, 406–412. https://doi.org/10.2174/15701786116666140311005612

[5] Patil, S. B. Heliyon **2019**, 9, e16773. https://doi.org/10.1016/j.heliyon.2023.e16773

[6] Nammalwar, B.; Bunce, R. A. Pharmaceuticals **2024**, 17, 104. https://doi.org/10.3390/ph17010104

[7] Han, Q.; Yin, Z.; Sui, J.; Wang, Q.; Sun, Y. J. Braz. Chem. Soc. **2019**, 30, 1483–1493. https://doi.org/10.21577/0103-5053.20190044

[8] Mallandur, B. K.; Rangaiah, G.; Harohally, N. V. Synth. Commun. **2017**, 47, 1065–1070. https://doi.org/10.1080/00397911.2017.1309668

[9] Miniyar, P. B.; Barmade, M. A.; Mahajan, A. A. J. Saudi Chem. Soc. **2015**, 19, 655–660. https://doi.org/10.1016/j.jscs.2013.12.004

[10] Da Silva, C. M.; et al. J. Adv. Res. **2011**, 2, 1–8. https://doi.org/10.1016/j.jare.2010.05.004

[11] Farghaly, A. M.; Habib, N. S.; Khalil, M. A.; El-Sayed, O. A.; Bistawroos, A. E. Arch. Pharm. **1990**, 323, 247–251. https://doi.org/10.1002/ardp.19903230414

[12] Khakhariya, A. D.; Savaniya, N. P.; Ladva, K. D. Asian J. Chem. **2024**, 36, 655–660. https://doi.org/10.14233/ajchem.2024.31022

[13] Kaur, K.; Jain, M.; Reddy, R. P.; Jain, R. Eur. J. Med. Chem. **2010**, 45, 3245–3264. https://doi.org/10.1016/j.ejmech.2010.04.011

[14] Vandekerckhove, S.; D'hooghe, M. Bioorg. Med. Chem. **2015**, 23, 5098–5119. https://doi.org/10.1016/j.bmc.2014.12.018

[15] Kishanrao, J.; et al. World J. Pharm. Pharm. Sci. **2018**, 2, 3373–3381.

[16] El-Feky, S. A. H.; et al. Bioorg. Chem. **2015**, 58, 104–116. https://doi.org/10.1016/j.bioorg.2014.12.003

[17] Keri, R. S.; Patil, S. A. Biomed. Pharmacother. **2014**, 68, 1161–1175. https://doi.org/10.1016/j.biopha.2014.10.007

[18] Cao, H. T.; Gree, R. Tetrahedron Lett. **2009**, 50, 1493–1494. https://doi.org/10.1016/j.tetlet.2009.01.080

[19] Maguire, M. P.; Sheets, K. R.; McVety, K.; Spada, A. P.; Zilberstein, A. J. Med. Chem. **1994**, 37, 2129–2137. https://doi.org/10.1021/jm00040a003

[20] Medapi, B.; et al. Bioorg. Med. Chem. **2015**, 23, 2062–2078. https://doi.org/10.1016/j.bmc.2015.03.004

[21] Gamage, S. A.; et al. J. Med. Chem. **1999**, 42, 2383–2393. https://doi.org/10.1021/jm980687m

[22] Raghu Prasad, M. A.; Kishore, D. P. **2001**.

[23] Saczewski, J.; et al. J. Heterocycl. Chem. **2009**, 46, 1259–1265. https://doi.org/10.1002/jhet.236

[24] Nayak, S. G.; Poojary, B.; Kamat, V.; Puthran, D. Arch. Pharm. **2021**, 354, 2000103. https://doi.org/10.1002/ardp.202000103

[25] Tayebee, R.; Javadi, F.; Argi, G. J. Mol. Catal. A Chem. **2013**, 368–369, 16–22. https://doi.org/10.1016/j.molcata.2012.11.011

[26] Erfaninia, N.; et al. Appl. Organomet. Chem. **2018**, 32, e4047. https://doi.org/10.1002/aoc.4047

[27] Triloknadh, S.; et al. Bioorg. Med. Chem. Lett. **2018**, 28, 1663–1667. https://doi.org/10.1016/j.bmcl.2018.03.030

[28] Fyfe, T. J.; et al. J. Med. Chem. **2019**, 62, 174–185. https://doi.org/10.1021/acs.jmedchem.8b01000

[29] Raghu Prasad, M.; Kishore, D. P. Chem. Pharm. Bull. **2007**, 55, 776–779. https://doi.org/10.1248/cpb.55.776

[30] Patil, S. K.; Vibhute, B. T. Arab. J. Chem. **2021**, 14, 103285. https://doi.org/10.1016/j.arabjc.2021.103285