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Synthesis and Antibacterial Activity of Some New Benzo[5,6]chromeno[2,3-*d*]pyrimidines[1]

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Abstract—The synthesis and antibacterial activity of some new benzo[5,6]chromeno[2,3-*d*]pyrimidine derivatives are described. The title compounds were obtained by the reaction of 1*H*-benzo[*f*]chromenes with aliphatic and aromatic amines. The structures of all newly synthesized compounds were confirmed by IR, ^{1}H NMR, ^{13}C NMR, and NOESY experiments. The compounds exhibited potent antibacterial activity against gram-positive and gram-negative bacterial species. 10-Methyl-12-(4-hydroxyphenyl)-10,12-dihydro-11*H*-benzo[5,6]chromeno[2,3-*d*] pyrimidin-11-imine displayed greater antibacterial activity against gram-negative bacterial species than did ciprofloxacinandamoxicillin.

Keywords: benzo[5,6]chromeno[2,3-*d*]pyrimidine, NOESY experiment, antibacterial activity, MIC

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INTRODUCTION

Resistance to antimicrobial agents is recognized as an important global public health problem, so that the discovery of new antibacterial compounds has become increasingly critical in fighting infectious disease. On the other hand, nitrogen heterocyclic compounds are of immense interests, because they constitute an important class of natural and non-natural products. Among numerous heterocycles, pyranopyrimidines are an important class of heterocyclic pharmaceuticals. They exhibit interesting biological properties, such as antimicrobial [1], antibacterial [2], antigenotoxic [3], antifungal activities [4–6], antithrombotic [7], anti-inflammatory, and antiphlogistic activity [8, 9]. Taking all these facts into consideration and in continuation of our studies on the synthesis of new bioactive heterocyclic compounds [10–14], we have synthesized some new benzo [5, 6]chromeno[2,3-*d*]pyrimidine derivatives via the reaction of 1*H*-benzo[*f*]chromenes with aliphatic and aromatic amines in high yields. Antibacterial activities of the new compounds against gram-positive and gram-negative bacteria species were also studied.

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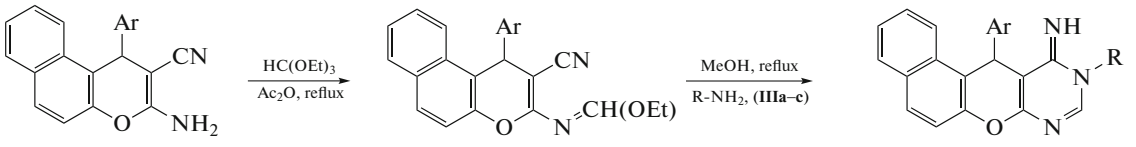
RESULTS AND DISCUSSION

The synthesis of new compounds was started with preparation of new 1*H*-benzo[*f*]chromen-2-carbonitriles (**IIa–d**) from naphtopyran derivatives (**Ia–d**) [15] using excess triethyl orthoformate treatment in acetic anhydride (Scheme 1). The reaction of compounds (**IIa–d**) with aliphatic and aromatic amines (**IIIa–c**) led to formation of new benzo [5, 6]chromeno[2,3-*d*]pyrimidinederivatives (**IVa–g**) in MeOH solution in high yields.

The structural assignments of compounds (**IVa–g**) were based on analytical and spectral data. For example, in the ^{1}H NMR spectrum of compound (**IVd**), the signals at 1.33 (t J = 7.2 Hz, 3H, CH_3) and 4.37(q, J = 7.2 Hz, 2H, OCH_2) ppm attributed to ethoxy (EtO-) group of compound (**IIa**) were absent but instead there was a signal at 8.63 ppm for an exchangeable proton (NH group) that is a clear indication of the cyclization step which leading to formation of the fourth aromatic ring. In the IR spectrum of compound (**IVd**), the absorption band at 2220 cm^{-1} assignable to CN group of compound (**IIa**) was not present but instead an absorption band attributed to NH group appeared at 3450 cm^{-1}. Moreover, the ^{13}C NMR spectrum, molecular ion peak at m/z 460 (M^+) and micro analytical data strongly support the tetracyclic structure of compound (**IVd**).



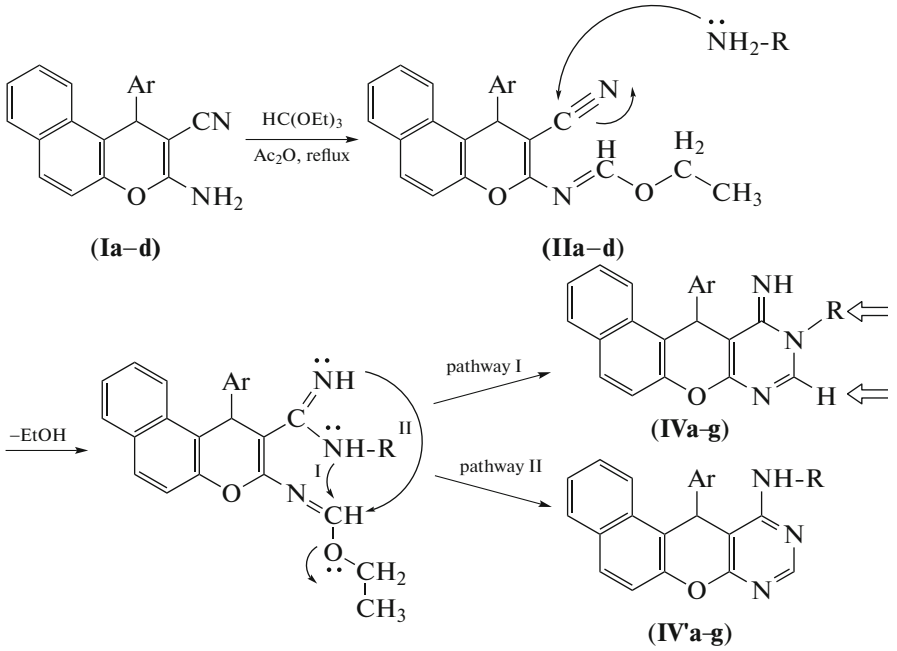
(Ia–d) **(Ia, IIa)**: Ar = 3-$O_2NC_6H_4$
(Ib, IIb): Ar = 4-HOC_6H_4
(Ic, IIc): Ar = 4-ClC_6H_4
(Id, IId): Ar = 2-ClC_6H_4

(IIa–d) **(IIIa)**: R = Me
(IIIb): R = $C_6H_5CH_2$
(IIIc): R = C_6H_5

(IVa): Ar = 3-$O_2NC_6H_4$, R = Me
(IVb): Ar = 4-HOC_6H_4, R = Me
(IVc): Ar = 4-ClC_6H_4, R = Me
(IVd): Ar = 3-$O_2NC_6H_4$, R = $C_6H_5CH_2$
(IVe): Ar = 3-$O_2NC_6H_4$, R = C_6H_5
(IVf): Ar = 4-HOC_6H_4, R = C_6H_5
(IVg): Ar = 2-ClC_6H_4, R = C_6H_5

Scheme 1. Synthesis of new benzo[5, 6]chromeno[2,3-*d*]pyrimidines (**IVa–g**).

However, these spectral characteristics are consistent with another possible structure that is isomeric with compounds (**IVa–g**). As depicted in Scheme 2, the cyclization step can occur by two different pathways because of the ability of C–C band to rotate in compounds (**IIa–d**).



Scheme 2. Two possible structures for the cyclization of (**IIa–d**).

In order to clarify the exact structure of the cyclization products of compounds (**IIa–d**), a NOESY experiment was performed with compound (**IVc**). The data of NOESY experiment showed a massive cross-peak between the proton of pyrimidine ring (δ_H 8.13, s) and the methyl group (δ_H 3.31, s), confirming that cyclization of compounds (**IIa–d**) resulted in formation of compounds (**IVa–g**) (Fig. 1).

The antibacterial activity of compounds (**IIa–d**) and (**IVa–g**) was tested against standard strains of two gram-positive bacteria (*Staphylococcus aureus* ATCC 29213 and *Bacillus subtilis* ATCC 6633) and two gram-negative bacteria (*Escherichia coli* ATCC 10538 and *Salmonella typhimurium* ATCC 14028) species (Table 1), using the broth microdilution method as previously described [16]. We used amoxicillin and ciprofloxacin as reference compounds in the study on the antibacterial activity. The lowes tconcentration of the antibacterial agent that prevents growth of the test organism, as detected by lack of visual turbidity (matching the negative growth control), is assigned to the minimum inhibitory concentration (MIC).

As demonstrated in the table, in spite of the very high activity of compounds (**IVa–g**) against both gram-positive and gram-negative bacteria, compounds (**IIa–d**) were not very effective against the organisms mentioned (MIC > 250). This implies that

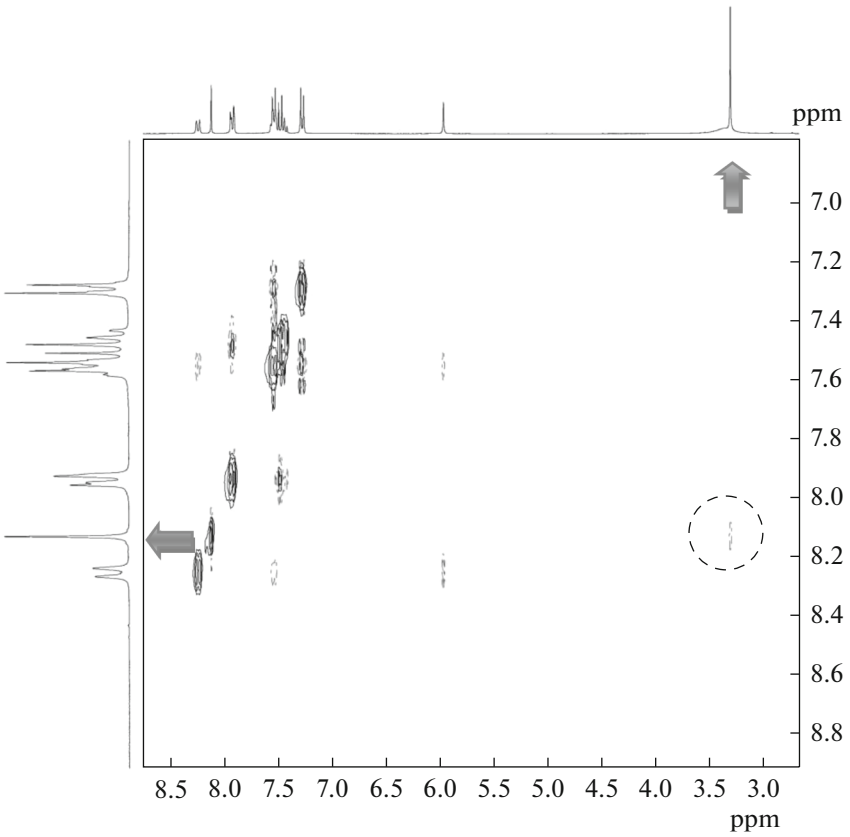


Fig. 1. NOESY spectrum of compound (**IVc**).

the role of pyrimidine moiety is very significant for increasing the antibacterial activity in these heterocyclic compounds. Comparison of the MIC values of the synthesized compounds (**IVa**–**g**) Table 1) revealed the effect of substituent on their antibacterial activity. The test shows that compounds (**IVb**), (**IVf**), (**IVc**), and (**IVg**), whose Ar groups are 4-OHC_6H_5, 4-ClC_6H_5, and 2-ClC_6H_5 showed higher inhibitory effects against *S. aureus*, *B. subtilis*, *E. coli*, and *S. typhimurium* strains tested in comparison with other synthesized compounds. Moreover, the data presented in Table 1 display that the role of aromatic substituents in decreasing the MIC values is higher than that of the R groups. Compound (**IVb**) with Ar = 4-OHC_6H_5 and R = Me showed the highest antibacterial activity among the titled compounds. Also, this compound demonstrated antibacterial activity against *S. aureus*, *E. coli*, and *S. typhimurium* strains higher than that of the well-known antibacterial agents ciprofloxacin and amoxicillin (Table 1).We propose that the hydroxyl and methyl groups might change the binding characteristics of the ligand to their respective receptors and, thereby, improve the biological activity.

CONCLUSION

We have synthesized some new derivatives of benzo [5, 6]chromeno[2,3-*d*]pyrimidine and shown them to be very effective against standard strains of gram-positive and gram-negative bacteria growth inhibitors. Such compounds appear to offer a suitable template for the design of more powerful antibacterial agents and further studies are under way to this end in our laboratory.

EXPERIMENTAL

General

All reagents and solvents used in this work were purchased from Merck. Amoxicillin, ciprofloxacin, and potassium hydroxide were purchased from Sigma-Aldrich. The microorganisms *Staphylococcus aureus* ATCC 29213, *Bacillus subtilis* ATCC 6633, *Escherichia coli* ATCC 10538, and *Salmonella typhimurium* ATCC 14028 were purchased from Pasteur Institute of Iran. Compounds (**Ia**–**d**) were synthesized according to a literature method [15]. All solvents were dried according to standard procedures.

Melting points were measured on an Electrothermal type-9100 melting-point apparatus. IR spectra (KBr; ν, cm^{-1}) were recorded on a Tensor 27 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX-300 FT spectrometer at 300 MHz for ^1H and 75 MHz for ^{13}C using DMSO-d_6 as a solvent. The ^1H and ^{13}C NMR chemical shifts were refer-

Table 1. Inhibitory activity (MIC, μg mL^{-1}) of thereferences and compounds (**IIa–d**) and (**IVa–g**)

Compound	*Staphylococcus aureus* (ATCC 29213)	*Bacillus subtilis* (ATCC 6633)	*Escherichia coli* (ATCC 10538)	*Salmonella typhimurium* (ATCC 14028)
(IIa–d)	>250	>250	>250	>250
(IVa)	75	5	15	25
(IVb)	15	0.5	0.5	25
(IVc)	50	0.5	5	50
(IVd)	75	15	15	50
(IVe)	50	15	20	50
(IVf)	25	1	1	35
(IVg)	25	1	15	50
Ciprofloxacin	16	0.05	1	>128
Amoxicillin	25	0.06	150	>128

enced to tetramethylsilane (TMS) as internal standard and are reported as δ, ppm. The mass spectra were recorded on a Varian Mat, CH-7, at 70 eV. Elemental analysis was performed on a Thermo Finnigan Flash EA microanalyzer.

Determination of the Minimum Inhibitory Concentration (MIC)

The MIC values of compounds (**IIa–d**) and (**IVa–g**) were determined in dilution test tube method, which had been introduced by NCCLS (National Committee for Clinical Laboratory Standards) [16]. For broth dilution methods, in which decreasing concentrations of the antimicrobial agents must be tested, the medium usually prepared in serial two-fold dilutions of a broth is placed in tubes which will support the growth of the test microorganism (10^4 CFU mL^{-1}). After sufficient incubation (18 h), the tubes are examined for turbidity, indicating growth of the microorganism. The organism grows in the tube that does not contain enough antimicrobial agents to inhibit growth. For further confidence, the samples were cultured onto Petri dishes containing Muller–Hinton agar (18 h at 37°C). The lowest concentration of the antibacterial agent that prevents growth of the test organism, as detected by lack of visual turbidity (matching the negative growth control), is designated as the minimum inhibitory concentration (MIC). Serial dilutions of tested compounds (final concentration of 400 to 0.4 μg mL^{-1}) were added to the test bacteria in Mueller–Hinton broth and were incubated at 37°C for 18 h. Growth was presented in the medium control and was absent from the inoculums control [16].

General Procedure for the Synthesis of (IIa–d) from (Ia–d)

Naphtopyrans (**Ia–d**) (1 mmol) and excess triethyl orthoformate (2 mL) in acetic anhydride (1 mL) were heated under reflux for 4 h, then the precipitate was collected and recrystallized from EtOH to give pure compounds (**IIa–d**).

Ethyl-*N*-(2-cyano-1-(3-nitrophenyl)-1*H*-benzo[*f*]-chromen-3-yl)-formimidate (IIa) was obtained as colorless crystals (EtOH), yield 82%, mp 170–172°C. IR: 2207 (CN), 1531, 1347 (NO_2). ^{1}H NMR: 1.33 (t, J = 7.2 Hz, 3H, CH_3), 4.35 (q, J = 7.2 Hz, 2H, OCH_2), 5.94 (s, 1H, CH-pyran), 7.44–7.52 (m, 2H, Ar-H), 7.54 (d, J = 9Hz, 1H, Ar-H), 7.63 (t, J = 7.8Hz, 1H, Ar-H), 7.76–8.19 (m, 6H, Ar-H), 8.77 (s, 1H, N=CH). ^{13}C NMR: 14.3, 64.5, 80.5, 113.4, 117.7, 118.1, 122.5, 122.9, 124.6, 125.8, 128.0, 129.1, 130.2, 130.9, 131.1, 131.7, 134.7, 146.2, 147.7, 148.5, 158, 162.9. MS (*m/z*): 399 (M^+). Anal. calcd. for $C_{23}H_{17}N_3O_4$ (399.4): C, 69.17; H, 4.29; N, 10.52. Found: C, 68.87; H, 4.26; N, 10.69.

Ethyl-*N*-(2-cyano-1-(4-hydroxyphenyl)-1*H*-benzo[*f*]-chromen-3-yl)-formimidate (IIb) was obtained as colorless crystals (EtOH), yield 88%, mp 191–192°C. IR: 2205 (CN), 3445 (OH). ^{1}H NMR: 1.32 (t, J = 6.6 Hz, 3H, CH_3), 4.35 (q, J = 6.6 Hz, 2H, OCH_2), 5.65 (s, 1H, CH-pyran), 7.07 (d, J = 7.3 Hz, 2H, Ar-H), 7.33 (d, J = 7.3 Hz, 2H, Ar-H), 7.80–8.02 (m, 6H, Ar-H), 8.74 (s, 1H, CH-pyrimidine). ^{13}C NMR: 14.3, 64.4, 81.4, 114.3, 117.6, 118.4, 122.7, 124.1, 125.7, 127.7, 129, 130.4, 131.6, 141.6, 147.5, 149.8, 157.4, 162.3, 169.5. MS (*m/z*): 370 (M^+). Anal. calcd. for $C_{23}H_{18}N_2O_3$ (370.4): C, 74.58; H, 4.90; N, 7.56. Found: C, 74.37; H, 4.88; N, 7.78.

Ethyl-*N*-(2-cyano-1-(4-chlorophenyl)-1*H*-benzo[*f*]-chromen-3-yl)-formimidate (IIc) was obtained as colorless crystals (EtOH), yield 90%, mp 200–202°C.

IR: 2209 (CN). ^{1}H NMR: 1.32 (t, J = 7.2 Hz, 3H, CH_3), 4.34 (q, J = 7.2 Hz, 2H, OCH_2), 5.65 (s, 1H, CH-pyran), 7.3–7.95 (m, 9H, Ar-H) 8.0 (d, J = 9 Hz, 1H, Ar-H), 8.73 (s, 1H, N=CH). ^{13}C NMR: 14.3, 64.4, 81.1, 114, 117.6, 118.3, 124.1, 125.7, 127.7, 129, 129.3, 129.9, 130.4, 130.5, 131.6, 132.3, 143.2, 147.5, 157.5, 162.5. MS (*m/z*): 390 [M(^{37}Cl)]$^+$). Anal. calcd. for $C_{23}H_{17}ClN_2O_2$ (388.8): C, 71.04; H, 4.41; N, 7.20. Found: C, 70.85; H, 4.37; N, 6.97.

Ethyl-*N*-(2-cyano-1-(2-chlorophenyl)-1*H*-benzo[*f*]-chromen-3-yl)-formimidate (IId) was obtained as colorless crystals (EtOH), yield 85%, mp 172–173°C. IR: 2209 (CN). ^{1}H NMR: 1.33 (t, J = 7.2 Hz, 3H, CH_3), 4.35 (q, J = 7.2 Hz, 2H O-CH_2), 5.96 (s, 1H, CH-pyran), 7.12–7.53 (m, 7H, Ar-H), 7.62 (d, J = 7.5Hz, 1H, Ar-H), 7.94–8.03 (m, 2H, Ar-H), 8.76 (s, 1H, CH-pyrimidine). ^{13}C NMR: 14.3, 64.5, 79.7, 113.7, 117.6, 117.8, 123.2, 125.8, 128, 128.8, 129.2, 129.6, 130.2, 130.4, 130.7, 131.3, 131.6, 131.9, 141.2, 147.8, 157.7, 162.6. MS (*m/z*): 390 [M(^{37}Cl)]$^+$). Anal. calcd. for $C_{23}H_{17}ClN_2O_2$ (388.8): C, 71.04; H, 4.41; N, 7.20. Found: C, 70.81; H, 4.36; N, 7.37.

*General Procedure for the Synthesis of Benzochromenopyrimidines (**IVa–d**)*

Method A. To a solution of aliphaticamine **(IIIa,b)** (1 mmol) in MeOH, compound **(IIa–c)** (1 mmol) was added under reflux condition. After 10–20 min, the precipitate was collected and recrystallized from EtOH.

Method B. Compound **(IIa–c)** (1 mmol) was added to a solution of aliphaticamine **(IIIa,b)** (1 mmol) in MeOH at rt. After1 h, the precipitate was collected and recrystallized from EtOH.

10-Methyl-12-(3-nitrophenyl)-10,12-dihydro-11*H*-benzo[5, 6]chromeno[2,3-*d*]pyrimidin-11-imine (IVa) was obtained as pale yellow crystals (EtOH), yield 80%, mp 212–213°C. IR: 3425 (NH), 1521 and 1348 (NO_2). ^{1}H NMR: 3.3 (s, 3H, N–CH_3), 6.18 (s, 1H, CH-pyran), 7.46–7.98 (m, 8H, Ar-H and exchangeable by D_2O, NH), 8.10 (s, 1H, CH-pyrimidine), 8.25 (s, 1H, Ar-H), 8.44 (s, 1H, Ar-H). ^{13}C NMR: 35.9, 99.1, 116.3, 117.9, 122.4, 122.7, 123.6, 125.5, 127.8, 129.1, 130.3, 130.4, 130.7, 131.4, 135, 146.5, 148, 148.1, 152.1, 156.8. MS (*m/z*): 384 (M$^+$). Anal. calcd. for $C_{22}H_{16}N_4O_3$ (384.4): C, 68.74; H, 4.20; N, 14.58. Found: C, 68.50; H, 4.18; N, 14.44.

10-Methyl-12-(4-hydroxyphenyl)-10,12-dihydro-11*H*-benzo [5, 6]chromeno [2,3-*d*] pyrimidin-11-imine (IVb) was obtained as pale yellow crystals (EtOH), yield 86%, mp 239–241°C. IR: 3326 (NH), 3415 (OH). ^{1}H NMR: 3.31 (s, 3H, N-CH_3), 5.79 (s, 1H, CH-pyran), 6.57–7.92 (m, 10H, Ar-H and NH), 8.09 (s, 1H, CH), 8.28 (d, J = 7.8 Hz, 1H, Ar-H), 9.26 (s, 1H, OH).^{13}C NMR: 35.8, 100, 115.4, 117.7, 117.8, 124.1, 125.2, 127.3, 128.9, 129.4, 129.5, 130.9, 131.3, 134.8, 147.5, 151.4, 156.2, 156.4. MS (*m/z*): 355 (M$^+$). Anal. calcd. for $C_{22}H_{17}N_3O_2$ (355.4): C, 74.35; H, 4.82; N, 11.82. Found: C, 74.23; H, 4.78; N, 12.01.

10-Methyl-12-(4-chlorophenyl)-10,12-dihydro-11*H*-benzo [5, 6]chromeno[2,3-*d*]pyrimidin-11-imine (IVc) was obtained as pale yellow crystals (EtOH), yield 90%, mp 245–247°C. IR: 3.340 (NH). ^{1}H NMR: 3.31 (s, 3H, N–CH_3), 5.98 (s, 1H, CH-pyran), 7.27–7.95 (m, 10H, Ar-H, NH), 8.13 (s, 1H, CH-pyrimidine), 8.25 (d, J = 8.4 Hz, 1H, Ar-H). ^{13}C NMR: 35.9, 99.4, 116.8, 117.9, 123.8, 125.4, 127.5, 128.8, 129, 129.9, 130.30, 130.8, 131.3, 131.7, 143.3, 147.7, 151.8, 156, 156.5. MS (*m/z*): 375 [M(^{37}Cl)]$^+$. Anal. calcd. for $C_{22}H_{16}ClN_3O$ (373.8): C, 70.68; H, 4.31; N, 11.24. Found: C, 70.47; H, 4.34; N, 10.97.

10-Benzyl-12-(3-nitrophenyl)-10*H*-benzo[5,6]-chromeno[2,3-*d*]pyrimidin-11(12*H*)-imine (IVd) was obtained as pale yellow crystals (EtOH), yield 89%, mp 210–211°C. IR: 3450 (NH), 1518 and 1346 (NO_2). ^{1}H NMR: 4.57 (dd, J_1 = 15, J_2 = 5.1 Hz, 1H, CH_2), 4.83 (dd, J_1 = 18.3, J_2 = 5.3 Hz, 1H, CH_2), 6.42 (s, 1H, CH-pyran), 7.15–7.66 (m, 9H, Ar-H), 7.81 (d, J = 7.8 Hz, 1H, Ar-H), 8.01 (t, J = 9 Hz, 3H, Ar-H), 8.12 (t, J = 5.7 Hz, 1H, Ar-H), 8.18 (d, J = 8.7 Hz, 1H, Ar-H), 8.23 (s, 1H, CH-pyrimidine), 8.63 (s, 1H, NH). ^{13}C NMR: 44.4, 97.3, 116.8, 118.2, 122.4, 122.5, 123.1, 125.6, 127.2, 127.3, 127.9, 128.6, 129.3, 130.4, 130.9, 131.3, 134.6. 139.7, 145.9, 148, 148.3, 157.1, 160.8, 162.0. MS (*m/z*): 460 (M$^+$). Anal. calcd. for $C_{28}H_{20}N_4O_3$ (460.5): C, 73.03; H, 4.38; N, 12.17. Found: C, 72.88; H, 4.36; N, 12.38.

*General Procedure for the Synthesis of Benzochromenopyrimidines (**IVe–g**)*

To a solution of aromatic amine **(IIIc)** (1 mmol) in MeOH (10 mL), compounds **(IIa, b)** and **(IId)** (1 mmol) were added under reflux condition in the presence of DABCO (10% mol) as catalyst. After 10–12 h (monitored by TLC), the precipitate was collected and washed with cold water and then recrystallized from EtOAC–*n*-hexane, 1 : 3.

12-(3-Nitrophenyl)-10-phenyl-10*H*-benzo[5,6]-chromeno[2,3-*d*]pyrimidin-11(12*H*)-imine (IVe) was obtained as pale yellow crystals, yield 88%, mp 225–227°C. IR: 3438 (NH), 1517 and 1343 (NO_2). ^{1}H NMR: 6.71 (s, 1H, CH-pyran), 7.12 (t, J = 7.2 Hz, 1H, Ar-H), 7.38 (t, J = 8.1 Hz, 2H, Ar-H), 7.48–7.7 (m, 6H, Ar-H), 7.91 (d, J = 7.8Hz, 1H), 7.98–8.05 (m, 3H, Ar-H), 8.28 (d, J = 8.4 Hz, 1H, Ar-H), 8.36 (s, 1H, CH-pyrimidine), 8.60 (s, 1H, Ar-H) 9.24 (s, 1H, NH). ^{13}C NMR: 98.9, 116.7, 118.1, 122.2, 122.7, 123.3, 124.2, 125.7, 128, 129, 129.3, 130.6, 130.7, 131, 131.4, 134.4, 139.4, 145.9, 148.2, 148.3, 156.9, 159.1, 162.7. MS (*m/z*): 446 (M$^+$). Anal. calcd. for

$C_{27}H_{18}N_4O_3$ (446.5): C, 72.64; H, 4.06; N, 12.55. Found: C, 72.47; H, 4.09; N, 12.70.

4-(11-Imino-10-phenyl-11,12-dihydro-10*H*-benzo-[5,6]chromeno[2,3-*d*]pyrimidin-12-yl)phenol (IVf) was obtained as pale yellow crystals, yield 87%, mp 273–274°C. IR: 3423 (NH, OH). ^{1}H NMR: 6.39 (s, 1H, CH-pyran), 6.61 (d, J = 8.4 Hz, 2H, Ar-H), 7.10 (t, J = 7.2 Hz, 1H, Ar-H), 7.33–7.73 (m, 9H, Ar-H), 7.97 (d, J = 8.7 Hz, 2H, Ar-H), 8.33 (d, J = 9.3 Hz, 2H, Ar-H and CH-pyrimidine), 8.96 (s, 1H, NH), 9.32 (s, 1H, OH). ^{13}C NMR: 100.3, 115.8, 118, 118.2, 122, 123.8, 123.9, 125.4, 127.4, 129, 129.1, 129.7, 130.9, 131.3, 134.6, 139.8, 147.9, 156.2, 156.6, 158.9, 162.5. MS (m/z): 417 (M^+). Anal. calcd. for $C_{27}H_{19}N_3O_2$ (417.5): C, 77.68; H, 4.59; N, 10.07. Found: C, 77.39; H, 4.56; N, 10.29.

12-(2-Chlorophenyl)-10-phenyl-10*H*-benzo [5, 6]-chromeno[2,3-*d*]pyrimidin-11(12*H*)-imine (IVg) was obtained as pale yellow crystals, yield 81%, mp 258–260°C. IR: 3415 (NH).^{1}H NMR: 6.76 (s, 1H, CH-pyran), 7.06 (t, J = 7.2 Hz, 1H, Ar-H), 7.16 (t, J = 7.2 Hz, 1H, Ar-H), 7.27 (t, J = 6.6 Hz, 1H, Ar-H), 7.32–7.37 (m, 3H, Ar-H), 7.5 (t, J = 7.2 Hz, 1H, Ar-H), 7.56–8.8 (m, 7H, Ar-H), 8.2 (d, J = 8.7 Hz, 1H, Ar-H), 8.4 (s, 1H, CH-pyrimidine), 8.62 (s, 1H, NH). ^{13}C NMR: 98.6, 116.1, 118, 120.9, 123.4, 123.5, 125.5, 127.7, 128.5, 129.1, 129.3, 129.6, 130.5, 130.7, 131, 131.3, 131.6, 132.1, 139.7, 140.8, 148.4, 156.7, 159, 162.8. MS (m/z): 437 [M(^{37}Cl)]$^+$. Anal. calcd. for $C_{27}H_{18}ClN_3O$ (435.9): C, 74.39; H, 4.16; N, 9.64. Found: C, 74.27; H, 4.14; N, 9.70.

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