Indian Journal of Chemistry
Vol. 61, October 2022, pp. 1097-1102
DOI: 10.56042/ijc.v61i10.59435

One-pot Michael addition and cyclo-elimination cascade synthesis of thiazolo-[4,5-*b*]pyridin-6-carbonitrile scaffold

Shailendra Tiwari[a,*], Vishal Kumar Singh[a], Shahla Rahmani[a], Akeel Ahmad[b] & Kahkashan Begum[c]

[a] Department of Chemistry, University of Allahabad, Allahabad 211 002, India
[b] Department of Chemistry, Mirza Ghalib College, Gaya 823 001, India
[c] Department of Chemistry, Gandhi Faiz-E-Aam College, Shahjahanpur 242 001, India
*E-mail: drshailendratiwariau@gmail.com

Received 19 January 2022; accepted (revised) 16 September 2022

A series of thiazolo [4,5-*b*]- pyridine-6-carbonitriles scaffold have been synthesized conveniently and smoothly in a single step in good yields. These compounds have been screened for their antibacterial and antifungal activity against different pathogenic strains of bacteria and fungi. The minimum inhibitory concentration (MBC) and minimum fungicidal concentration (MFC) have been determined for the test compounds as well as for reference standards. Compounds **3c**, **3d**, **3e**, **3f**, **4c**, **4d**, **4e** and **4f** have shown good antibacterial as well as antifungal activity.

Keywords: 3-Benzyl-4-thiazolidinon-2-thione, Carbonitrile, Antibacterial and antifungal activity

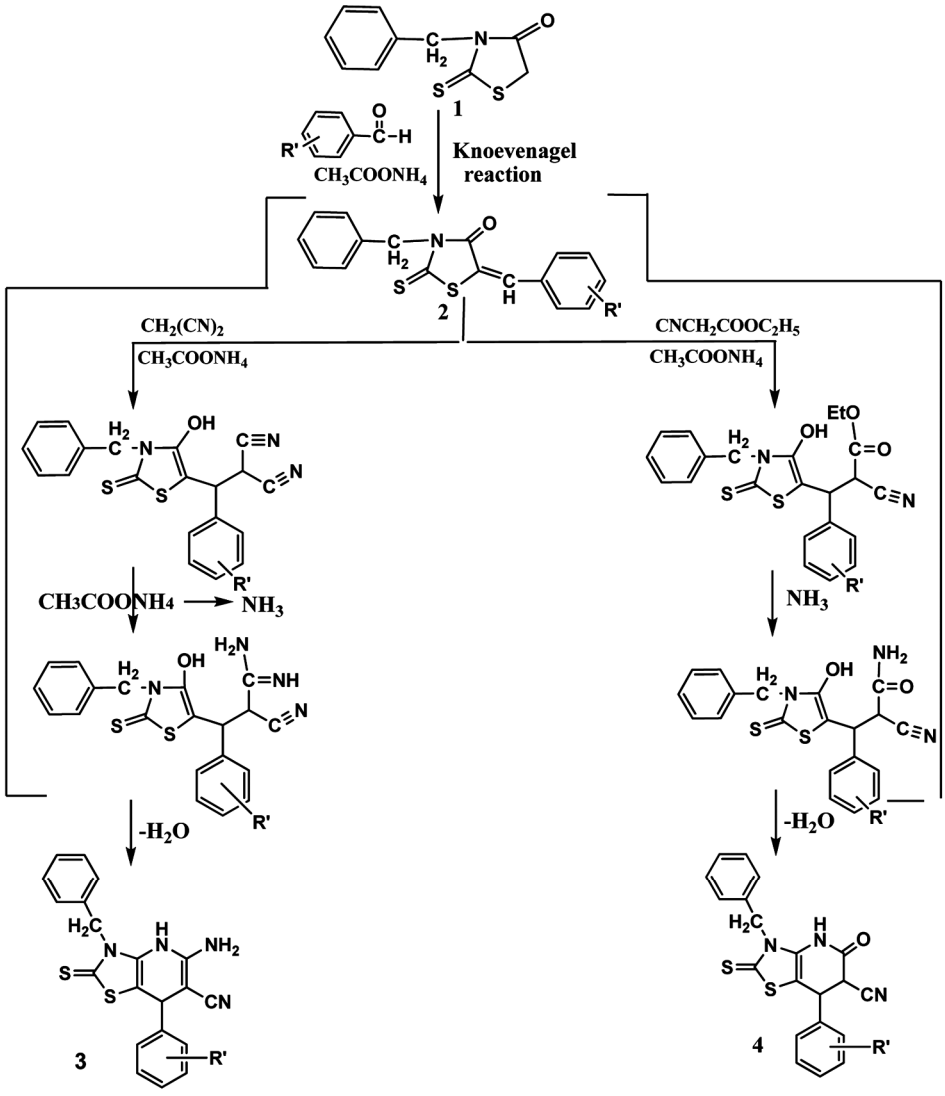
One pot synthesis of drug-like small molecules has been interest for medicinal chemists and chemical biologists because, this provides the important scaffolds in fewer steps and these molecules play very important role in drug discovery processes[1]. Several bacterial infections such as diarrhea, food poisoning, rheumatic salmonellosis, extraintestinal and intestinal wall infections are caused by gram-negative and gram-positive pathogens[2,3]. The resistance of pathogens bacteria towards available antibiotics is rapidly becoming a major threat to human health world-wide[4]. In addition, fungal infections continue to increase dramatically because of growing number of immunocompromised hosts such as AIDS patients or those undergoing anticancer chemotherapy and transplantation[5-7]. Resistance to know antibiotics is becoming great concern in scientific community and big challenge to develop new scaffold as biologically active molecules. Therefore, design of new antimicrobial compounds to deal with these problems is of prime interest.

Michael addition of nucleophiles to electron deficient alkenes is one of the most powerful and widely used synthetic tools for the formation of carbon-carbon hetero bonds in organic chemistry[8-12]. Hetero Michael additions, *viz*. aza-michael, thia-michael etc, are the most exploited organic reactions and are the mainstay of efficient synthetic tools for the construction of druggable heterocyclic scaffolds and natural products[13-15]. Construction of molecules architecture by two or more bond formation in one-step operation *via* Michael reaction has been one of the current interests in synthetic organic chemistry[16,17].

The high therapeutic properties of the compounds incorporating nitrogen heterocyclics have encouraged the medicinal chemist to synthesize large number of novel therapeutic agents. Thiazole and pyridine rings are the active cores of various bio-active thiazoles. These are a class of heterocycles which have attracted significant interest in medicinal chemistry and they have a wide range of pharmaceutical and biological activities including antibacterial[18-20], antifungal[21-24], antitubercular[25,26], analgesic[27], agents. Pyrimidines represent one of the most active classes of compounds possessing a wide spectrum of biological activity[28]. Derivatives of [3,4-b] pyridine skeleton have proven to be interesting classes of heterocycles due to diverse biological properties including antitubercular, antibacterial and antioxidant activities[29-32]. The cyno group is a stable and useful functional group[12,32] that can be transformed to various other functional groups such as acyl, carboxy, formyl, carbamoyl, etc.[33-36] The past seven decades has witnessed the transition of organic nitriles from a position of laboratory curiosities to that of large tonnage chemicals of

commercial importance. On the other hand, reactions involving C-C bond formation are one of the main stays in synthetic organic chemistry. The use of nitrile for C-C bond formation reaction occupies an important position in organic chemistry[37,38].

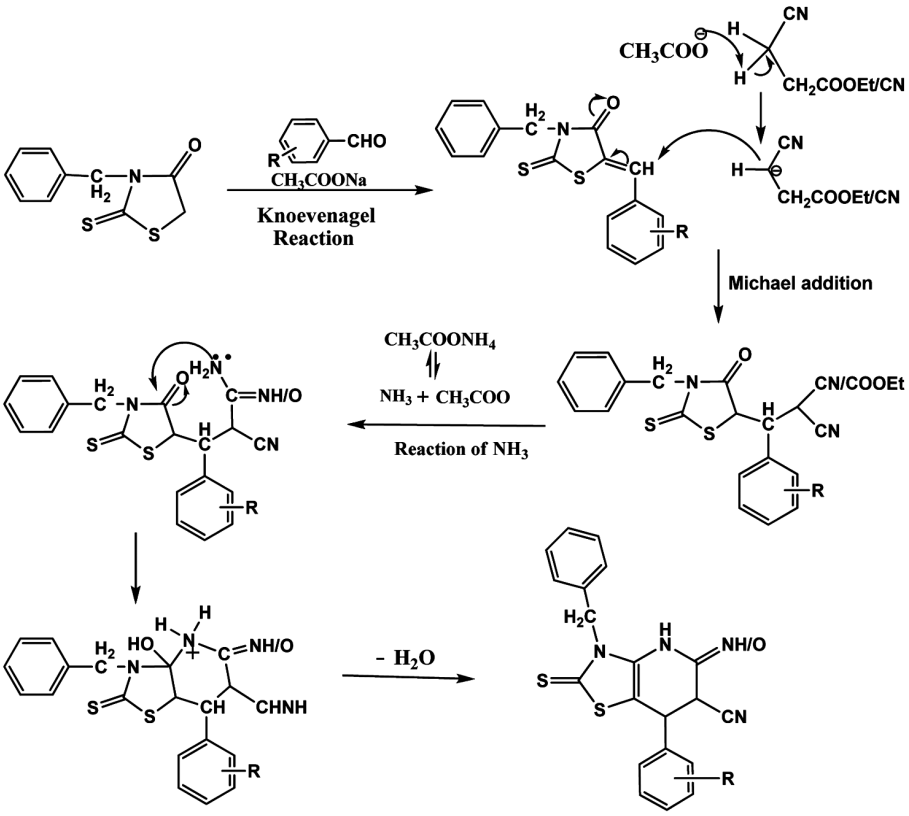
In the light of above literature facts, we report herein, a convenient, effective one pot synthesis of thiazolo [4,5-*b*] pyridine-6-carbonitriles scaffold *via* Michael addition and cyclo-elimination (Scheme 1). A plausible mechanism for the formation of titled thiazolo [4,5-*b*] pyridine-6-carbonitrile scaffold is given in Scheme 2. The intermediate **2** formed by the reaction of substituted benzaldehyde and 3-benzyl-4-thiazolidin-2-thione, by virtue of having α, β- unsaturated ketonic linkage served as Michael acceptor while carbanion, generated from malononitrile/ethyl cyanoacetate by acetate ion as Michael donor. The Michael adducts thus formed on cycloelimination gave the desired scaffold. The titled



a R' = H
b R' = 2-Cl
c R' = 4-Cl
d R' = 4-F
e R' = 3-NO_2
f R' = 3, 4-$(OCH_3)_2$

a R' = H
b R' = 2-Cl
c R' = 4-Cl
d R' = 4-F
e R' = 3-NO_2
f R' = 3, 4-$(OCH_3)_2$

Scheme 1



Scheme 2

compounds by virtue of having these moieties in a single molecule may show pronounced biocidal activity. The structure of these compounds established by the IR, ^{1}H and ^{13}C NMR and elemental analysis. The required starting material 3-benzyl-2-thio-4-thiazolidinone **1** was prepared according to the known methods[39].

Antimicrobial activity

The antimicrobial activity of synthesized compounds **3a-f** and **4a-f** was determined *in vitro* against four bacterial strains. For this study, the test cultures of bacterial strains *Escherichia coli*, *Salmonella typhi*, *Bacillus subtilis* and S*taphylococcus aureus* were maintained in nutrient agar slants at 37°C. The antimicrobial activity of compounds against test bacteria was determined by agar well diffusion method[40] using standards antibiotic ciprofloxacin as positive control and DMSO as negative control. All the experiments were performed in triplicate.

The results of present investigation showed that compounds **3c**, **3d**, **3e**, **3f**, **4c**, **4d**, **4e** and **4f** have promises activity against all the test organisms. Except **3f** and **4f** all the compounds showed moderate to good activity. Most of the other compounds were either active or inactive against test organisms. Compounds **3c**, **3d**, **3e**, **4c**, **4d** and **4e** is found to be most effective against all test organisms (Table 1).

Fungicidal activity

In vitro antifungal activity of all compounds was studied against two fungal strains, *Candida albicans* and *Aspergillus niger*. Intraconazole was employed as standard to compare the results. Among all the compounds, compound **3c**, **3d**, **4c** and **4d** displayed good antifungal activity. Compounds **3f** and **4f** displayed moderate antifungal activity and the remaining compounds are found to be inactive (Table 2).

The structure-activity relationship (SAR) of the tested compounds for antibacterial as well as antifungal activity can be summarized as follows:

(i) In the series of the substituted thiazolo [4,5-*b*] pyridine-6-carbonitrile derivatives has shown better antibacterial and antifungal activity than the O-substituted groups.

(ii) Presence of one or more polar groups/-OCH_3 in phenyl ring is an important scaffold for better antibacterial as well as antifungal activity.

Table 1 — Zone of inhibition in mm at concentration 100 µg/mL

Compound	*B. subtilis*	*S. aureus*	*E. coli*	*S. typhi*
3c	33	24	29	28
3d	25	20	25	24
3e	22	21	15	–
3f	–	12	–	–
4c	31	22	28	27
4d	23	21	24	22
4e	19	20	17	–
4f	–	–	16	–
Ciprofloxacin	36	46	40	40

Table 2 — Antifungal activity of compounds 3c, 3d, 3f, 4c,4d and 4f

	Fungal species and MIC (µg/mL)	
Compound	*C. albicans*	*A. niger*
3c	10	17
3d	12	19
3f	6	8
4c	9	16
4d	11	15
4f	8	10
Intraconazole	26	28

Experimental Section

Melting points were recorded in Richerf-Thermover instrument and are uncorrected. The IR spectra were recorded on Perkin-Elmer-RXI spectrometer in KBr. ^{1}H and ^{13}CMR spectra were recorded on Bruker 300 and Bruker Advance II 400 spectrometer using tetra methyl silane (TMS) as on internal standards and DMSO-d_6/$CDCl_3$as solvent. The micro analytical data were collected on Elemental Vario EL III elemental analyser. All chemicals used were purchased from Merck and Fluka Chemicals. The homogeneity of compound was checked by thin layer Chromatography (TLC) on glass plates coated with silica gel GF254 (Merck, Mumbai, India) using chloroform-methanol (3:1) mixture as mobile phase.

General procedure for synthesis of 5-amino-3-benzyl-7-substituted phenyl-2-thioxo-2,3,4,7-tetrahydrothiazolo[4,5-*b*] pyrdine-6-carbonitrile (R' = 4-OCH_3)

A mixture of 4-methoxybenzaldehyde (1.20 g, 0.01 mol), 3-benzyl-4-thiazolidinon-2-thione 2.3 g, 0.01 mol), and ammonium acetate (1.54 g ,0.02 mol) was fused for 2 h. Malononitrile (0.66 g, 0.01 mol) and ammonium acetate (4.6 g, 0.06 mol) was added and the mixture was fused again further for 2 h. Dioxane (15.0 mL) was added and the mixture was refluxed for 2 h. The resulting solution was cooled and poured into water. The solid product obtained was filtered and washed with water, dried and purified by recrystallization from ethanol to get crystalline solid products **3a-3f**.

3a: Colorless solid; Yield 67%; m.p.100°C; IR: 3476, 3247, 3183, (NH_2 and N-H), 2890, 2748 (C-H aliph) 2325 (CN), 1598, 1580, 1508, 1467 (aromatic ring), 1289, 1143 (C-N-C), 1198 cm^{-1} (C=S); ^{1}H NMR (DMSO-d_6): δ 9.07 (s, 1H, N-H), 7.25-7.32 (m, 5H, benzene ring), 7.08-7.19 (m, 5H, benzene ring), 6.49 (s, 2H, N-H), 4.45 (s, 2H, sp^3, C-H), 4.41 (s, 1H, sp^3, C-H); ^{13}C NMR (DMSO-d_6): δ 187.4, 161.3, 142.1, 138.6, 135.9, 128.3, 127.5, 126.6, 126.4, 125.5, 117.1, 71.5, 57.4, 49.8, 40.6.

3b: Colorless solid; Yield 70%; m.p.120°C; IR: 3440, 3230, 3160, (NH_2 and N-H), 2860, 2770 (C-H aliph) 2340 (CN), 1590, 1575, 1500, 1460 (Arom ring), 1280, 1150 (C-N-C), 1190 cm^{-1} (C=S); ^{1}H NMR (DMSO-d_6): δ 9.09 (s, 1H, N-H), 7.65 (d, 1H, benzene ring), 7.38 (d, 1H, benzene ring), 7.28 (m, 1H, benzene ring), 7.26 (m, 2H, benzene ring), 7.26-7.32 (m, 5H, benzene ring), 6.49 (s, 2H, N-H), 4.45 (s, 2H, sp^3, C-H), 4.43 (s, 1H, sp^3, C-H); ^{13}C NMR (DMSO-d_6): δ 187.3, 161.4, 143.5, 139.4, 136.3, 131.2, 128.5, 128.3, 127.1, 126.5, 126.2, 117.1, 71.8, 57.4, 49.9, 35.5.

3c: Colorless solid; Yield 70%; m.p.80°C; IR: 3460, 3250, 3180 (NH_2 and N-H), 2880, 2752 (C-H aliph) 2350 (CN), 1585, 1575, 1505, 1470 (Arom ring) 1290, 1160 (C-N-C), 1210 cm^{-1} (C=S); ^{1}H NMR (DMSO-d_6): δ 9.07 (s, 1H, N-H), 7.15-7.21 (m, 4H, benzene ring), 7.26-7.32 (m, 5H, benzene ring), 6.49 (s, 2H, N-H), 4.45 (s, 2H, sp^3, C-H), 4.43 (s, 1H, sp^3, C-H); ^{13}C NMR (DMSO-d_6): δ 187.5, 161.5, 140.1, 139.4, 136.3, 131.2, 130.2, 128.6, 128.4, 126.7, 126.5, 117.1, 72.0, 57.4, 50.1, 40.6.

3d: Colorless solid. Yield 90%. m.p.60°C; IR: 3390, 3260, 3170 (NH_2 and N-H), 2890, 2760 (C-H aliph) 2330 (CN), 1580, 1560, 1510, 1470 (Arom ring), 1285, 1155 (C-N-C), 1205 cm^{-1} (C=S); ^{1}H NMR (DMSO-d_6): δ 9.07 (s, 1H, N-H), 7.16-7.42 (m, 4H, benzene ring), 7.26-7.32 (m, 5H, benzene ring), 6.49 (s, 2H, N-H), 4.45 (s, 2H, sp^3, C-H), 4.43 (s, 1H, sp^3, C-H); ^{13}C NMR (DMSO-d_6): δ 187.5, 161.4, 159.7, 139.4, 137.6, 136.3, 130.4, 128.3, 126.7, 126.4, 117.1, 115.2, 72.0, 57.4, 50.1, 40.7.

3e: Colorless solid; Yield 70%; m.p.110°C; IR: 3430, 3270, 3140, (NH_2 and N-H), 2880, 2750 (C-H aliph), 2340 (CN), 1580, 1570, 1510, 1480 (Arom ring) 1280, 1160 (C-N-C), 1190 cm^{-1} (C=S); ^{1}H NMR

(DMSO-d_6): δ 9.12 (s, 1H, N-H), 7.26-7.32 (m, 5H, benzene ring), 7.57-8.38 (m, 4H, benzene ring), 6.49 (s, 2H, N-H), 4.45 (s, 2H, sp^3, C-H), 4.43 (s, 1H, sp^3, C-H); ^{13}C NMR (DMSO-d_6): δ 187.6, 161.5, 145.2, 143.1, 139.6, 136.5, 134.2, 128.3, 126.9, 126.7, 121.8, 120.9, 117.3, 72.0, 57.6, 50.1, 39.8.

3f: Colorless solid; Yield 79%; m.p.130°C; IR: 3475, 3245, 3180 (NH_2 and N-H), 2885, 2745 (C-H aliph), 2330 (CN), 1590, 1575, 1510, 1460 (Arom ring), 1280, 1140, (C-N-C), 1195 cm^{-1} (C=S); ^{1}H NMR (DMSO-d_6): δ 9.11 (s, 1H, N-H), 7.24-7.34 (m, 5H, benzene ring), 6.80-6.84 (m, 3H, benzene ring), 6.46 (s, 2H, N-H), 4.43 (s, 2H, sp^3, C-H), 4.41 (s, 1H, sp^3, C-H), 3.81 (s, 3H, sp^3, C-H), 3.73 (s, 3H, sp^3, C-H); ^{13}C NMR (DMSO-d_6): δ 187.5, 161.4, 149.6, 146.6, 139.4, 136.3, 135.3, 128.3, 126.6, 126.5, 122.1, 117.1, 113.9, 112.1, 71.8, 57.4, 55.9, 49.9, 57.4.

General procedure for synthesis of 3-benzyl-7-substituted phenyl-5-oxo-2-thioxo-2,3,4,5,6,7-hexahydrothiazolo [4,5-*b*] pyridine-6-carbonitrile (R' = 4-OCH_3)

A mixture of 4-methoxybenzaldehyde (1.20 g, 0.01 mol), 3-benzyl-4-thiazolidinon-2-thione 2.3 g, 0.01 mol) and ammonium acetate (1.54 g ,0.02 mol) was fused for 2 h. Ethylcyanoacetate (1.13 g, 0.01 mol) and ammonium acetate (4.6 g, 0.06 mol) was added and the mixturewas fused again for 2 h. Dioxane (15.0 mL) was added and the mixture was reflux for 2 h. The resulting solution was cooled and poured into water. The solid product obtained was filtered and washed with water, dried and purified by crystallization from ethanol to get crystalline solid products **4a-4f**.

4a: Colorless solid; Yield 40%; m.p.105°C; IR: 3081 (NH), 2325 (CN), 1660 (CONH), 1305, 1165 (C-N-C), 1261, 1094 (C-S-C), 1198 cm^{-1} (C=S); ^{1}H NMR (DMSO-d_6): δ 10.97 (s, 1H, N-H), 7.26-7.32 (m, 5H, benzene ring), 7.30-7.35 (m, 5H, benzene ring), 4.44 (s, 2H, sp^3 C-H), 3.84 (d, 1H, sp^3 C-H); 3.78 (d, 1H, sp^3 C-H); ^{13}C NMR (DMSO-d_6): δ 187.5, 161.5, 142.2, 139.6, 136.5, 128.6, 128.5, 127.7, 126.9, 126.7, 125.7, 117.3, 72.0, 57.6, 50.1, 40.8.

4b: Colorless solid; Yield 44%; m.p.80°C; IR: 3100 (NH), 2320 (CN), 1650 (CONH), 1310, 1160 (C-N-C), 1260, 1085 (C-S-C), 1190 cm^{-1} (C=S); ^{1}H NMR (DMSO-d_6): δ 10.95 (s, 1H, N-H), 7.18-7.63 (m, 4H, benzene ring), 7.23-7.34 (m, 5H, benzene ring), 4.42 (s, 2H, sp^3 C-H), 3.86 (d, 1H, sp^3 C-H), 3.77 (d, 1H, sp^3 C-H); ^{13}C NMR (DMSO-d_6): δ 187.5, 171.8, 138.2, 136.4, 133.0, 129.1, 128.7, 128.5, 127.3, 126.9, 126.7, 116.8, 80.8, 49.7, 37.2, 26.6.

4c: Colorless solid; Yield 63%; m.p.85°C; IR: 3090 (NH), 2330 (CN), 1665 (CONH), 1307, 1164 (C-N-C), 1265, 1090 (C-S-C), 1195 cm^{-1} (C=S); ^{1}H NMR (DMSO-d_6): δ 10.96 (s, 1H, N-H), 7.40 (s, 4H, benzene ring), 7.24-7.30 (m, 5H, benzene ring), 4.42 (s, 2H, sp^3 C-H), 3.82 (d, 1H, sp^3 C-H), 3.76 (d, 1H, sp^3 C-H); ^{13}C NMR (DMSO-d_6): δ 187.5, 171.8, 138.7, 136.5, 131.5, 129.1, 128.7, 128.5, 126.9, 126.7, 116.8, 80.8, 49.7, 37.7, 31.7.

4d: Colorless solid; Yield 61%; m.p.98°C; IR: 3085 (NH), 2320 (CN), 1655 (CONH), 1307, 1164 (C-N-C), 1265, 1090 (C-S-C), 1195 cm^{-1} (C=S); ^{1}H NMR (DMSO-d_6): δ 9.06 (s, 1H, N-H), 7.14-7.40 (m, 4H, benzene ring), 7.24-7.30 (m, 5H, benzene ring), 6.47 (s, 2H, N-H), 4.41 (s, 2H, sp^3 C-H), 4.38 (s, 1H, sp^3 C-H); ^{13}C NMR (DMSO-d_6): δ 187.5, 161.5, 159.9, 139.6, 137.8, 136.5, 130.6, 128.5, 126.9, 126.7, 117.3, 115.4, 72.0, 57.6, 50.1, 40.8.

4e: Colorless solid; Yield 95%; m.p.60°C; IR: 3080 (NH), 2327 (CN), 1665 (CONH), 1310, 1170 (C-N-C), 1260, 1090 (C-S-C), 1195 cm^{-1} (C=S); ^{1}H NMR (DMSO-d_6): δ 9.06 (s, 1H, N-H), 7.59-8.36 (m, 4H, benzene ring), 7.21-7.30 (m, 5H, benzene ring), 6.44 (s, 2H, N-H), 4.40 (s, 2H, sp^3 C-H), 4.36 (s, 1H, sp^3 C-H); ^{13}C NMR (DMSO-d_6): δ 187.5, 161.5, 145.2, 143.1, 139.6, 136.5, 134.2, 128.5, 126.9, 126.7, 121.8. 120.9, 117.3, 72.0, 57.6, 50.1, 39.8.

4f: Colorless solid; Yield 72%; m.p.78°C; IR: 3085 (NH), 2330 (CN), 1665 (CONH), 1310, 1170 (C-N-C), 1260, 1095 (C-S-C), 1195 cm^{-1} (C=S); ^{1}H NMR (DMSO-d_6): δ 10.96 (s, 1H, N-H), 7.42 (s, 4H, benzene ring), 7.23-7.29 (m, 5H, benzene ring), 4.40 (s, 2H, sp^3 C-H), 3.81 (d, 1H, sp^3 C-H), 3.78 (d, 1H, sp^3 C-H); ^{13}C NMR (DMSO-d_6): δ 187.5, 171.8, 138.7, 136.4, 131.5, 129.1, 128.7, 126.9, 126.7, 116.8, 80.8, 49.7, 37.7, 31.7.

Conclusion

In the present investigation, series of new fused heterocycles have been synthesized and screened for their antifungal and antibacterial activity. The activity reveals that the synthesized compounds possess moderate to good activity profile. The insights gained in this study will be useful for development of new anti-infective agents.

Acknowledgements

The authors Shailendra Tiwari, Vishal Kumar Singh and Shahla Rahmani are thankful to the Head, Department of Chemistry, University of Allahabad. Akeel Ahmad is thankful to the Principal/Head MGPG College Gaya, Kahkashan Begum is thankful to the Principal/Head GFPG College Shahjahanpur for providing necessary facilities. The authors would also like to thank SAIF, CDRI, Lucknow and SAIF, Punjab University, Chandigarh for spectral and analytical data and Centre of Biotechnology, University of Allahabad, Allahabad for antimicrobial data.

References

1 Kumar S, Kishore D, Paliwal S, Chauhan R, Dwivedi J & Mishra A, *Mol Drivers*, 20 (2016) 85.
2 Gold S H & Moellering Jr R C, *New Eng J Med*, 335 (1996) 1445.
3 Tiwari S, Pathak P, Singh K P & Sagar R, *Bioorg Med Chem Lett*, 27 (2017) 3802.
4 Garbars G, *Drugs*, 61 (2001) 1.
5 Perkoic I, Butala I &Kralj M, *Eur J Med Chem*, 51 (2012) 227.
6 Zhanz H J, Qian Y, Zhu D D, Yang X G & Zhu H L, *Eur J Med Chem*, 46 (2011) 4702.
7 Mavrova A T, Wesselinova D, Tsenov J A & Lubenova L A, *Eur J Med Chem*, 86 (2014) 676.
8 Krause N & Hoffmann-Rode A, *Synthesis*, 2 (2001) 171.
9 Sibi M P &Manyem S, *Tetrahedron*, 41 (56) (2000) 8033.
10 Basu B, Das P & Hossain I, *Synlett*, 14 (2004) 2630.
11 Tiwari S, Ahmad A & Singh V K, *Indian J Chem*, 59B (2020) 1586.
12 Ahmad A & Tiwari S, *Indian J Chem*, 59B (2020) 724.
13 Sharma Y O & Degani M S, *J Mol Cat*: *Chemical*, 277 (2007) 215.
14 Movassagh B & Shaygan P, *Arkivoc*, Xii (2006) 130.
15 Wang Y, Yuan Y Q & Guo S R, *Molecules*, 14 (11) (2009) 4779.
16 Fan Y C & Kwon O, *Molecules*, 16 (2011) 3802.
17 Yaragorla S & Kumar G S, *Indian J Chem*, 54B (2015) 240.
18 Kadi A A, Brollsy N R, Al-Deeb O A, Hibib E E, Ibrahim T M & El-Emam A A, *Eur J Med Chem*, 42 (2007) 235.
19 Tiwari S, *Indian J Chem*, 57B (2018) 1416.
20 Begum K, Ahmed A & Tiwari S, *Indian J Chem*, 60B (2021) 1490.
21 Tiwari S, Tiwari N, Agrawal T, Khan M H & Nizamuddin, *Indian J Chem*, 34B (1995) 1010.
22 Tiwari S H, *Oxidation Commun*, 36 (2013) 254.
23 Tiwari S & Nizamuddin, *J Indian Chem Soc*, 90 (2013) 267.
24 Khan M H, Tiwari S, Begum K & Nizamuddin, *Indian J Chem*, 37B (1998) 1075.
25 Solak N & Rollas S, *Arkivoc*, (2006) 173.
26 Mamolo M G, Falagiani V, Zampieri D, Vio L, Banfi E & Scialino G, *Il Farmaco*, 58 (2003) 631.
27 Schenone S, Brullo C, Bruno O, Bondavalli F, Ranise A, Filippelli W, Rinaldi B, Capuano A & Falcone G, *Bioorg Med Chem Lett*, 14 (2016) 1698.
28 Sondhi S M, Singh N, Johar M & Kumar A, *Bioorg Med Chem*, 13 (2005) 6158.
29 Mishra R N, Rawlins D B, Xiao H, Shan W, Bursuker I, Kellar K A, Mulheraon J G, Sack J S, Tokarski J S, Kimball S D & Webster K R, *Bioorg Med Chem Lett*, 13 (2003) 1133.
30 Straub A, Buckholz J, Frode R, Kern A, Kohlsdorfer Ch, Schmitt P, Schwarz Th, Siefert H & Stasch J, *Bioorg Med Chem Lett*, 10 (2002) 1711.
31 Gouda M A, *Arch Pharm*, 344 (2011) 543.
32 Tiwari S & Ahmad A, *Indian J Chem*, 58B (2019) 1407.
33 Diaa A I & Nasser S M I, *Eur J Med Chem*, 46 (2011) 5825.
34 Nasr M N &Gineinah M M, *Arch Pharm* (*Weinheim*), 335 (2002) 289.
35 Alam O, Khan S A, Siddiqui N, Ahsan W, Verma S P & Gilani S J, *Eur J Med Chem*, 45 (2010) 5113.
36 Sakamoto T & Ohsawa K, *J Chem Soc*, *Perkin Trans 1*, (1999) 2323.
37 Collier S J & Langer P, *Science of Synthesis*, 19, (2004) 403.
38 Arseniyadis S, Kyler K S & Watt D S, *Org React*, 31 (1984) 1.
39 Sahoo B, Tripathi P B & Rout M K, *J Indian Chem Soc*, 36 (1959) 421.
40 Tiwari S, Pathak P & Sagar R, *Bioorg Med Chem Lett*, 26 (2016) 2513.