© 2017 IJSRST | Volume 3 | Issue 7 | Print ISSN: 2395-6011 | Online ISSN: 2395-602X
Themed Section: Science and Technology

A One-Pot Synthesis of 1,4-dihydropyrimido[1,2-a] benzimidazoles and their Antimicrobial Activity

Kalpesh V. Vilapara[1], Rajendra M. Jadav*[2], Sagar P. Gami[2]
[1]Department of Chemistry, Saurashtra University, Rajkot, Gujarat, India
[2]Department of chemistry, Bhavan'ssheth R. A. college of science, Ahmedabad, Gujarat, India

ABSTRACT

A one-pot synthesis of 1,4-dihydropyrimido[1,2-a]benzimidazole were carried out by Biginelli like cyclocondensation of aromatic aldehydes and acetoacetic acid derivatives with 2-amino benzimidazole containing a guanidine fragment. The newly synthesized compounds were characterized by IR, NMR and Mass spectroscopy.

Keywords: Pyrimidine, Benzimidazole, Cyclocondensation, Antimicrobial

I. INTRODUCTION

Synthetic studies of fused pyrimidine have been reported extensively because of their structural diversity and association with a wide spectrum of biological activity. It has been observed over the years that poly substituted pyrimido[1,2-a]benzimidazolespossess a wide spectrum of biological activities like Antimicrobial[1,2],antimalarial[3], antiproliferative[4], antiInflammatory[5,6], antitumor[7], antimycotic[8], anti asthmati[9] and diuretie[10,11].Several procedures for the synthesis ofpyrimido[1,2-a]benzimidazole have been studied. Over all the reported synthesis more efficient synthesis is Biginelli like three-component cyclocondensation reaction of an aromatic aldehydes, acetoacetic acid derivatives and 2-aminobenzimidazole affording the pyrimido[1,2-*a*]benzimidazoles[12-16]. Another synthetic path for pyrimido[1,2-*a*]benzimidazoles from aminobenzimidazolewith α, β-unsaturated nitriles,especiallyarylidenemalononitriles and arylidenecyanoacetates have been reported[17,18].

II. RESULT AND DISCUSSION

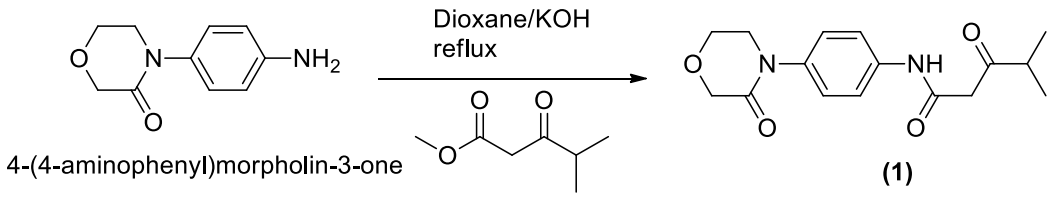
The biological importance of 1,4-dihydropyrimido[1,2-*a*]benzimidazoles is well documented. Over the years, various substituted derivatives of these heterocycles have shown utility against a range of biological targets.

One of the synthetic pathways to 1,4-dihydropyrimido[1,2-*a*]benzimidazoles by treatment of 2-amino benzimidazole with aldehydes and 1,3-diketones. The cyclocondensations were achieved by heating of the starting materials with reflux conditions using dimethylformamide (DMF) as solvent.

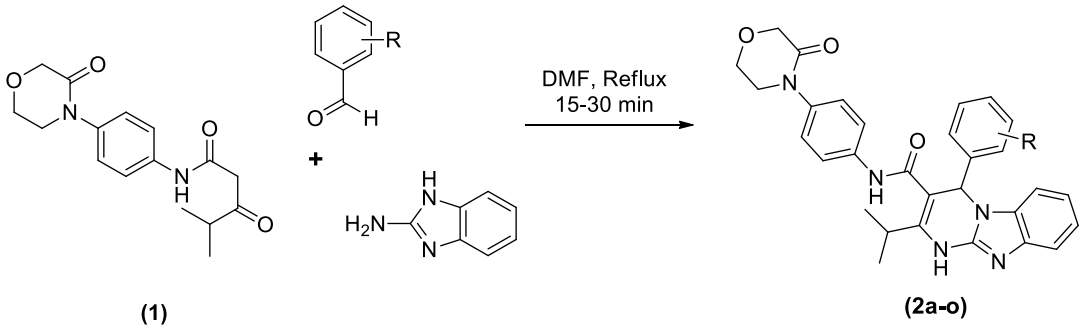
Recognizing these facts, we have synthesised new series of 1,4-dihydropyrimido[1,2-a]benzimidazoles containing an acetoacetamide fragment.The reaction of various aldehydes with 2-aminobenimidazole and INT-I trace amount of DMF at reflux affords substitutedbenzimidazolopyrimidines**(2a-o)(table-1)**.
4-methyl-3-oxo-N-(4-(3-oxomorpholino)phenyl)pentanamide (**1**) was synthesized by refluxing methyl 4-methyl-3-

oxopentanoate and 4-(4-aminophenyl)morpholin-3-one with potassium hydroxide in dioxane.

The structures of all the newly synthesized compounds were elucidated by FT-IR, mass spectra, ^{1}H NMR and elemental analyses. The newly synthesized compounds were subjected to antimicrobial activity**(table 2)**.



Scheme-1 Synthesis of INT-I



Scheme-2 Synthesis of 1,4-dihydroprimido[1,2-*a*]benzimidazole

Table 1. Synthesis of substituted benzimidazolopyrimidine

Entry	R	Time, min	M.W.	Yield %	mp°C
2a	H	25	507	71	271
2b	4-OCH_3	18	537	69	264
2c	4-CH_3	24	521	73	248
2d	4-$N(CH_3)_2$	20	550	76	234
2e	2,5-di-OCH_3	22	567	72	240
2f	4-OH	24	523	66	227
2g	4-Cl	18	542	74	252
2h	4-Br	15	586	81	284
2i	4-F	20	525	77	245
2j	3-Br	25	586	83	274
2k	2-Cl	21	542	67	198
2l	2-Br	24	586	69	228
2m	4-CN	18	532	86	260
2n	4-NO_2	17	552	89	279

2o	2-NO_2	20	552	84	251

Table 2. Antimicrobial Sensitivity Assay

Compound	MIC(μg/mL)					
	Antibacterial activity				Antifungal activity	
	E.coli (MTCC443)	S. typhi (MTCC98)	B. subtillis (MTCC441)	S.aureus (MTCC96)	A. niger (MTCC282)	A.clavatus (MTCC1323)
2a	**200**	500	**100**	500	500	1000
2b	**100**	**200**	500	250	**100**	**100**
2c	250	500	250	500	500	500
2d	**200**	**200**	**100**	500	>1000	1000
2e	250	500	500	500	1000	500
2f	500	**100**	250	**100**	**100**	250
2g	**100**	**100**	**100**	250	500	>1000
2h	500	250	500	500	1000	1000
2i	500	250	500	500	500	>1000
2j	250	250	500	**100**	>1000	500
2k	**100**	500	**100**	**50**	**100**	**100**
2l	500	250	500	250	1000	500
2m	250	**100**	**100**	500	>1000	1000
2n	**100**	**100**	250	**100**	**200**	**100**
2o	250	**100**	250	500	500	500
Gentamicin	0.05	1	0.25	0.5	-	-
Ampicillin	100	100	250	100	-	-
Chloramphenicol	50	50	50	50	-	-
Ciprofloxacin	25	25	50	50	-	-
Norfloxacin	10	10	10	10	-	-
Nystatin	-	-	-	-	100	100
Griseofulvin	-	-	-	-	100	100

III. EXPERIMENTAL SECTION

All research chemicals were purchased from Sigma-Aldrich Chemicals and used as received. Reactions were monitored by thin layer chromatography (TLC) on pre-coated silica gel GF254 plates (E-Merck Co) by using appropriate solvent systems. Melting points were determined in open capillaries and are uncorrected. Infrared (IR) spectra (KBr pellets) were recorded on a Shimadzu-FTIR-8400 spectrophotometer over frequencies ranging from 4000-400 cm-1. The NMR Spectra (1HNMR &13C NMR) were recorded on a BrukerAvance-III Spectrospin 400 MHz spectrometer using CDCl3 as solvents and TMS as an internal standard. Mass spectra were recorded on a Shimadzu GC-MS-QP-2010 spectrometer by using Electron Impact (EI) (0.7 kV) ionization source. The ion source temperature was 220 oC and interface temperature was 240 °C.

Synthesis of 4-methyl-N-(4-morpholinophenyl)-3-oxopentanamide (1)

A mixture 4-(4-aminophenyl)morpholin-3-one (10 mmol), methyl 4-methyl-

3-oxopentanoate (10 mmol) and catalytic amount of sodium or potassium hydroxide lie (10 %) in 1,4-dioxane (50ml) was refluxed at 110 oC for 12-15 h. The reaction was monitored by TLC. After completion of reaction, the crude material was poured in to cold dilute hydrochloric acid and filtered the separated solid was with n-hexane.

General Synthesis of Imidazolopyrimidine (2a-o)

A mixture of the 2-aminobenzimidazole (0.01 mol), 4-methyl-3-oxo-N-(4-(3-oxomorpholino)phenyl)pentanamide (0.01 mol) and an appropriate aromatic aldehyde (0.01 mol) was refluxed in 0.4 mL of DMF for 15-25 min. After cooling, methanol (~10 mL) was added. The reaction mixture was allowed to stand overnight and then filtered to give the solid imidazolopyrimidine products 2a to 2o, which were crystallized from ethanol and subsequently dried in air.

IV. SPECTRAL DATA

2-isopropyl-*N*-(4-(3-oxomorpholino)phenyl)-4-phenyl-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2a): Off white solid; mp 271 °C; R_f 0.47 (4:6–EtOAc-hexane);IR (KBr): 3319, 3234, 3057, 2974, 1660, 1595, 1566, 1512, 1452, 1400, 1311, 1282, 1247, 1122, 1076, 1004, 922, 839, 738, 694 cm^{-1};^{1}H NMR (400 MHz, DMSO-d_6): ^{1}H NMR: δ 10.10 (s, 1H, -NH amide), 10.00 (s, 1H, -NH, pyrimidine ring), 7.56 (d, *J*= 8.0 Hz, 2H, Ar-H), 7.34-7.19 (m, 9H, Ar-H), 7.05-7.00 (m, 2H, Ar-H), 6.90 (t, 1H, Ar-H), 6.61 (s, 1H, -CH pyrimidine ring), 4.18 (s, 2H, -CH_2- in morpholinone ring near ketone), 3.95 (t, 2H, -CH_2- in morpholinone ring), 3.67 (t, 2H, -CH_2- in morpholinone ring), 3.34-3.27 (m, 1H, ipr-CH), 1.30 (d, *J*= 6.8 Hz, 3H, -$(CH_3)_2$), 1.21 (d, *J*= 6.8 Hz, 3H, -$(CH_3)_2$) ^{13}C NMR (400 MHz, DMSO-d_6): 165.95, 165.20, 147.13, 143.49, 142.53, 140.64, 137.45, 136.82, 131.57, 128.80, 128.08, 126.64, 125.90, 121.63, 119.82, 119.59, 116.31, 109.39, 103.30, 67.75, 63.51, 57.50, 49.12, 28.90, 19.78, 19.52; MS (*m/z*): 507 (M^+);Elemental analysis: Calcd. for $C_{30}H_{29}N_5O_3$: C, 70.99; H, 5.76; N, 13.80; Found: C, 71.24; H, 5.58; N, 13.68.

2-isopropyl-4-(4-methoxyphenyl)-*N*-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2b): Off white solid; mp264 °C; R_f 0.52 (4:6–EtOAc-hexane);IR (KBr): 3306, 3053, 2970, 1666, 1560, 1523, 1456, 1251, 1180, 1126, 1072, 1024, 842, 736, 678, 569 cm^{-1};MS (*m/z*): 537 (M^+);Elemental analysis: Calcd. for $C_{31}H_{31}N_5O_4$: C, 69.26; H, 5.81; N, 13.03; Found: C, 69.35; H, 5.69; N, 13.31.

2-isopropyl-*N*-(4-(3-oxomorpholino)phenyl)-4-(*p*-tolyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2c): Off white solid; mp248 °C; R_f 0.56 (4:6–EtOAc-hexane); IR (KBr): 3300, 3167, 3053, 2968, 1656, 1565, 1564, 1512, 1456, 1342, 1311, 1282, 1255, 1224, 1128, 1074, 898, 835, 738, 678, 513 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.07 (s, 1H, -NH amide), 9.96 (s, 1H, -NH, pyrimidine ring), 7.57 (d, *J*= 8.0 Hz, 2H, Ar-H), 7.33-7.27 (m, 4H, Ar-H), 7.14 (d, *J*= 7.6 Hz, 2H, Ar-H), 7.08 (d, *J*= 7.6 Hz, 2H, Ar-H), 7.04-6.99 (m, 2H, Ar-H), 6.89 (t, 1H, Ar-H), 6.57 (s, 1H, -CH- pyrimidine ring), 4.18 (s, 2H, -CH_2- in morpholinone ring near ketone), 3.95 (t, 2H, -CH_2- in morpholinone ring), 3.68 (t, 2H, -CH_2- in morpholinone ring), 3.34-3.27 (m, 1H, ipr-CH), 2.19 (s, 3H, -CH_3), 1.29 (d, *J*= 6.8 Hz, 3H, -$(CH_3)_2$), 1.20 (d, *J*= 6.4 Hz, 3H, -$(CH_3)_2$); ^{13}C NMR (400 MHz, DMSO-d_6): 165.93, 165.19, 147.09, 143.35, 142.52, 137.73, 137.31, 136.78, 131.58, 129.33, 126.53, 125.87, 121.55, 119.75, 119.52, 116.24, 109.40, 103.38, 67.73, 63.50, 57.23, 49.11, 28.85, 20.65, 19.75, 19.52;MS (*m/z*): 521 (M^+); Elemental analysis: Calcd. for $C_{31}H_{31}N_5O_3$: C, 71.38; H, 5.99; N, 13.43; Found: C, 70.51; H, 6.12; N, 13.62.

4-(4-(dimethylamino)phenyl)-2-isopropyl-*N*-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-

carboxamide (2d): Off white solid; mp234 °C; R_f 0.52 (4:6–EtOAc-hexane); IR (KBr): 3360, 3205, 2958, 2868, 1710, 1660, 1629, 1546, 1512, 1460, 1348, 1315, 1232, 1203, 1126, 997, 922, 817, 736, 533 cm^{-1};MS (*m/z*): 550 (M^+);Elemental analysis: Calcd. for $C_{32}H_{34}N_6O_3$: C, 69.80; H, 6.22; N, 15.26; Found: C, 69.72; H, 6.39; N, 15.08.

4-(2,5-dimethoxyphenyl)-2-isopropyl-*N*-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2e): Off white solid; mp240 °C; R_f 0.49 (4:6–EtOAc-hexane);IR (KBr): 3341, 3267, 3042, 2972, 1664, 1586, 1552, 1471, 1411, 1313, 1248, 1161, 1081, 1012, 923, 848, 750, 679, 523 cm^{-1}; MS (*m/z*): 567 (M^+); Elemental analysis: Calcd. for $C_{32}H_{33}N_5O_5$: C, 67.71; H, 5.86; N, 12.34; Found: C, 67.86; H, 5.66; N, 12.52.

4-(4-hydroxyphenyl)-2-isopropyl-*N*-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2f): Off white solid; mp227 °C; R_f 0.47 (4:6–EtOAc-hexane);IR (KBr): 3406, 3217, 2966, 2872, 1666, 1633, 1599, 1564, 1512, 1458, 1408, 1342, 1278, 1234, 1128, 1001, 922, 829, 744, 686, 653, 547, 503 cm^{-1};MS (*m/z*): 523 (M^+);Elemental analysis: Calcd. for $C_{30}H_{29}N_5O_4$: C, 68.82; H, 5.58; N, 13.38; Found: C, 68.59; H, 5.74; N, 13.10.

4-(4-chlorophenyl)-2-isopropyl-N-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carboxamide (2g): White solid; mp252 °C; R_f 0.54 (4:6–EtOAc-hexane);IR (KBr): 3296, 3174, 3051, 2970, 1654, 1620, 1595, 1564, 1512, 1462, 1344, 1313, 1286, 1251, 1128, 1074, 997, 833, 740, 675 cm^{-1};MS (*m/z*): 542 (M^+);Elemental analysis: Calcd. for $C_{30}H_{28}ClN_5O_3$: C, 66.48; H, 5.21; N, 12.92; Found: C, 66.72; H, 5.48; N, 13.06.

4-(4-bromophenyl)-2-isopropyl-*N*-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2h): Off white solid; mp284 °C; R_f 0.56 (4:6–EtOAc-hexane);IR (KBr): 3294, 3053, 2970, 2870, 1708, 1654, 1597, 1564, 1512, 1460, 1313, 1284, 1126, 1074, 1004, 922, 831, 740, 675 cm^{-1};^{1}H NMR (400 MHz, DMSO-d_6):δ 10.09 (s, 1H, -NH amide), 10.02 (s, 1H, -NH, pyrimidine ring), 7.56 (d, *J*= 6.0 Hz, 2H, Ar-H), 7.49 (s, 3H, Ar-H), 7.29 (s, 2H, Ar-H), 7.20 (d, *J*= 6.2 Hz, 2H, Ar-H), 6.92 (d, *J*= 6.8, 1H, Ar-H), 6.59 (s, 1H, -CH- pyrimidine ring), 4.18 (s, 2H, $-CH_2-$ in morpholinone ring near ketone), 3.95 (s, 2H, $-CH_2-$ in morpholinone ring), 3.86 (t, 2H, $-CH_2-$ in morpholinone ring), 3.27-3.244 (m, 1H, ipr-CH), 1.94 (d, *J*= 6.2 Hz, 3H, $-(CH_3)_2$), 1.25 (d, *J*= 6.4 Hz, 3H, $-(CH_3)_2$) ^{13}C NMR (400 MHz, DMSO-d_6): 165.93, 165.08, 148.92, 142.46, 140.02, 137.35, 136.93, 131.74, 128.77, 126.06, 125.90, 121.63, 119.82, 118.45, 116.34, 109.30, 102.92, 67.74, 63.51, 56.83, 49.10, 29.05, 19.69, 19.50;MS (*m/z*): 586 (M^+);Elemental analysis: Calcd. for $C_{30}H_{28}BrN_5O_3$: C, 61.44; H, 4.81; N, 11.94; Found: C, 61.24; H, 4.98; N, 12.21.

4-(4-fluorophenyl)-2-isopropyl-*N*-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2i): White solid; mp245 °C; R_f 0.52 (4:6–EtOAc-hexane);IR (KBr): 3304, 3163, 3055, 2972, 1654, 1618, 1597, 1564, 1512, 1460, 1313, 1286, 1257, 1226, 1014, 922, 898, 792, 738, 680, 615, 555 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6):δ 10.10 (s, 1H, -NH amide), 10.02 (s, 1H, -NH, pyrimidine ring), 7.57 (d, *J*= 8.4 Hz, 2H, Ar-H), 7.35-7.29 (m, 5H, Ar-H), 7.13 (t, 2H, Ar-H), 7.05 (t, 2H, Ar-H), 6.91 (t, 1H, Ar-H), 6.63 (s, 1H, -CH- pyrimidine ring), 4.19 (s, 2H, $-CH_2-$ in morpholinone ring near ketone), 3.95 (t, 2H, $-CH_2-$ in morpholinone ring), 3.68 (t, 2H, $-CH_2-$ in morpholinone ring), 3.32-3.25 (m, 1H, ipr-CH), 1.31 (d, *J*= 6.8 Hz, 3H, $-(CH_3)_2$), 1.22 (d, *J*= 6.4 Hz, 3H, $-(CH_3)_2$) ^{13}C NMR (400 MHz, DMSO-d_6): 165.18, 160.45, 147.02, 143.39, 142.52, 137.39, 136.88, 131.48, 128.82, 128.74, 125.91, 121.71, 119.86, 116.35, 115.76, 115.54, 109.40, 103.25, 67.75, 63.51, 56.76, 49.13, 29.01, 19.74,

19.53;MS (*m/z*): 525 (M^+);Elemental analysis: Calcd. for $C_{30}H_{28}FN_5O_3$: C, 68.56; H, 5.37; N, 13.33; Found: C, 68.73; H, 5.20; N, 13.54.

4-(3-bromophenyl)-2-isopropyl-*N*-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2j): Off white solid; mp274 °C; R_f 0.55(4:6–EtOAc-hexane);IR (KBr): 3288, 3174, 3063, 2970, 1664, 1611, 1579, 1559, 1523, 1472, 1325, 1275, 1246, 1036, 952, 835, 767, 663, 564 cm^{-1};MS (*m/z*): 586 (M^+);Elemental analysis: Calcd. for $C_{30}H_{28}BrN_5O_3$: C, 61.44; H, 4.81; N, 11.94; Found: C, 61.19; H, 4.68; N, 11.76.

4-(2-chlorophenyl)-2-isopropyl-*N*-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2k):White solid; mp 198 °C; R_f 0.51 (4:6–EtOAc-hexane);IR (KBr): 3284, 3048, 2974, 2868, 1668, 1589, 1557, 1468, 1317, 1291, 1138, 1057, 1012, 931, 849, 751, 659, 537 cm^{-1}; MS (*m/z*): 542 (M^+); Elemental analysis: Calcd. for $C_{30}H_{28}ClN_5O_3$: C, 66.48; H, 5.21; N, 12.92; Found: C, 66.62; H, 5.47; N, 12.69.

4-(2-bromophenyl)-2-isopropyl-*N*-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2l):White solid; mp 228 °C; R_f 0.47 (4:6–EtOAc-hexane);IR (KBr): 3287, 3178, 3034, 2976, 1668, 1579, 1551, 1507, 1462, 1368, 1316, 1275, 1219, 1163, 1087, 869, 842, 751, 668, 542 cm^{-1}; MS (*m/z*): 586 (M^+); Elemental analysis: Calcd. for $C_{30}H_{28}BrN_5O_3$: C, 65.34; H, 5.08; N, 14.48; Found: C, 65.52; H, 4.83; N, 14.21.

4-(4-cyanophenyl)-2-isopropyl-*N*-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2m):Off White solid; mp 260 °C; R_f 0.53 (4:6–EtOAc-hexane);IR (KBr): 3325, 3254, 3061, 2966, 1672, 1596, 1525, 1485, 1408, 1315, 1259, 1152, 1074, 1030, 916, 862, 739, 659, 537 cm^{-1}; MS (*m/z*): 532 (M^+); Elemental analysis: Calcd. for $C_{31}H_{28}N_6O_3$: C, 69.91; H, 5.30; N, 15.78; Found: C, 69.75; H, 5.62; N, 15.57.

2-isopropyl-4-(4-nitrophenyl)-*N*-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2n):White solid; mp 279 °C; R_f 0.56 (4:6–EtOAc-hexane); IR (KBr): 3249, 3075, 2974, 1668, 1584, 1534, 1472, 1313, 1262, 1174, 1114, 1064, 928, 831, 768, 641, 536 cm^{-1}; MS (*m/z*): 552 (M^+); Elemental analysis: Calcd. for $C_{30}H_{28}N_6O_5$: C, 65.21; H, 5.11; N, 15.21; Found: C, 65.48; H, 5.29; N, 15.04.

2-isopropyl-4-(2-nitrophenyl)-*N*-(4-(3-oxomorpholino)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*]pyrimidine-3-carboxamide (2o):White solid; mp 279 °C; R_f 0.56 (4:6–EtOAc-hexane);IR (KBr): 3338, 3151, 3034, 2976, 1648, 1569, 1528, 1479, 1328, 1286, 1240, 1031, 941, 878, 764, 751, 663, 635, 548 cm^{-1}; MS (*m/z*): 552 (M^+); Elemental analysis: Calcd. for $C_{30}H_{28}N_6O_5$: C, 65.21; H, 5.11; N, 15.21; Found: C, 64.91; H, 4.84; N, 15.48.

V. CONCLUSION

In summary, we have prepared a library of imidazopyrimidine analogues by one pot Biginally type multicomponent reaction. The process has several advantages like neat reaction and easy workup and purification steps. All the synthesized compounds were evaluated for their antimicrobial activity. The investigation of antimicrobial and antifungal screening data revealed that all the tested compounds showed moderate to significant activity.

VI. REFERENCES

[1]. Abdelhamid, A. O.; Abdelall, Eman K. A.; Abdel-Riheem, Nadia A.; Ahmed, Sayed A. Phosphorus, Sulfur and Silicon2010, 185, 709.

[2]. Shaabani, M. R. Heterocycles2008, 75, 3005.

[3]. Werbel, L. M.; Curry, A.; Elslager, E. F.; Hess, C. A.; Hutt, M. P.; Youngstrom, C. Journal of Heterocyclic Chemistry1969, 6, 787.
[4]. Nawrocka, W. P.; Sztuba, B.; Drys, A.; Wietrzyk, J.; Kosendiak, J.; Opolski, A. Polish Journal of Chemistry2006, 80, 279.
[5]. Sondhi, S. M.; Magan, A.; Sahu, R.; Mahesh, V. K.; Shukla, R.; Patnaik, G. K. Synthesis 1994, 11, 1175.
[6]. Srinivasan, N., Balaji A., Nagrajan, G., Suthakaran, R., Kumar, Y. ;Asian J. Chem., 2008, 20, 4934.
[7]. Berg, D., Büchel, K. H., Plempel, M., Zywietz, A.; Mycoses, 1986, 29, 221.
[8]. Leonard, J. T.; Jeyaseeli, L., Kumar, M., Sivakumar, R.; Asian J. Chem., 2006, 18, 1104.
[9]. Orjales, A., Cires, L. A., Tudanca, P. L., Tapia, I., Mosquera, R., Labeaga, L.; Eur. J. Med. Chem., 1999, 34, 415.
[10]. Wahe, H.; Asobo, P. F.; Cherkasov, R. A.; Nkengfack, A. E.; Folefoc, G. N.; Fomum, Z. T.; Doepp, D. Arkivoc2003, 14, 170.
[11]. Kumar, B. B., Rao, P. V. ;Asian J. Chem., 2006, 18, 3060..
[12]. Shaabani, A.; Rahmati, A.; Naderi, S. Bioorg. Med.Chem. Lett.2005, 15, 5553.
[13]. Yao, C.; Lei, S.; Wang, C.; Yu, C.; Shao, Q.; Tu, S..Chin. J. Chem. 2008, 26, 2107.
[14]. Shaabani, A.; Rahmati, A.; Rezayan, A. H.; Darvishi, M.; Badri, Z.; Sarvari, A. QSAR & Combinatorial Science 2007, 26, 973.
[15]. Tu, S.; Shao, Q.; Zhou, D.; Cao, L.; Shi, F.; Li, C..J. Heterocycl. Chem. 2007, 44, 1401.
[16]. Gladkov, E. S.; Chebanov, V. A.; Desenko, S. M.; Shishkin, O. V.; Shishkina, S. V.; Dallinger, D.; Kappe, C. O., Heterocycles 2007, 73 469.
[17]. Nofal, Z. M.; Fahmy, H. H.; Mohamed, H. S. Arch.Pharm. Res.2002, 25, 28.
[18]. Abdelhamid, A. O.; Riad, B. Y.; Aziz, S. I. Fac. Sci., Cairo Univ., Giza, Egypt. Arch.Pharm. 1987, 320, 642.