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Synthesis and antimicrobial importance of oxazine bearing pyridine scaffold

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A highly efficient method for the synthesis of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((arylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles is described. The structures have been confirmed by IR, ^{1}H and ^{13}C NMR, and mass spectral techniques. The synthesized compounds have been tested for antimicrobial activity. The title compounds **4a-o** have been studied against strains of bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pyogenes*) and fungi (*Candida albicans*, *Aspergillus niger* and *Aspergillus clavatus*) by serial dilution method. Compounds **4b** (-2-OH), **4f** (-4-NO_2), **4h** (-3-Cl), **4j** (-4-OCH_3), **4l** (-4-OH-3-OCH_3) and **4m** (-N,N'-$(CH_3)_2$) exhibit good *in vitro* antimicrobial activity.

Keywords: Oxazine, pyridine, antibacterial activity, antifungal activity, SAR study

Pathogens, like bacteria and fungi cause a wide range of serious illnesses such as infections of the soft tissues, skin, hair, nails and internal organs. To treat these illnesses, antimicrobials have been used. But the worldwide use of antimicrobials has increased and due to this, their efficacy has been found to decrease rapidly in last three decades. Misuse or overuse of antimicrobials create resistant microbes[1,2]. Drug resistance causes serious difficulties in the routine therapy for curing common microbial infections. Thus it is very essential to develop new antimicrobial agents which can offer alternative treatments.

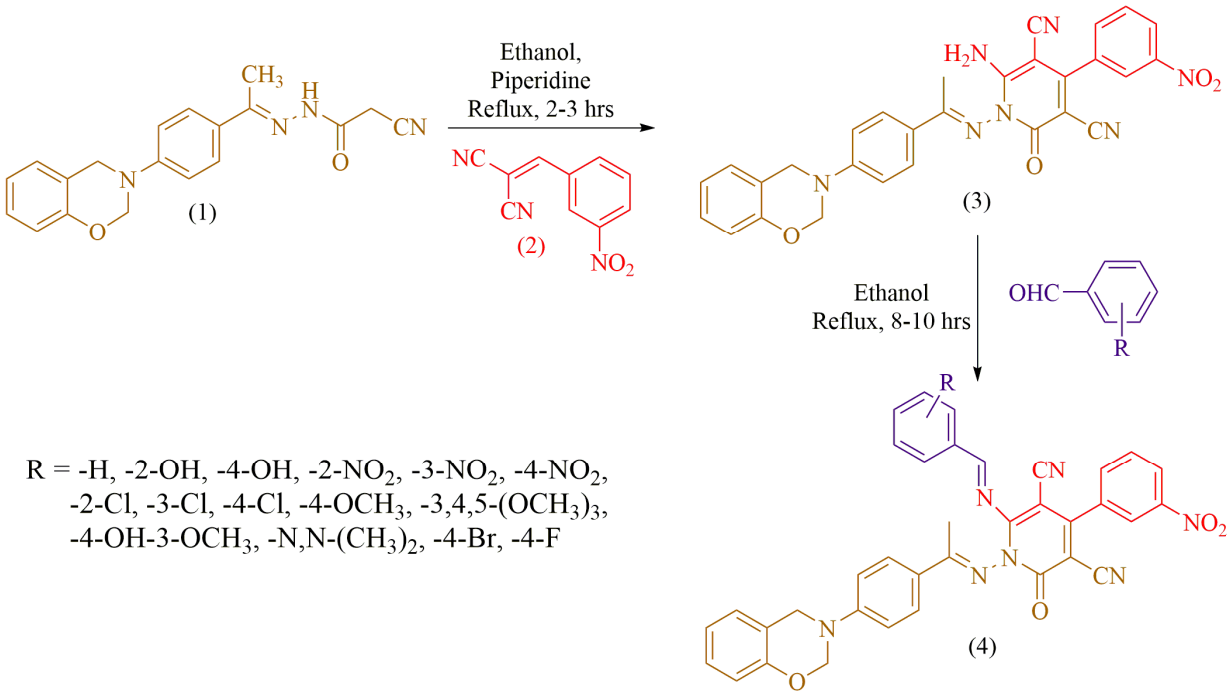
Two or more heterocyclic moieties, clubbed with each other in a single compound, can have medicinal properties[3-8]. In the present paper we have applied this approach. Here, new oxazine and pyridine motifs clubbed compounds are synthesized, characterized and screened for their antimicrobial properties. In the titled work, oxazine moiety has been chosen due to its broad range of pharmacological properties[9-13]. Pyridine is the most wide spread heterocycle in medicinal chemistry because of its various biological activities[14-19]. Commercially available drugs, having similarities in the structure of final compounds are shown in Figure 1. Milrinone and ciclopirox having 2-oxopyridine nucleus and linezolid having oxazine nucleus. Milrinone is useful in heart failure[20], linezolid is used to treat bacterial infections[21] and ciclopirox is used to treat fungal infections[22].

Results and Discussion

Chemistry

The synthetic pathway of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((arylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles **4a-o** is described in the Scheme I. *N'*-(1-(4-(2*H*-Benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)-2-cyanoacetohydrazide **1**, which on reaction with benzylidenemalononitrile **2** in the presence of piperidine produce intermediate **3**. Nucleophilic attack of the nitrogen on the carbon of the nitrile followed by a proton transfer and a tautomerization explain the formation of intermediate **3**. Intermediate **3** refluxed with different substituted benzaldehydes for 8-10 h furnished the reported compounds **4a-o**.

The structures of newly synthesized compounds of the series **4a-o** were confirmed by IR, ^{1}H and ^{13}C NMR, and mass spectral analysis. IR spectra of compound **4k** (Figure 2) showed the bands observed at 2255 and 2218 cm^{-1} which indicated the presence of -C≡N group attached to pyridine ring. Absorption band at 1701 cm^{-1} indicated the >C=O stretching of cyclic amide present on pyridine ring. The presence of oxazine moiety was confirmed by the



Scheme I — Synthetic pathway of reported compounds **4a-o**

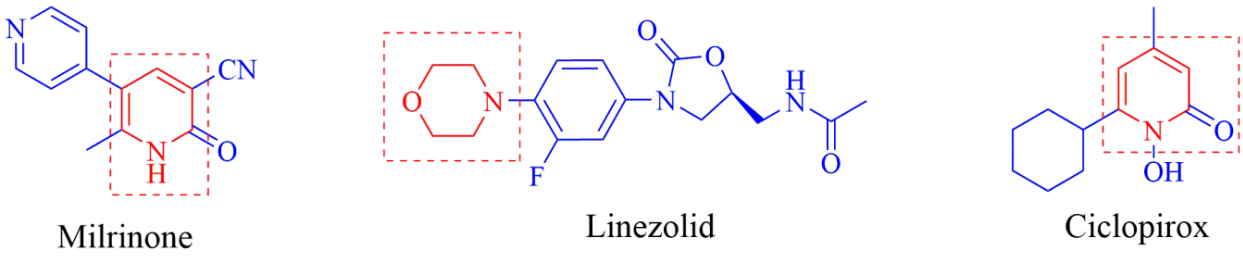


Figure 1 — Commercially available drug candidates containing 2-oxopyridone and oxazine

sharp absorption bands at 1118 and 1085 cm^{-1} of C-O-C stretching.

The ^{1}H NMR spectra of the title compound **4k** showed two -O-C*H*$_2$-N< oxazine protons as a singlet at δ 6.05 whereas two protons of Ar-C*H*$_2$-N< were observed as a singlet at δ 4.65. Fourteen protons of phenyl rings showed multiplet peaks of aromatic protons between δ 6.60 –7.80. Presence of substituted methoxyl group was confirmed by the presence of a singlet at δ 3.70 and 3.85. Ar-C*H*=N- showed a singlet at δ 9.35 while, the three protons of Ar-C(C*H*$_3$)=N- were observed as a singlet at δ 3.05. On the basis of ^{13}C NMR of the final compound **4k**, carbon of pyridine showed a chemical shift at δ 114.6–169.8. Carbon of oxazine moiety appeared at δ 59.8 - 157.5. Carbons of aromatic rings exhibited chemical shift at δ 104.3 - 152.5.

Determination of antibacterial and antifungal activities

Antimicrobial activity data are reported in Table I and Table II respectively. Compound **4f** (-4-NO_2) exhibited excellent activity against *E. coli* at MIC 12.5 µg/mL. Compounds **4b** (-2-OH) and **4h** (-3-Cl) showed very good activity against *E. coli* at MIC 25 µg/mL. Compound **4e** (-3-NO_2) demonstrated good activity against *E. coli* at MIC 50 µg/mL. Amongst the synthesized compounds, 4**b** (-2-OH) was found to be most potent as compared to standard drug at MIC 12.5 µg/mL against *P. aeruginosa*. Compound **4f** (-4-NO_2) showed very good activity against *P. aeruginosa* at MIC 25 µg/mL. Compound **4c** (-4-OH) and **4i** (-4-Cl) exhibited good activity against *P. aeruginosa* at MIC 50 µg/mL. Highest inhibition is possessed by compound **4f** (-4-NO_2) against *S.*

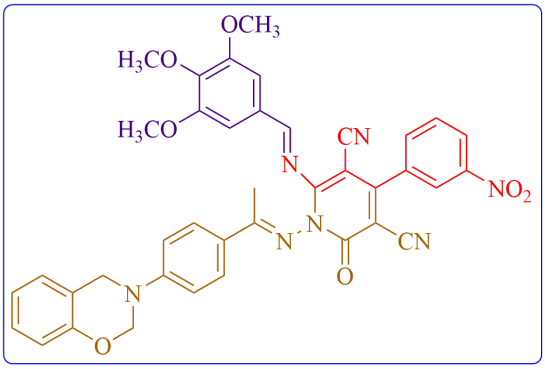


Figure 2 — Newly synthesized compound **4k**

Table I — Results of antibacterial activities of compounds **4a-o**

Compd	-R	Minimum inhibitory concentration (MIC) in µg/mL			
		E. c. MTCC (443)	*P. a.* MTCC (1688)	*S. a.* MTCC (96)	*S. p.* MTCC (442)
4a	-H	500	100	250	250
4b	-2-OH	25	12.5	100	50
4c	-4-OH	250	50	100	500
4d	-2-NO_2	100	200	250	250
4e	-3-NO_2	50	250	500	100
4f	-4-NO_2	12.5	25	25	50
4g	-2-Cl	500	100	500	250
4h	-3-Cl	25	100	200	250
4i	-4-Cl	100	50	100	100
4j	-4-OCH_3	100	500	100	100
4k	-3,4,5-$(OCH_3)_3$	500	500	500	250
4l	-4-OH-3-OCH_3	500	250	500	250
4m	-N,N'-$(CH_3)_2$	100	100	250	50
4n	-4-Br	250	100	250	100
4o	-4-F	250	100	100	100
	Ampiciline	100	100	250	100

E. c. Escherichia coli, P. a. Pseudomonas aeruginosa, S. a. Staphylococcus aureus, S. p. Streptococcus pyogenes

*aureus*at MIC 25 µg/mL. While compounds **4b** (-2-OH) and **4f** (-4-NO_2) exhibited good activity against *S. pyogenes* at MIC 50 µg/mL. Compound **4j** (-4-OCH_3) revealed excellent activity against *C. albicans* at MIC 12.5 µg/mL. When we installed the functional groups like in **4l** (-4-OH, 3-OCH_3) and **4m** (-*N,N*'-$(CH_3)_2$) the resulting compounds showed good activity against *C. albicans* at MIC 50 µg/mL. Compounds **4j** (-4-OCH_3) and **4k** (-3,4,5-$(OCH_3)_3$ possessed good activity against *A. niger* at MIC 25 µg/mL and MIC 50 µg/mL respectively. Installation of group like (-4-OH-3-OCH_3) on compound **4l** furnished highest inhibition against *A. clavatus* at MIC 25 µg/mL. Compound **4j** (-4-OCH_3) and **4k** (-3,4,5-$(OCH_3)_3$) exhibited good activity against *A. clavatus* at MIC 50 µg/mL.

Table II — Results of antifungal activities of compounds **4a-o**

Compd	-R	Minimum inhibitory concentration (MIC) in µg/mL		
		C. a. MTCC (227)	*A. n.* MTCC (282)	*A. c.* MTCC (1323)
4a	-H	100	500	250
4b	-2-OH	500	100	100
4c	-4-OH	500	250	250
4d	-2-NO_2	500	100	100
4e	-3-NO_2	500	250	500
4f	-4-NO_2	100	250	250
4g	-2-Cl	250	500	500
4h	-3-Cl	100	100	500
4i	-4-Cl	500	250	500
4j	-4-OCH_3	12.5	25	50
4k	-3,4,5-$(OCH_3)_3$	100	50	50
4l	-4-OH-3-OCH_3	50	100	25
4m	-N,N'-$(CH_3)_2$	50	100	250
4n	-4-Br	500	250	500
4o	-4-F	500	250	100
	Griseofulvin	500	100	100

C.a. Candida albicans, A. n. Aspergillus niger, A. c. Aspergillus clavatus

Structure Activity Relationship (SAR)

The results of antimicrobial activity were highly affected by the different substituents on the aromatic ring of compounds **4a-o**. The introduction of electron withdrawing group on the aromatic ring increased antibacterial potency of the compounds. Nitro group at *para* position, containing compound **4f** showed maximum effect against *E. coli. i.e.* inhibition at MIC 12.5 µg/mL. Compounds **4b** and **4h** containing hydroxyl and chloro groups showed significant inhibition against *E. coli* at MIC 25 µg/mL. Installation of hydroxy and nitro group at the substituted benzene ring showed very good activity against *P. aeruginosa* at MIC 12.5 µg/mL and MIC 25 µg/mL respectively. Compound **4f**, with nitro group at 4th position showed significant potency against *S. aureus* at MIC 25 µg/mL. Compounds **4b**, **4f** and **4m** showed good activity against *S. pyogens* bacteria. MIC results displayed that substitution of electron donating groups on the benzene ring showed lesser potency than electron withdrawing groups. Data of antifungal activity revealed that methoxy group on 4-OCH_3 substitution of benzene ring showed excellent activity against *C. albicans* at 12.5 µg/mL. Significant inhibition was shown by compound **4j** against *A. niger* at concentration of 25 µg/mL. Compound **4l** containing -4-OH-3-OCH_3 group exhibited maximum potency at MIC 25 µg/mL against *A. clavatus*.

Antimicrobial Assay

The titled compounds were evaluated against *S. aureus*, *S. pyogenes*, *E. coli, P. aeruginosa* and three strains of fungi like *C. albicans, A. niger* and *A. clavatus*. The MIC (μg/mL) values of test compounds **4a-o** are listed in Table I and Table II along with the MIC values of reference compounds which are ampicillin and griseofulvin. The results have shown that majority of synthesized compounds exhibited different degrees of inhibition against several strains of microbes. The antimicrobial activity of newly synthesized compounds can be linked to structural alterations and modifications of the respective compounds.

Antibacterial Assay

"Mueller Hinton Broth dilution method (Becton Dickinson, USA) was used for antibacterial assay of synthesized compounds[23]. The strains used for antimicrobial activity of newly synthesized compounds, were procured from the IMTECH, Chandigarh. The compounds **4a-o** were screened for their antibacterial activity in triplicate sets against these bacteria at different concentrations of 1000, 500, 250 and 200 μg/mL. The drugs which were found to be active in primary analysis were further diluted and evaluated. 10 μg/mL suspensions were further inoculated on appropriate media and the growth was noted after one or two days. Minimum inhibitory concentration is the lowest concentration, which showed no growth of microbes after spot subculture for each drug. The test mixture should contain 108 cells/mL. In this study, Ampicillin was the standard drug for evaluating the antibacterial activity.

Antifungal Assay

The newly prepared compounds **4a-o** were screened for their antifungal activity as primary screens in six sets against *C. albicans*, *A. niger*, and *A. clavatus* at various concentrations of 1000, 500, and 250 μg/mL[23]. The primary active compounds were similarly diluted to obtain 200, 125, 100, 62.5, 50, 25, and 12.5 μg/mL concentrations for secondary screening to test in a second set of dilutions against all fungi. The fungal activity of each compound was compared with 'griseofulvin' as a standard drug, which showed 500, 100, and 100 μg/mL MIC against *C. albicans*, *A. niger*, and *A. clavatus*, respectively. For fungal growth, in the present protocol, we have used Sabouraud's dextrose broth at 28°C in aerobic condition for 48 h. DMSO and sterilized distilled water was used as negative control while griseofulvin (1 U strength) was used as a positive control."

Experimental Section

Materials and methods

Completion of the reaction and homogeneity of compounds were checked on Aluminum coated TLC plates [60 F_{245} (E. Merck)]. Ethyl acetate: *n*-hexane (3:7 V/V) used as mobile phase and TLC plates visualized in an iodine chamber. An electro thermal melting point apparatus was used to determine melting points which are uncorrected. Elemental analysis (% C, H, N) was confirmed by a Perkin-Elmer 2400 CHN analyzer. A Perkin-Elmer FT-IR spectrophotometer was used to record IR spectra by using KBr. ^{1}H NMR spectra were recorded on a Bruker Avance II 400 MHz while ^{13}C NMR spectra on Varian Mercury-400, 100 MHz in DMSO-d_6 as a solvent and tetramethylsilane (TMS) as an internal standard using 5 mm tube. Mass spectra were obtained on Shimadzu LC-MS 2010 spectrometer.

***N'*-(1-(4-(2*H*-Benzo[e][1,3]oxazin-3(4*H*)-yl) phenyl)ethylidene)-2-cyanoacetohydrazide, 1** was prepared by our previously reported method[24].

Benzylidenemalononitrile, 2 was prepared by the literature procedure[25].

1-((1-(4-(2*H*-Benzo[e][1,3]oxazin-3(4*H*)-yl) phenyl)ethylidene)amino)-6-amino-4-(3-nitro-phenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbo-nitrile, 3

A mixture containing *N'*-(1-(4-(2*H*-benzo[e] [1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)-2-cyano acetohydrazide (0.01 mole), benzylidenemalono nitrile (0.01 mole) and 2 drops of piperidine in ethanol (95%) (50 mL) was refluxed for 2-3 hrs. The mixture was then cooled down to RT and diluted with few drops of water. The crystals formed were filtered, air dried and recrystallized from aqueous DMF. Yield: 69%; m.p.: 159-162°C;IR (λ_{max}, cm^{-1}, KBr): 3089 (C-H stretching, aromatic ring), 2972 (C-H stretching, -CH_3 group), 2893 (C-H stretching, -CH_2 group), 2230, 2223 (C≡N stretching), 1718 (C=O stretching, cyclic amide), 1647, 1581 (N-H bending, -RNH_2), 1634, 1565, 1547 (C=C, C=N stretching, aromatic ring), 1236 (C-H bending), 1206, 1092 (C-O-C stretching, cyclic ether group), 814 (1:4-substituted benzene ring), 742 (1:2-

substituted benzene ring)). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.94 (s, 3H, -N=C-CH_3), 4.64 (s, 2H, -N-CH_2), 6.45 (s, 1H, pyridine ring-N*H*), 6.75-8.16 (m, 12H, Ar-*H*), 6.09 (s, 2H, -O-CH_2-N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.3 (1C, -C(=N)CH_3), 59.5 (1C, C_4 oxazine ring), 76.5, (1C, C_3 pyridine ring), 93.2 (1C, C_2 oxazine ring), 111.7 (2C, C_3 & C_5 aromatic ring), 112.4 (1C, C_2 aromatic ring), 115.5 (1C, C_5 pyridine ring), 115.9 (2C, -C≡N), 120.2 (1C, C_2 aromatic ring with -NO_2 group), 120.4 (1C, C_4 aromatic ring), 122.3 (1C, C_6 aromatic ring), 123.3 (1C, C_4 aromatic ring with -NO_2 group), 127.6 (1C, C_3 aromatic ring), 128.3 (1C, C_3 aromatic ring), 128.7 (1C, C_5 aromatic ring), 129.4 (1C, C_5 aromatic ring with -NO_2 group), 130.3 (2C, C_2 & C_6 aromatic ring), 133.3 (1C, C_1aromatic ring with -NO_2 group), 135.7 (1C, C_2 aromatic ring with -NO_2 group), 147.6 (1C, C_3aromatic ring with -NO_2 group), 151.7 (1C, C_4 aromatic ring), 157.4 (1C, C_1 aromatic ring), 159.6 (1C, C_2 pyridine ring), 160.5 (1C, C_6 pyridine ring), 163.5 (1C, -C(=N)CH_3), 169.6 (1C, C_4 pyridine ring).LC-MS (m/z): 531.19 [M^+]; Anal. Calcd for $C_{29}H_{21}N_7O_4$: C, 65.53; H, 3.98; N, 18.45; Found: C, 65.39; H, 4.15; N, 18.72 %.

1-((1-(4-(2*H*-Benzo[e][1,3]oxazin-3(4*H*)-yl)-phenyl)ethylidene)amino)-6-((arylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles, 4a-o

Synthesis of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((arylidene) amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles **(4a-o)** is illustrated in Scheme I. Because of the nucleophilic addition of benzaldehyde derivatives to 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-amino-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile (3)in the presence of ethanol (95%), as a solvent, titled compounds **(4a-o)** obtained. Physicochemical characteristics of the synthesized compounds **(4a-o)** are mentioned in Table III and spectral characterization in Table IV.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3-(4*H*)-yl)phenyl)ethylidene)amino)-6-((benzylidene) amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4a

IR (λ_{max}, cm^{-1}, KBr): 3096 (C-H stretching, aromatic ring), 2992 (C-H stretching, -CH_3 group), 2891 (C-H stretching, -CH_2 group), 2239, 2201(C≡N stretching), 1713 (C=O stretching, cyclic amide), 1638, 1562, 1539 (C=C, C=N stretching, aromatic ring), 1237 (C-H bending), 1201, 1091 (C-O-C stretching, cyclic ether group), 814 (1:4-substituted benzene ring), 732 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.97 (s, 3H, Ar-C(CH_3)=N-), 4.64 (s, 2H, Ar-CH_2-N<), 6.03 (s, 2H, -O-CH_2-N<), 6.81-8.11 (m, 17H, Ar-H), 9.51 (s, 1H, Ar-CH=N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.4 (1C, -CH_3), 59.6 (1C, C_4 oxazine ring), 93.5 (1C, C_2 oxazine ring), 111.7 (2C, C_2& C_6 aromatic ring), 112.3 (1C, C_2 aromatic ring), 114.7 (1C, C_5 2-oxopyridine ring), 115.2 (2C, -C≡N), 115.4 (1C, C_3 2-oxopyridine ring), 120.2 (1C, C_2 aromatic ring with -NO_2 group), 120.5 (1C, C_4 aromatic ring), 122.3 (1C, C_5 oxazine ring), 123.4 (1C, C_4 aromatic ring with -NO_2 group), 126.7 (1C, C_1 aromatic ring), 128.4 (1C, C_3 aromatic ring), 128.5 (2C, C_3& C_5 aromatic ring), 129.2 (1C, C_5 aromatic ring), 129.7

Table III — Physicochemical characteristics of the synthesized compounds

Compd	-R	Mol. formula	Mol. wt. (g/mol)	Rf value	Yield (%)	m.p. (°C)
4a	-H	$C_{36}H_{25}N_7O_4$	619	0.54	69	218-20
4b	-2-OH	$C_{36}H_{25}N_7O_5$	635	0.46	67	171-73
4c	-4-OH	$C_{36}H_{25}N_7O_5$	635	0.82	63	178-80
4d	-2-NO_2	$C_{36}H_{24}N_8O_6$	664	0.73	73	218-20
4e	-3-NO_2	$C_{36}H_{24}N_8O_6$	664	0.59	76	228-30
4f	-4-NO_2	$C_{36}H_{24}N_8O_6$	664	0.74	75	218-20
4g	-2-Cl	$C_{36}H_{24}ClN_7O_4$	654	0.69	63	208-10
4h	-3-Cl	$C_{36}H_{24}ClN_7O_4$	654	0.65	69	194-96
4i	-4-Cl	$C_{36}H_{24}ClN_7O_4$	654	0.71	72	187-89
4j	-4-OCH_3	$C_{37}H_{27}N_7O_5$	649	0.58	65	167-69
4k	-3,4,5-$(OCH_3)_3$	$C_{39}H_{31}N_7O_7$	709	0.82	72	203-205
4l	-4-OH-3-OCH_3	$C_{37}H_{27}N_7O_6$	665	0.68	68	157-59
4m	-N,N'-$(CH_3)_2$	$C_{38}H_{30}N_8O_4$	662	0.63	71	168-70
4n	-4-Br	$C_{36}H_{24}BrN_7O_4$	698	0.73	68	118-20
4o	-4-F	$C_{36}H_{24}FN_7O_4$	637	0.49	73	205-207

Table IV — Characterization of the synthesized compounds

Compd	R	^{1}H NMR	^{13}C NMR	IR	LC-MS (*m/z*)
4a	-H	2.97, 4.64, 6.03, 6.81-8.11, 9.51.	17.4, 93.5, 111.7, 112.3, 114.7, 115.2, 115.4, 120.2, 120.5, 122.3, 123.4, 126.7, 128.4, 128.5, 129.2, 129.7, 129.8, 130.4, 131.2, 133.5, 133.6, 135.2, 148.0, 152.6, 153.6, 157.9, 160.5, 163.6, 163.7, 169.9.	3096, 2992, 2891, 2239, 2201, 1713, 1638, 1562, 1539, 1237, 1201, 1091, 814, 732.	619.20
4b	-2-OH	2.98, 4.63, 5.97, 6.74-8.17, 9.49, 11.15.	17.5, 59.3, 93.7, 111.2, 112.4, 114.8, 115.4, 115.5, 118.4, 118.6, 120.4, 120.5, 121.6, 122.2, 123.1, 126.7, 128.6, 128.9, 129.4, 129.9, 132.3, 132.6, 133.8, 135.4, 148.1, 152.4, 153.5, 158.1, 160.7, 161.4, 163.5, 163.8, 169.5.	3461, 3084, 3002, 2894, 2245, 2211, 1719, 1629, 1568, 1545, 1231, 1215, 1096, 806, 731.	635.19
4c	-4-OH	3.04, 4.58, 6.04, 6.80-8.16, 9.50, 9.71.	17.1, 93.8, 111.6, 112.0, 114.6, 115.4, 115.5, 116.5 , 120.5, 120.6, 122.7, 123.3, 126.2, 126.6, 128.5, 129.2, 129.6, 129.8, 130.5, 133.4, 135.3, 148.3, 152.4, 153.5, 158.2, 160.5, 160.7, 163.4, 163.7, 169.7.	3390, 3089, 2999, 2879, 2230, 2214, 1719, 1634, 1568, 1530, 1227, 1195, 1090, 823, 722.	635.19
4d	-2-NO_2	3.00, 4.59, 6.05, 6.83-8.11, 9.46.	17.4, 93.3, 111.5, 112.4, 114.6, 115.1, 115.2, 120.3, 120.4, 122.6, 123.5, 124.4, 126.8, 128.1, 128.5, 129.4, 129.7, 129.9, 130.3, 132.2, 133.6, 134.7, 135.4, 147.7, 148.3, 152.7, 153.8, 158.2, 160.7, 163.7, 163.9, 169.4.	3098, 2996, 2890, 2243, 2205, 1717, 1642, 1563, 1531, 1528, 1357, 1239, 1213, 1097, 819, 732	664.18
4e	-3-NO_2	3.06, 4.65, 6.11, 6.73-8.50, 9.50.	17.1, 59.4, 93.3, 111.8, 112.4, 114.9, 115.1, 115.4, 120.3, 120.7, 121.8, 122.6, 123.5, 126.4, 126.9, 128.5, 129.0, 129.4, 129.6, 133.6, 134.8, 135.4, 147.8, 152.5, 153.7, 158.1, 160.6, 163.4, 163.9, 169.6.	3087, 3005, 2898, 2233, 2216, 1725, 1644, 1568, 1537, 1530, 1344, 1228, 1214, 1098, 811, 737.	664.18
4f	-4-NO_2	2.99, 4.60, 6.02, 6.76-8.37, 9.49.	17.2, 59.3, 93.2, 111.9, 112.4, 114.5, 115.3, 115.6, 120.4, 120.7, 122.4, 123.6, 124.2, 126.8, 127.9, 128.4, 129.3, 129.5, 129.9, 133.4, 135.4, 140.0, 148.2, 150.4, 152.4, 153.7, 158.8, 160.7, 163.4, 163.8, 169.6.	3093, 2990, 2889, 2249, 2201, 1732, 1633, 1559, 1546, 1531, 1349, 1239, 1210, 1031, 816, 738.	664.18
4g	-2-Cl	2.91, 4.64, 6.09, 6.77-8.19, 9.48.	17.0, 59.5, 93.8, 11.5, 112.6, 114.9, 115.3, 115.7, 120.4, 120.7, 122.5, 123.5, 126.5, 126.8, 127.5, 128.2, 129.3, 129.4, 129.5, 130.3, 132.6, 133.3, 133.7, 134.3, 135.3, 148.2, 152.5, 153.8, 157.6, 160.4, 163.5, 163.8, 169.5.	3091, 2998, 2893, 2241, 2205, 1718, 1631, 1567, 1535, 1230, 1210, 1097, 809, 830, 739.	653.16
4h	-3-Cl	3.01, 4.64, 6.03, 6.80-8.17, 9.51.	17.5, 59.7, 93.7, 111.6, 112.4, 114.8, 115.4, 115.6, 120.3, 120.7, 122.4, 123.6, 126.6, 126.9, 127.5, 128.5, 129.3, 129.6, 129.9, 130.3, 131.4, 133.4, 134.6, 135.3, 135.4, 148.4, 152.3, 152.8, 158.2, 160.7, 163.5, 163.7, 169.4.	3096, 2992, 2891, 2239, 2201, 1713, 1638, 1562, 1539, 1237, 1201, 1091, 815, 837, 732.	653.16
4i	-4-Cl	3.05, 4.67, 6.06, 6.73-8.16, 9.48.	17.5, 59.8, 93.3, 111.4, 112.2, 114.5, 115.3, 115.7, 120.1, 120.6, 122.5, 123.6, 126.8, 128.6, 128.7, 129.3, 12936, 129.7, 130.8, 132.0, 133.7, 135.4, 136.8, 147.9, 152.5, 153.5, 157.6, 160.7, 163.4, 163.7, 170.2.	3090, 2987, 2895, 2231, 2206, 1718, 1630, 1565, 1534, 1236, 1205, 1099, 809, 843, 729.	653.16
4j	-4-OCH_3	2.91, 3.84, 4.67, 5.97, 6.76-8.19, 9.45.	17.3, 55.4, 59.8, 93.3, 111.5, 112.4, 114.4, 114.5, 115.3, 115.6, 120.3, 120.4, 122.6, 123.7, 126.3, 126.9, 128.2, 129.1, 129.4, 129.6, 130.4, 133.3, 135.6, 148.2, 152.4, 153.2, 157.7, 160.4, 162.7, 163.4, 163.8, 169.7.	3097, 2990, 2897, 2237, 2203, 1714, 1633, 1561, 1536, 1233, 1205, 1097, 822, 734.	649.21

(*Contd.*)

Table IV — Characterization of the synthesized compounds—(*Contd*.)

Compd	R	^{1}H NMR	^{13}C NMR	IR	LC-MS (*m/z*)
4k	-3,4,5-$(OCH_3)_3$	3.05, 3.70, 3.85, 4.65, 6.05, 6.60-7.80, 9.35.	17.6, 56.4, 59.8, 61.0, 93.2, 104.3, 111.6, 112.2, 114.6, 115.4, 115.6, 120.3, 120.6, 122.4, 123.5, 126.9, 128.2, 128.4, 129.2, 129.5, 129.6, 133.3, 135.4, 141.7, 148.4, 152.5, 153.1, 153.4, 157.5, 160.2, 163.4, 163.5, 169.8.	3105, 3009, 2860, 2255, 2218, 1701, 1625, 1598, 1557, 1285, 1118, 1085, 810, 775.	709.23
4l	-4-OH-3-OCH_3	2.98, 3.86, 4.65, 5.94, 6.72-8.15, 9.50, 9.58.	17.1, 56.4, 59.3, 93.4, 111.6, 112.0, 112.4, 114.9, 115.3, 115.6, 117.3, 120.4, 120.7, 122.4, 123.1, 123.6, 126.8, 127.5, 128.5, 129.3, 129.6, 129.8, 133.6, 135.3, 148.2, 149.5, 151.2, 152.7, 153.9, 157.7, 160.4, 163.6, 163.3, 170.2.	3396, 3106, 3015, 2898, 2825, 2231, 2208, 1714, 1647, 1569, 1547, 1237, 1210, 1099, 829, 742.	665.20
4m	-N,N'-$(CH_3)_2$	2.97, 3.07, 4.64, 5.99, 6.72-8.19, 9.47.	17.5, 41.5, 59.7, 93.4, 111.9, 112.2, 112.5, 114.6, 115.3, 115.6, 120.3, 120.7, 122.4, 123.2, 123.6, 126.8, 128.2, 128.7, 129.0, 129.4, 129.8, 133.7, 135.1, 148.3, 152.7, 153.2, 153.8, 157.4, 160.2, 163.6, 163.8, 169.7.	3087, 2989, 2887, 2230, 2206, 1718, 1658, 1566, 1543, 1347, 1231, 1221, 1098, 823, 746.	662.24
4n	-4-Br	2.93, 4.57, 5.95, 6.79-8.17, 9.53.	17.1, 59.4, 93.3, 111.4, 112.5, 114.9, 115.4, 115.7, 120.3, 120.7, 122.4, 123.5, 125.6, 126.8, 128.1, 128.6, 129.3, 129.7, 129.9, 131.8, 132.5, 133.4, 135.6, 148.3, 152.6, 153.5, 157.7, 160.3, 163.5, 163.8, 169.4.	3102, 2987, 2894, 2237, 2211, 1724, 1637, 1552, 1543, 1231, 1207, 1105, 819, 725, 576.	697.11
4o	-4-F	2.97, 4.63, 6.01, 6.80-8.18, 9.43.	17.3, 59.5, 93.7, 111.9, 112.5, 114.6, 115.3, 115.4, 115.7, 120.3, 120.8, 122.3, 123.5, 126.8, 128.6, 129.1, 129.4, 129.5, 129.9, 130.5, 133.4, 135.3, 148.0, 152.2, 153.5, 158.0, 160.4, 163.4, 163.6, 165.6, 170.1.	3096, 2992, 2891, 2239, 2201, 1713, 1638, 1562, 1539, 1237, 1201, 1091, 1067, 806, 732.	637.19

(1C, C_5 aromatic ring with -NO_2 group), 129.8 (2C, C_2& C_6 aromatic ring), 130.4 (2C, C_2& C_6 aromatic ring), 131.2 (1C, C_4 aromatic ring), 133.5 (1C, C_1 aromatic ring with -NO_2 group), 133.6 (1C, C_1 aromatic ring), 135.2 (1C, C_6 aromatic ring with -NO_2 group), 148.0 (1C, C_3 aromatic ring with -NO_2 group), 152.6 (1C, C_4 aromatic ring), 153.6 (1C, C_6 2-oxopyridine ring), 157.9 (1C, C_6 oxazine ring), 160.5 (1C, C_6 2-oxopyridine ring), 163.6 (1C, -CH=N), 163.7 (1C, -C(=N)-CH_3), 169.9 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 619.20 [M^+]; Anal. Calcd for $C_{36}H_{25}N_7O_4$: C, 69.78; H, 4.07; N, 15.82; Found: C, 69.76; H, 4.05; N, 15.86 %.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3]-oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((2-hydroxybenzylidene) amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4b

IR (λ_{max}, cm^{-1}, KBr): 3461 (-O-H stretching, Ar-OH), 3084 (>C-H stretching, aromatic ring), 3002 (>C-H stretching, -CH_3 group), 2894 (>C-H stretching, -CH_2 group), 2245, 2211 (-C≡N stretching), 1719 (>C=O stretching, cyclic amide), 1629, 1568, 1545 (>C=C<, >C=N- stretching, aromatic ring), 1231 (>C-H bending), 1215, 1096 (>C-O-C< stretching, cyclic ether group), 806 (1:4-substituted benzene ring), 731 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.98 (s, 3H, Ar-C(CH_3)=N-), 4.63 (s, 2H, Ar-CH_2-N<), 5.97 (s, 2H, -O-CH_2-N<), 6.74-8.17 (m, 16H, Ar-H), 9.49 (s, 1H, Ar-CH=N-), 11.15 (s, 1H, -OH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.5 (1C, -CH_3), 59.3 (1C, C_4 oxazine ring), 93.7 (1C, C_2 oxazine ring), 111.2 (2C, C_2& C_6 aromatic ring), 112.4 (1C, C_2 aromatic ring), 114.8 (1C, C_5 2-oxopyridine ring), 115.4 (2C, -C≡N), 115.5 (1C, C_3 2-oxopyridine ring), 118.4 (1C, C_3 aromatic ring), 118.6 (1C, C_1 aromatic ring), 120.4 (1C, C_4 aromatic ring), 120.5 (1C, C_2 aromatic ring with -NO_2 group), 121.6 (1C, C_5 aromatic ring), 122.2 (1C, C_5 oxazine ring), 123.1 (1C, C_4 aromatic ring with -NO_2 group), 126.7 (1C, C_1 aromatic ring), 128.6 (1C, C_3 aromatic ring), 128.9 (1C, C_5 aromatic ring), 129.4 (2C, C_2& C_6 aromatic ring), 129.9 (1C, C_5 aromatic ring with -NO_2 group), 132.3 (1C, C_6 aromatic ring), 132.6 (1C, C_4 aromatic ring), 133.8 (1C, C_1 aromatic ring with -NO_2 group), 135.4 (1C, C_6 aromatic ring with -NO_2 group), 148.1 (1C, C_3 aromatic ring with -NO_2 group), 152.4

(1C, C_4 aromatic ring), 153.5 (1C, C_6 2-oxopyridine ring), 158.1 (1C, C_6 oxazine ring), 160.7 (1C, C_6 2-oxopyridine ring), 161.4 (1C, C_2 aromatic ring-OH), 163.5 (1C, -CH=N), 163.8 (1C, -C(=N)-CH_3), 169.5 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 635.19 [M^+]; Anal. Calcd for $C_{36}H_{25}N_7O_5$: C, 68.03; H, 3.96; N, 15.43; Found: C, 68.06; H, 3.94; N, 15.44 %.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3] oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((4-hydroxybenzylidene) amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4c

IR (λ_{max}, cm^{-1}, KBr): 3390 (-O-H stretching, Ar-OH), 3089 (>C-H stretching, aromatic ring), 2999 (>C-H stretching, -CH_3 group), 2879 (>C-H stretching, -CH_2 group), 2230, 2214 (-C≡N stretching), 1719 (>C=O stretching, cyclic amide), 1634, 1568, 1530 (>C=C<, >C=N- stretching, aromatic ring), 1227 (>C-H bending), 1195, 1090 (>C-O-C< stretching, cyclic ether group), 823 (1:4-substituted benzene ring), 722 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.04 (s, 3H, Ar-C(CH_3)=N-), 4.58 (s, 2H, Ar-CH_2-N<), 6.04 (s, 2H, -O-CH_2-N<), 6.80-8.16 (m, 16H, Ar-H), 9.50 (s, 1H, Ar-CH=N-), 9.71 (s, 1H, -OH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.1 (1C, -CH_3), 59.5 (1C, C_4 oxazine ring), 93.8 (1C, C_2 oxazine ring), 111.6 (2C, C_2& C_6 aromatic ring), 112.0 (1C, C_2 aromatic ring), 114.6 (1C, C_5 2-oxopyridine ring), 115.4 (2C, -C≡N), 115.5 (1C, C_3 2-oxopyridine ring), 116.5 (2C, C_3& C_5 aromatic ring), 120.5 (1C, C_2 aromatic ring with -NO_2 group), 120.6 (1C, C_4 aromatic ring), 122.7 (1C, C_5 oxazine ring), 123.3 (1C, C_4 aromatic ring with -NO_2 group), 126.2 (1C, C_1 aromatic ring), 126.6 (1C, C_1 aromatic ring), 128.5 (1C, C_3 aromatic ring), 129.2 (2C, C_2& C_6 aromatic ring), 129.6 (1C, C_5 aromatic ring), 129.8 (1C, C_5 aromatic ring with -NO_2 group), 130.5 (2C, C_2& C_6 aromatic ring), 133.4 (1C, C_1 aromatic ring with -NO_2 group), 135.3 (1C, C_6 aromatic ring with -NO_2 group), 148.3 (1C, C_3 aromatic ring with -NO_2group), 152.4 (1C, C_4 aromatic ring), 153.5 (1C, C_6 2-oxopyridine ring), 158.2 (1C, C_6 oxazine ring), 160.5(1C, C_4 aromatic ring-OH), 160.7 (1C, C_6 2-oxopyridine ring), 163.4 (1C, -CH=N), 163.7 (1C, -C(=N)-CH_3), 169.7 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 635.19 [M^+]; Anal. Calcd for $C_{36}H_{25}N_7O_5$: C, 68.03; H, 3.96; N, 15.43; Found: C, 68.07; H, 3.95; N, 15.46 %.

Characterization of 1-((1-(4-(2*H*-benzo[e] [1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((2-nitrobenzylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4d

IR (λ_{max}, cm^{-1}, KBr): 3098 (>C-H stretching, aromatic ring), 2996 (>C-H stretching, -CH_3 group), 2890 (>C-H stretching, -CH_2 group), 2243, 2205 (-C≡N stretching), 1717 (>C=O stretching, cyclic amide), 1642, 1563, 1531 (>C=C<, >C=N- stretching, aromatic ring), 1528, 1357 (-N=O stretching), 1239 (>C-H bending), 1213, 1097 (>C-O-C< stretching, cyclic ether group), 819 (1:4-substituted benzene ring), 732 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.00 (s, 3H, Ar-C(CH_3)=N-), 4.59 (s, 2H, Ar-CH_2-N<), 6.05 (s, 2H, -O-CH_2-N<), 6.83-8.11 (m, 16H, Ar-H), 9.46 (s, 1H, Ar-CH=N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.4 (1C, -CH_3), 59.5 (1C, C_4 oxazine ring), 93.3 (1C, C_2 oxazine ring), 111.5 (2C, C_2& C_6 aromatic ring), 112.4 (1C, C_2 aromatic ring), 114.6 (1C, C_5 2-oxopyridine ring), 115.1 (2C, -C≡N), 115.2 (1C, C_3 2-oxopyridine ring), 120.3 (1C, C_2 aromatic ring with -NO_2 group), 120.4 (1C, C_4 aromatic ring), 122.6 (1C, C_5 oxazine ring), 123.5 (1C, C_4 aromatic ring with -NO_2 group), 124.4 (1C, C_3 aromatic ring), 126.8 (1C, C_1 aromatic ring), 128.1 (1C, C_1 aromatic ring), 128.5 (1C, C_3 aromatic ring), 129.4 (1C, C_5 aromatic ring), 129.7 (2C, C_2& C_6 aromatic ring), 129.9 (1C, C_5 aromatic ring with -NO_2 group), 130.3 (1C, C_2 aromatic ring), 132.2 (1C, C_4 aromatic ring), 133.6 (1C, C_1 aromatic ring with -NO_2 group), 134.7 (1C, C_3 aromatic ring), 135.4 (1C, C_6 aromatic ring with -NO_2 group), 147.7 (1C, C_4 aromatic ring-NO_2), 148.3 (1C, C_3 aromatic ring with -NO_2 group), 152.7 (1C, C_4aromatic ring), 153.8 (1C, C_6 2-oxopyridine ring), 158.2 (1C, C_6 oxazine ring), 160.7 (1C, C_6 2-oxopyridine ring), 163.7 (1C, -C(=N)-CH_3), 163.9 (1C, -CH=N), 169.4 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 664.18 [M^+]; Anal. Calcd for $C_{36}H_{24}N_8O_6$: C, 65.06; H, 3.64; N, 16.86; Found: C, 65.02; H, 3.62; N, 16.85 %.

Characterization of 1-((1-(4-(2*H*-benzo[e] [1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((3-nitrobenzylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4e

IR (λ_{max}, cm^{-1}, KBr): 3087 (>C-H stretching, aromatic ring), 3005 (>C-H stretching, -CH_3 group), 2898 (>C-H stretching, -CH_2 group), 2233, 2216 (-C≡N stretching), 1725 (>C=O stretching, cyclic amide), 1644, 1568, 1537 (>C=C<, >C=N- stretching,

aromatic ring), 1530, 1344 (-N=O stretching), 1228 (>C-H bending), 1214, 1098 (>C-O-C< stretching, cyclic ether group), 811 (1:4-substituted benzene ring), 737 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.06 (s, 3H, Ar-C(CH_3)=N-), 4.65 (s, 2H, Ar-CH_2-N<), 6.11 (s, 2H, -O-CH_2-N<), 6.73-8.50 (m, 16H, Ar-H), 9.50 (s, 1H, Ar-CH=N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.1 (1C, -CH_3), 59.4 (1C, C_4 oxazine ring), 93.3 (1C, C_2 oxazine ring), 111.8 (2C, C_2& C_6 aromatic ring), 112.4 (1C, C_2 aromatic ring), 114.9 (1C, C_5 2-oxopyridine ring), 115.1 (1C, C_3 2-oxopyridine ring), 115.4 (2C, -C≡N), 120.3 (1C, C_2 aromatic ring with -NO_2 group), 120.7 (1C, C_4 aromatic ring), 121.8 (1C, C_2 aromatic ring), 122.6 (1C, C_5 oxazine ring), 123.5 (1C, C_4 aromatic ring with -NO_2 group), 126.4 (1C, C_4 aromatic ring), 126.9 (1C, C_1 aromatic ring), 128.5 (1C, C_3 aromatic ring), 129.0 (1C, C_5 aromatic ring), 129.4 (2C, C_2& C_6 aromatic ring), 129.6 (2C, C_5 aromatic ring with -NO_2 group), 133.6 (1C, C_1 aromatic ring with -NO_2 group), 134.8 (1C, C_1 aromatic ring), 135.4 (2C, C_6 aromatic ring with -NO_2 group), 147.8 (2C, C_3 aromatic ring with -NO_2 group), 152.5 (1C, C_4 aromatic ring), 153.7 (1C, C_6 2-oxopyridine ring), 158.1 (1C, C_6 oxazine ring), 160.6 (1C, C_6 2-oxopyridine ring), 163.4 (1C, -CH=N), 163.9 (1C, -C(=N)-CH_3), 169.6 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 664.18 [M^+]; Anal. Calcd for $C_{36}H_{24}N_8O_6$: C, 65.06; H, 3.64; N, 16.86; Found: C, 65.03; H, 3.66; N, 16.87 %.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((4-nitrobenzylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4f

IR (λ_{max}, cm^{-1}, KBr): 3093 (>C-H stretching, aromatic ring), 2990 (>C-H stretching, -CH_3 group), 2889 (>C-H stretching, -CH_2 group), 2249, 2201 (-C≡N stretching), 1732 (>C=O stretching, cyclic amide), 1633, 1559, 1546 (>C=C<, >C=N- stretching, aromatic ring), 1531, 1349 (-N=O stretching), 1239 (>C-H bending), 1210, 1031 (>C-O-C< stretching, cyclic ether group), 816 (1:4-substituted benzene ring), 738 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.99 (s, 3H, Ar-C(CH_3)=N-), 4.60 (s, 2H, Ar-CH_2-N<), 6.02 (s, 2H, -O-CH_2-N<), 6.76-8.37 (m, 16H, Ar-H), 9.49 (s, 1H, Ar-CH=N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.2 (1C, -CH_3), 59.3 (1C, C_4 oxazine ring), 93.2 (1C, C_2 oxazine ring), 111.9 (2C, C_2& C_6 aromatic ring), 112.4 (1C, C_2 aromatic ring), 114.5 (1C, C_5 2-oxopyridine ring), 115.3 (2C, -C≡N), 115.6 (1C, C_3 2-oxopyridine ring), 120.4 (1C, C_2 aromatic ring with -NO_2 group), 120.7 (1C, C_4 aromatic ring), 122.4 (1C, C_5 oxazine ring), 123.6 (1C, C_4 aromatic ring with -NO_2 group), 124.2 (2C, C_3& C_5 aromatic ring), 126.8 (1C, C_1 aromatic ring), 127.9 (2C, C_2& C_6 aromatic ring), 128.4 (1C, C_3 aromatic ring), 129.3 (1C, C_5 aromatic ring), 129.5 (2C, C_2& C_6 aromatic ring), 129.9 (1C, C_5 aromatic ring with -NO_2 group), 133.4 (1C, C_1 aromatic ring with -NO_2 group), 135.4 (1C, C_6 aromatic ring with -NO_2 group), 140.0 (1C, C_1 aromatic ring), 148.2 (1C, C_3 aromatic ring with -NO_2 group), 150.4 (1C, C_4 aromatic ring-NO_2), 152.4 (1C, C_4 aromatic ring), 153.7 (1C, C_6 2-oxopyridine ring), 158.8 (1C, C_6 oxazine ring), 160.7 (1C, C_6 2-oxopyridine ring), 163.4 (1C, -CH=N), 163.8 (1C, -C(=N)-CH_3), 169.6 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 664.18 [M^+]; Anal. Calcd for $C_{36}H_{24}N_8O_6$: C, 65.06; H, 3.64; N, 16.86; Found: C, 65.04; H, 3.65; N, 16.87 %.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((2-chlorobenzylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4g

IR (λ_{max}, cm^{-1}, KBr): 3091 (>C-H stretching, aromatic ring), 2998 (>C-H stretching, -CH_3 group), 2893 (>C-H stretching, -CH_2 group), 2241, 2205 (-C≡N stretching), 1718 (>C=O stretching, cyclic amide), 1631, 1567, 1535 (>C=C<, >C=N- stretching, aromatic ring), 1230 (>C-H bending), 1210, 1097 (>C-O-C< stretching, cyclic ether group), 809 (1:4-substituted benzene ring), 830 (>C-Cl stretching), 739 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.91 (s, 3H, Ar-C(CH_3)=N-), 4.64 (s, 2H, Ar-CH_2-N<), 6.09 (s, 2H, -O-CH_2-N<), 6.77-8.19 (m, 16H, Ar-H), 9.48 (s, 1H, Ar-CH=N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.0 (1C, -CH_3), 59.5 (1C, C_4 oxazine ring), 93.8 (1C, C_2 oxazine ring), 111.5 (2C, C_2& C_6 aromatic ring), 112.6 (1C, C_2 aromatic ring), 114.9 (1C, C_5 2-oxopyridine ring), 115.3 (2C, -C≡N), 115.7 (1C, C_3 2-oxopyridine ring), 120.4 (1C, C_2 aromatic ring with -NO_2 group), 120.7 (1C, C_4 aromatic ring), 122.5 (1C, C_5 oxazine ring), 123.5 (1C, C_4 aromatic ring with -NO_2 group), 126.5 (1C, C_5 aromatic ring), 126.8 (1C, C_1 aromatic ring), 127.5 (1C, C_6 aromatic ring), 128.2 (1C, C_3 aromatic ring), 129.3 (1C, C_5 aromatic ring), 129.4 (1C, C_5 aromatic ring with -NO_2 group), 129.5 (2C, C_2& C_6 aromatic ring), 130.3 (1C, C_3 aromatic ring), 132.6 (1C, C_4 aromatic ring), 133.3 (1C, C_1

aromatic ring), 133.7 (1C, C_1 aromatic ring with -NO_2 group), 134.3 (1C, C_2 aromatic ring with -Cl), 135.3 (1C, C_6 aromatic ring with -NO_2 group), 148.2 (1C, C_3 aromatic ring with -NO_2 group), 152.5 (1C, C_4 aromatic ring), 153.8 (1C, C_6 2-oxopyridine ring), 157.6 (1C, C_6 oxazine ring), 160.4 (1C, C_6 2-oxopyridine ring), 163.5 (1C, -C(=N)-CH_3), 163.8 (1C, -CH=N), 169.5 (1C, C_4 2-oxopyridine ring).LC-MS (m/z): 653.16 [M^+]; Anal. Calcd for $C_{36}H_{24}ClN_7O_4$: C, 66.11; H, 3.70; N, 14.99; Found: C, 66.13; H, 3.71; N, 14.96 %.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((3-chlorobenzylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4h

IR (λ_{max}, cm^{-1}, KBr): 3096 (>C-H stretching, aromatic ring), 2992 (>C-H stretching, -CH_3 group), 2891 (>C-H stretching, -CH_2 group), 2239, 2201 (-C≡N stretching), 1713 (>C=O stretching, cyclic amide), 1638, 1562, 1539 (>C=C<, >C=N- stretching, aromatic ring), 1237 (>C-H bending), 1201, 1091 (>C-O-C< stretching, cyclic ether group), 815 (1:4-substituted benzene ring), 837 (>C-Cl stretching), 732 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.01 (s, 3H, Ar-C(CH_3)=N-), 4.64 (s, 2H, Ar-CH_2-N<), 6.03 (s, 2H, -O-CH_2-N<), 6.80-8.17 (m, 16H, Ar-H), 9.51 (s, 1H, Ar-CH=N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.5 (1C, -CH_3), 59.7 (1C, C_4 oxazine ring), 93.7 (1C, C_2 oxazine ring), 111.6 (2C, C_2& C_6 aromatic ring), 112.4 (1C, C_2 aromatic ring), 114.8 (1C, C_5 2-oxopyridine ring), 115.4 (2C, -C≡N), 115.6 (1C, C_3 2-oxopyridine ring), 120.3 (1C, C_2 aromatic ring with -NO_2 group), 120.7 (1C, C_4 aromatic ring), 122.4 (1C, C_5 oxazine ring), 123.6 (1C, C_4 aromatic ring with -NO_2 group), 126.6 (1C, C_1 aromatic ring), 126.9 (1C, C_2 aromatic ring), 127.5 (1C, C_6 aromatic ring), 128.5 (1C, C_3 aromatic ring), 129.3 (1C, C_5 aromatic ring), 129.6 (2C, C_2& C_6 aromatic ring), 129.9 (1C, C_5 aromatic ring with -NO_2 group), 130.3 (1C, C_5 aromatic ring), 131.4 (1C, C_4 aromatic ring), 133.4 (1C, C_1 aromatic ring with –NO_2 group), 134.6 (1C, C_3 aromatic ring with -Cl), 135.3 (1C, C_6 aromatic ring with -NO_2 group), 135.4 (1C, C_1 aromatic ring), 148.4 (1C, C_3 aromatic ring with -NO_2 group), 152.8 (1C, C_4 aromatic ring), 153.3 (1C, C_6 2-oxopyridine ring), 158.2 (1C, C_6 oxazine ring), 160.7 (1C, C_6 2-oxopyridine ring), 163.5 (1C, -C(=N)-CH_3), 163.7 (1C, -CH=N), 169.4 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 653.16 [M^+]; Anal. Calcd for $C_{36}H_{24}ClN_7O_4$: C, 66.11; H, 3.70; N, 14.99; Found: C, 66.13; H, 3.68; N, 15.02 %.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((4-chlorobenzylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4i

IR (λ_{max}, cm^{-1}, KBr): 3090 (>C-H stretching, aromatic ring), 2987 (>C-H stretching, -CH_3 group), 2895 (>C-H stretching, -CH_2 group), 2231, 2206 (-C≡N stretching), 1718 (>C=O stretching, cyclic amide), 1630, 1565, 1534 (>C=C<, >C=N- stretching, aromatic ring), 1236 (>C-H bending), 1205, 1099 (>C-O-C< stretching, cyclic ether group), 809 (1:4-substituted benzene ring), 843 (>C-Cl stretching), 729 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.05 (s, 3H, Ar-C(CH_3)=N-), 4.67 (s, 2H, Ar-CH_2-N<), 6.06 (s, 2H, -O-CH_2-N<), 6.73-8.16 (m, 16H, Ar-H), 9.48 (s, 1H, Ar-CH=N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.5 (1C, -CH_3), 59.8 (1C, C_4 oxazine ring), 93.3 (1C, C_2 oxazine ring), 111.4 (2C, C_2& C_6 aromatic ring), 112.2 (1C, C_2 aromatic ring), 114.5 (1C, C_5 2-oxopyridine ring), 115.3 (1C, C_3 2-oxopyridine ring), 115.7 (2C, -C≡N), 120.1 (1C, C_2 aromatic ring with -NO_2 group), 120.6 (1C, C_4 aromatic ring), 122.5 (1C, C_5 oxazine ring), 123.6 (1C, C_4 aromatic ring with -NO_2 group), 126.8 (1C, C_1 aromatic ring), 128.6 (1C, C_3 aromatic ring), 128.7 (2C, C_3& C_5 aromatic ring), 129.3 (1C, C_5 aromatic ring), 129.6 (2C, C_2& C_6 aromatic ring), 129.7 (1C, C_5 aromatic ring with -NO_2 group), 130.8 (2C, C_2& C_6 aromatic ring), 132.0 (1C, C_1 aromatic ring), 133.7 (1C, C_1 aromatic ring with -NO_2 group), 135.4 (1C, C_6 aromatic ring with -NO_2 group), 136.8 (1C, C_1 aromatic ring with -Cl), 147.9 (1C, C_3 aromatic ring with -NO_2 group), 152.5 (1C, C_4 aromatic ring), 153.5 (1C, C_6 2-oxopyridine ring), 157.6 (1C, C_6 oxazine ring), 160.7 (1C, C_6 2-oxopyridine ring), 163.4 (1C, -C(=N)-CH_3), 163.7 (1C, -CH=N), 170.2 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 653.16 [M^+]; Anal. Calcd for $C_{36}H_{24}ClN_7O_4$: C, 66.11; H, 3.70; N, 14.99; Found: C, 66.10; H, 3.72; N, 14.97 %.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((4-methoxybenzylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4j

IR (λ_{max}, cm^{-1}, KBr): 3097 (>C-H stretching, aromatic ring), 2990 (>C-H stretching, -CH_3 group), 2897 (>C-H stretching, -CH_2 group), 2237, 2203

(-C≡N stretching), 1714 (>C=O stretching, cyclic amide), 1633, 1561, 1536 (>C=C<, >C=N- stretching, aromatic ring), 1233 (>C-H bending), 1205, 1097 (>C-O-C< stretching, cyclic ether group), 822 (1:4-substituted benzene ring), 734 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.91 (s, 3H, Ar-C(CH_3)=N-), 3.84 (s, 3H, -OCH_3), 4.67 (s, 2H, Ar-CH_2-N<), 5.97 (s, 2H, -O-CH_2-N<), 6.76-8.19 (m, 16H, Ar-H), 9.45 (s, 1H, Ar-CH=N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.3 (1C, -CH_3), 55.4 (1C,-OCH_3), 59.8 (1C, C_4 oxazine ring), 93.3 (1C, C_2 oxazine ring), 111.5 (2C, C_2& C_6 aromatic ring), 112.4 (1C, C_2 aromatic ring), 114.4 (2C, C_3 & C_5 aromatic ring), 114.5 (1C, C_5 2-oxopyridine ring), 115.3 (2C, -C≡N), 115.6 (1C, C_3 2-oxopyridine ring), 120.3 (1C, C_4 aromatic ring), 120.4 (1C, C_2 aromatic ring with -NO_2 group), 122.6 (1C, C_5 oxazine ring), 123.7 (1C, C_4 aromatic ring with -NO_2 group), 126.3 (1C, C_1 aromatic ring), 126.9 (1C, C_1 aromatic ring), 128.2 (1C, C_3 aromatic ring), 129.1 (1C, C_5 aromatic ring), 129.4 (2C, C_2& C_6 aromatic ring), 129.6 (1C, C_5 aromatic ring with -NO_2 group), 130.4 (2C, C_2& C_6 aromatic ring), 133.3 (1C, C_1 aromatic ring with -NO_2 group), 135.6 (1C, C_6 aromatic ring with -NO_2 group), 148.2 (1C, C_3 aromatic ring with -NO_2 group), 152.4 (1C, C_4 aromatic ring), 153.2 (1C, C_6 2-oxopyridine ring), 157.7 (1C, C_6 oxazine ring), 160.4 (1C, C_6 2-oxopyridine ring), 162.7 (1C, C_4 aromatic ring with -OCH_3 group), 163.4 (1C, -CH=N), 163.8 (1C, -C(=N)-CH_3), 169.7 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 649.21 [M^+]; Anal. Calcd for $C_{37}H_{27}N_7O_5$: C, 68.41; H, 4.19; N, 15.09; Found: C, 68.40; H, 4.17; N, 15.06 %.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-4-(3-nitrophenyl)-2-oxo-6-((3,4,5-trimethoxybenzylidene)amino)-1,2-dihydropyridine-3,5-dicarbonitrile, 4k

IR (λ_{max}, cm^{-1}, KBr): 3105 (C-H stretching, aromatic ring), 3009 (C-H stretching, -CH_3 group), 2860 (C-H stretching, -CH_2 group), 2255, 2218 (C≡N stretching), 1701 (C=O stretching, cyclic amide), 1625, 1598, 1557 (C=C, C=N, N=O stretching, aromatic ring), 1285 (C-H bending), 1118, 1085 (C-O-C stretching, cyclic ether group), 810 (1:4-substituted benzene ring), 775 (1:4-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.05 (s, 3H, Ar-C(CH_3)=N-),3.70 (s, 3H, -O-CH_3 C_4 aromatic ring) 3.85 (s, 6H, -O-CH_3 C_3& C_5 aromatic ring), 4.65 (s, 2H, Ar-CH_2-N<), 6.05 (s, 2H, -O-CH_2-N<), 6.60-7.80 (m, 14H, Ar-H), 9.35 (s, 1H, Ar-CH=N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.6 (1C, -CH_3), 56.4 (2C, C_3& C_5 aromatic ring with -OCH_3), 59.8 (1C, C_4 oxazine ring), 61.0 (1C, -OCH_3), 93.2 (1C, C_2 oxazine ring), 104.3 (2C, C_2& C_6 aromatic ring), 111.6 (2C, C_2& C_6 aromatic ring), 112.2 (1C, C_2 aromatic ring), 114.6 (1C, C_5 2-oxopyridine ring), 115.4 (2C, -C≡N), 115.6 (1C, C_3 2-oxopyridine ring), 120.3 (1C, C_2 aromatic ring with -NO_2 group), 120.6 (1C, C_4 aromatic ring), 122.4 (1C, C_5 oxazine ring), 123.5 (1C, C_4 aromatic ring with -NO_2 group), 126.9 (1C, C_1 aromatic ring), 128.2 (1C, C_3 aromatic ring), 128.4 (1C, C_1 aromatic ring), 129.2 (2C, C_2& C_6 aromatic ring), 129.5 (1C, C_5 aromatic ring), 129.6 (1C, C_5 aromatic ring with –NO_2 group), 133.3 (1C, C_1 aromatic ring with -NO_2 group), 135.4 (1C, C_6 aromatic ring with -NO_2 group), 141.7 (1C, C_4 aromatic ring with -OCH_3 group), 148.4 (1C, C_3 aromatic ring with -NO_2 group), 152.5 (1C, C_4 aromatic ring), 153.1 (2C, C_3& C_5 aromatic ring with -OCH_3), 153.4 (1C, C_6 2-oxopyridine ring), 157.5 (1C, C_6 oxazine ring), 160.2 (1C, C_6 2-oxopyridine ring), 163.4 (1C, -C(=N)-CH_3), 163.5 (1C, -CH=N), 169.8 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 709.23 [M^+]; Anal. Calcd for $C_{39}H_{31}N_7O_7$: C, 66.00; H, 4.40; N, 13.82; Found: C, 66.02; H, 4.41; N, 13.85 %.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((4-hydroxy-3-methoxybenzylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4l

IR (λ_{max}, cm^{-1}, KBr): 3396 (-O-H stretching, Ar-OH), 3106 (>C-H stretching, aromatic ring), 3015 (>C-H stretching, -CH_3 group), 2898 (>C-H stretching, -CH_2 group), 2825 (>C-H, stretching in C-O-CH_3), 2231, 2208(-C≡N stretching), 1714 (>C=O stretching, cyclic amide), 1647, 1569, 1547 (>C=C<, >C=N- stretching, aromatic ring), 1237 (>C-H bending), 1210, 1099 (>C-O-C< stretching, cyclic ether group), 829 (1:4-substituted benzene ring), 742 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.98 (s, 3H, Ar-C(CH_3)=N-), 3.86 (s, 3H, -OCH_3), 4.65 (s, 2H, Ar-CH_2-N<), 5.94 (s, 2H, -O-CH_2-N<), 6.72-8.15 (m, 15H, Ar-H), 9.50 (s, 1H, Ar-CH=N-), 9.58 (s, 1H, -OH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.1 (1C, -CH_3), 56.4 (1C,-OCH_3), 59.3 (1C, C_4 oxazine ring), 93.4 (1C, C_2 oxazine ring), 111.6 (2C, C_2& C_6 aromatic ring), 112.0 (1C, C_2 aromatic ring), 112.4 (1C, C_2 aromatic ring), 114.9 (1C, C_5 2-oxopyridine ring), 115.3 (2C, -C≡N), 115.6 (1C, C_3 2-

oxopyridine ring), 117.3 (1C, C_5 aromatic ring), 120.4 (1C, C_2 aromatic ring with -NO_2 group), 120.7 (1C, C_4 aromatic ring), 122.4 (1C, C_5 oxazine ring), 123.1 (1C, C_6 aromatic ring), 123.6 (1C, C_4 aromatic ring with -NO_2 group), 126.8 (1C, C_1 aromatic ring), 127.5 (1C, C_1 aromatic ring), 128.5 (1C, C_3 aromatic ring), 129.3 (1C, C_5 aromatic ring), 129.6 (2C, C_2& C_6 aromatic ring), 129.8 (1C, C_5 aromatic ring with -NO_2 group), 133.6 (1C, C_1 aromatic ring with -NO_2 group), 135.3 (1C, C_6 aromatic ring with -NO_2 group), 148.2 (1C, C_3 aromatic ring with -NO_2 group), 149.5 (1C, C_3 aromatic ring with -OCH_3), 151.2 (1C, C_4 aromatic ring with -OH), 152.7 (1C, C_4 aromatic ring), 153.9 (1C, C_6 2-oxopyridine ring), 157.7 (1C, C_6 oxazine ring), 160.4 (1C, C_6 2-oxopyridine ring), 163.6 (1C, -C(=N)-CH_3), 163.3 (1C, -CH=N), 170.2 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 665.20 [M^+]; Anal. Calcd for $C_{37}H_{27}N_7O_6$: C, 66.76; H, 4.09; N, 14.73; Found: C, 66.75; H, 4.11; N, 14.75 %.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((4-(dimethylamino)benzylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4m

IR (λ_{max}, cm^{-1}, KBr): 3087 (>C-H stretching, aromatic ring), 2989 (>C-H stretching, -CH_3 group), 2887 (>C-H stretching, -CH_2 group), 2230, 2206 (-C≡N stretching), 1718 (>C=O stretching, cyclic amide), 1658, 1566, 1543 (>C=C<, >C=N- stretching, aromatic ring), 1347 (>C-N< stretching, tertiary amine), 1231 (>C-H bending), 1221,1098 (>C-O-C< stretching, cyclic ether group), 823 (1:4-substituted benzene ring), 746 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.97 (s, 3H, Ar-C(CH_3)=N-), 3.07 (s, 6H, Ar-N(CH_3)$_2$) 4.64 (s, 2H, Ar-CH_2-N<), 5.99 (s, 2H, -O-CH_2-N<), 6.72-8.19 (m, 16H, Ar-H), 9.47 (s, 1H, Ar-CH=N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.5 (1C, -CH_3), 41.5 (2C, -N,N(CH_3)$_2$), 59.7 (1C, C_4 oxazine ring), 93.4 (1C, C_2 oxazine ring), 111.9 (2C, C_2& C_6 aromatic ring), 112.2 (2C, C_3& C_5 aromatic ring), 112.5 (1C, C_2 aromatic ring), 114.6 (1C, C_5 2-oxopyridine ring), 115.3 (2C, -C≡N), 115.6 (1C, C_3 2-oxopyridine ring), 120.3 (1C, C_2 aromatic ring with -NO_2 group), 120.7 (1C, C_4 aromatic ring), 122.4 (1C, C_5 oxazine ring), 123.2 (1C, C_1 aromatic ring), 123.6 (1C, C_4 aromatic ring with -NO_2 group), 126.8 (1C, C_1 aromatic ring), 128.2 (1C, C_3 aromatic ring), 128.7 (2C, C_2& C_6 aromatic ring), 129.0 (1C, C_5 aromatic ring), 129.4 (2C, C_2& C_6 aromatic ring), 129.8 (1C, C_5 aromatic ring with -NO_2 group), 133.7 (1C, C_1 aromatic ring with -NO_2 group), 135.1 (1C, C_6 aromatic ring with -NO_2 group), 148.3 (1C, C_3 aromatic ring with -NO_2 group), 152.7 (1C, C_4 aromatic ring), 153.2 (1C, C_4 aromatic ring with -N,N(CH_3)$_2$), 153.8 (1C, C_6 2-oxopyridine ring), 157.4 (1C, C_6 oxazine ring), 160.2 (1C, C_6 2-oxopyridine ring), 163.6 (1C, -C(=N)-CH_3), 163.8 (1C, -CH=N), 169.7 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 662.24 [M^+]; Anal. Calcd for $C_{38}H_{30}N_8O_4$: C, 68.87; H, 4.56; N, 16.91; Found: C, 68.88; H, 4.54; N, 16.93 %.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((4-bromobenzylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4n

IR (λ_{max}, cm^{-1}, KBr): 3102 (>C-H stretching, aromatic ring), 2987 (>C-H stretching, -CH_3 group), 2894 (>C-H stretching, -CH_2 group), 2237, 2211 (-C≡N stretching), 1724 (>C=O stretching, cyclic amide), 1637, 1552, 1543 (>C=C<, >C=N- stretching, aromatic ring), 1231 (>C-H bending), 1207, 1105 (>C-O-C< stretching, cyclic ether group), 819 (1:4-substituted benzene ring), 725 (1:2-substituted benzene ring), 576 (>C-Br stretching). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.93 (s, 3H, Ar-C(CH_3)=N-), 4.57 (s, 2H, Ar-CH_2-N<), 5.95 (s, 2H, -O-CH_2-N<), 6.79-8.17 (m, 16H, Ar-H), 9.53 (s, 1H, Ar-CH=N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.1 (1C, -CH_3), 59.4 (1C, C_4 oxazine ring), 93.3 (1C, C_2 oxazine ring), 111.4 (2C, C_2& C_6 aromatic ring), 112.5 (1C, C_2 aromatic ring), 114.9 (1C, C_5 2-oxopyridine ring), 115.4 (2C, -C≡N), 115.7 (1C, C_3 2-oxopyridine ring), 120.3 (1C, C_2 aromatic ring with -NO_2 group), 120.7 (1C, C_4 aromatic ring), 122.4 (1C, C_5 oxazine ring), 123.5 (1C, C_4 aromatic ring with -NO_2 group), 125.6 (1C, C_1 aromatic ring with -Br), 126.8 (1C, C_1 aromatic ring), 128.1 (2C, C_2& C_6 aromatic ring), 128.6 (1C, C_3 aromatic ring), 129.3 (1C, C_5 aromatic ring), 129.7 (2C, C_2& C_6 aromatic ring), 129.9 (1C, C_5 aromatic ring with -NO_2 group), 131.8 (2C, C_2& C_6 aromatic ring), 132.5 (1C, C_1 aromatic ring), 133.4 (1C, C_1 aromatic ring with -NO_2 group), 135.6 (1C, C_6 aromatic ring with -NO_2 group), 148.3 (1C, C_3 aromatic ring with -NO_2 group), 152.6 (1C, C_4 aromatic ring), 153.5 (1C, C_6 2-oxopyridine ring), 157.7 (1C, C_6 oxazine ring), 160.3 (1C, C_6 2-oxopyridine ring), 163.5 (1C, -CH=N), 163.8 (1C, -C(=N)-CH_3), 169.4 (1C, C_4 2-oxopyridine ring).LC-MS (m/z): 697.11 [M^+]; Anal. Calcd for $C_{36}H_{24}BrN_7O_4$: C, 61.90; H, 3.46; N, 14.04; Found: C, 61.92; H, 3.45; N, 14.06 %.

Characterization of 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((4-flourobenzylidene)amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile, 4o

IR (λ_{max}, cm^{-1}, KBr): 3096 (>C-H stretching, aromatic ring), 2992 (>C-H stretching, -CH_3 group), 2891 (>C-H stretching, -CH_2 group), 2239, 2201(-C≡N stretching), 1713 (>C=O stretching, cyclic amide), 1638, 1562, 1539 (>C=C<, >C=N- stretching, aromatic ring), 1237 (>C-H bending), 1201, 1091 (>C-O-C< stretching, cyclic ether group), 1067 (>C-F stretching), 806 (1:4-substituted benzene ring), 732 (1:2-substituted benzene ring). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.97 (s, 3H, Ar-C(CH_3)=N-), 4.63 (s, 2H, Ar-CH_2-N<), 6.01 (s, 2H, -O-CH_2-N<), 6.80-8.18 (m, 16H, Ar-H), 9.43 (s, 1H, Ar-CH=N-). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 17.3 (1C, -CH_3), 59.5 (1C, C_4 oxazine ring), 93.7 (1C, C_2 oxazine ring), 111.9 (2C, C_2& C_6 aromatic ring), 112.5 (1C, C_2 aromatic ring), 114.6 (1C, C_5 2-oxopyridine ring), 115.3 (2C, C_3& C_5 aromatic ring), 115.4 (2C, -C≡N), 115.7 (1C, C_3 2-oxopyridine ring), 120.3 (1C, C_2 aromatic ring with -NO_2 group), 120.8 (1C, C_4 aromatic ring), 122.3 (1C, C_5 oxazine ring), 123.5 (1C, C_4 aromatic ring with -NO_2 group), 126.8 (1C, C_1 aromatic ring), 128.6 (1C, C_3 aromatic ring), 129.1 (1C, C_1 aromatic ring), 129.4 (1C, C_5 aromatic ring), 129.5 (2C, C_2& C_6 aromatic ring), 129.9 (1C, C_5 aromatic ring with -NO_2 group), 130.5 (2C, C_2& C_6 aromatic ring), 133.4 (1C, C_1 aromatic ring with -NO_2 group), 135.3 (1C, C_6 aromatic ring with -NO_2 group), 148.0 (1C, C_3 aromatic ring with -NO_2 group), 152.2 (1C, C_4 aromatic ring), 153.5 (1C, C_6 2-oxopyridine ring), 158.0 (1C, C_6 oxazine ring), 160.4 (1C, C_6 2-oxopyridine ring), 163.4 (1C, -CH=N), 163.6 (1C, -C(=N)-CH_3), 165.6 (1C, C_4 aromatic ring with -F), 170.1 (1C, C_4 2-oxopyridine ring). LC-MS (m/z): 637.19 [M^+]; Anal. Calcd for $C_{36}H_{24}FN_7O_4$: C, 67.81; H, 3.79; N, 15.38; Found: C, 67.83; H, 3.77; N, 15.36 %.

Conclusion

Synthesis of the 1-((1-(4-(2*H*-benzo[e][1,3]oxazin-3(4*H*)-yl)phenyl)ethylidene)amino)-6-((arylidene) amino)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles was achieved in good yield. The obtained results confirm that the nature of the substituents and substitution pattern on the oxazine clubbed pyridine heterocycles may have considerable impact on biological activities of the target products. Out of 15 reported derivatives, **4b** (-2-OH), **4f** (-4-NO_2), **4h** (-3-Cl), **4j** (-4-OCH_3), **4l** (-4-OH-3-OCH_3) and **4m** (-N,N'-$(CH_3)_2$) exhibited good *in vitro* antimicrobial activity. From the antimicrobial outcomes, it can be concluding that compounds containing electron-withdrawing group showed good activity against bacterial strains. On the other hand, compounds containing electron-donating group showed good activity against fungal strains. The results show that further research on biological profiles of these compounds is worth pursuing.

Supplementary Information

Supplementary information is available in the website http://nopr.niscair.res.in/handle/123456789/60.

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