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NOVEL PYRROLO[2,3-*b*]PYRIDINE AND PYRROLO[2,3-*d*] PYRIMIDINE DERIVATIVES: DESIGN, SYNTHESIS, AND STRUCTURE ELUCIDATION

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ABSTRACT. A cyclo condensation reaction is an effective method for a two-component reaction of 2-amino-1,5-diphenyl-1*H*-pyrrole-3-carbonitrile **3a-c** and active methylene compounds in acetic acid and catalytic hydrochloric acid to produce new substituted 1*H*-pyrrolo[2,3-*b*]pyridine **4a-c**, **5a-c**, and **6a-c** have been established. Additionally, a new series of substituted 1*H*-pyrrolo[2,3-*d*]pyrimidines **7a-c** and **8a-c** could be synthesized utilizing a feasible and efficient approach, including urea and thiourea substrates. Spectroscopic data IR, MS, ^{1}H, and ^{13}C NMR, as well as elemental analyses, elucidated these compounds' structures.

KEY WORDS: 1*H*-Pyrrolo[2,3-*b*]pyridine, 1*H*-Pyrrolo[2,3-*d*]pyrimidines, Active methylene compounds

INTRODUCTION

Polycyclic nitrogen compounds are a significant family of heterocyclic molecules that gained the significant interest of both medicinal and synthetic chemists due to their extensive bioactivity spectrum. In particular, 1*H*-pyrrolo[2,3-*b*]pyridine derivatives' pharmacological characteristics include anticonvulsant, anticancer, analgesic, anti-inflammatory, anti-MDR, anti-hypertensive, and antipyretic activities [1, 2]. In medicinal chemistry, a fused heterocyclic molecule, including 1*H*-pyrrolo[2,3-*b*]pyridine, is a substantial scaffold [3, 4]. A variety of natural compounds include 1*H*-pyrrolo[2,3-*b*] pyridines, particularly variolins obtained from the antarctic sponge by Kirkpatrick Avarialosa model [5, 6]. 7-Azaindoles, also referred to as 1*H*-pyrrolo[2,3-*b*]pyridines, and their derivatives have preferable bioactive applications to comparable indole moieties due to their essential physicochemical features [7, 8]. Numerous techniques have been published for 1*H*-pyrrolo[2,3-*b*]pyridine, but new approaches from inexpensive and readily accessible starting substrates are still required.

In this study, further modifications were carried out on 2-amino-1,5-diphenyl-1*H*-pyrrole-3-carbonitrile derivatives reported in our previous study. It has been found that functionalized different reagents containing active methylene group with donating and withdrawing substituents were diverse biological activity and strong coordination ability with our starting material **3a-c** afforded the desired 1*H*-pyrrolo[2,3-*b*]pyridines. Adding pyridine-containing fragments to the 2-amino-1,5-diphenyl-1*H*-pyrrole-3-carbonitrile yielded compounds **4a-c**, **5a-c**, and **6a-c**.

Due to various pharmacologically active chemicals that may be synthesized in the lab and isolated from natural sources, fused pyrimidines are a significant class of heterocyclic chemistry studied by medicinal chemists. Because the pyrrolo[2,3-*d*]pyrimidine rings resemble purines [9, 10] and pyrimidines, they are characterized by a variety of bioactivities, particularly those that inhibit enzymes, are antimicrobial, antiviral, anticancer, antifolates, antitumor, anti-inflammatory, antifungal, antiallergic [11-13]. The biological activities of pyrrolo[2,3-*d*]pyrimidine derivatives

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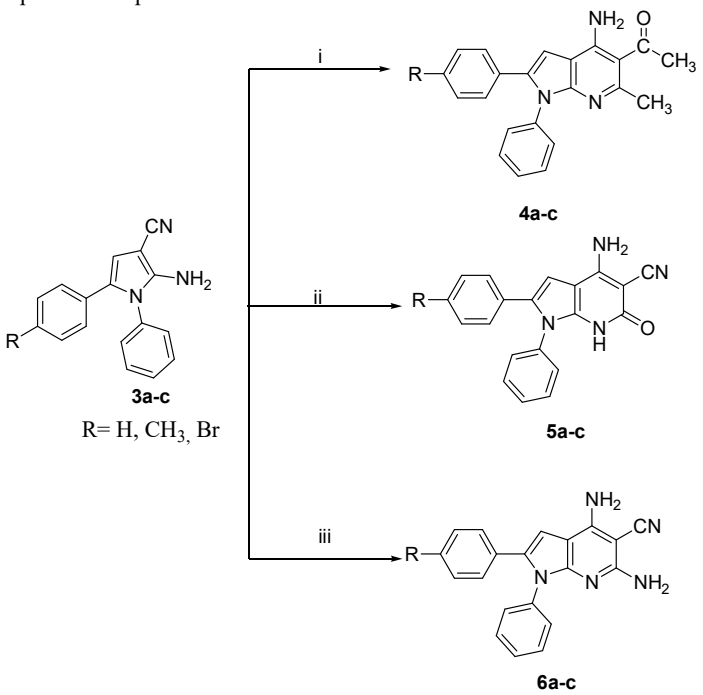
are distinct and include anticancer, antiviral, anti-diabetic, and anti-inflammatory effects [14, 15]. However, due to their antioxidant and tumor-preventing qualities, some pyrrolopyrimidine syntheses have received FDA and other country approval for treating several disorders undergoing phase I/II clinical trials [16].

Based on the previous findings and our attempt to find new synthetic pathways, we report the synthesis and assessment of pyrrolo[2,3-*d*]pyrimidine derivatives. The straightforward and practical synthesis of active nitrogen-containing heterocycles is an essential task in synthetic chemistry, and new artificial techniques are regularly reported. In this study, we provide a specific approach for synthesizing pyrrolo[2,3-*b*]pyridine and pyrrolo[2,3-*d*]pyrimidine utilizing substituted 2-amino-1,5-diphenyl-1*H*-pyrrole-3-carbonitrile and other simple aliphatic reagents via the cross-coupling process and condensation reactions, continuing our long-standing interest in the synthesis of heterocyclic compounds.

RESULTS AND DISCUSSION

The synthetic method (Scheme 1) successfully produced the target molecules **4a–c**, **5a-c**, and **6a-c**. Initially, 2-amino-1,5-diphenyl-1*H*-pyrrole-3-carbonitrile derivatives **3a-c** were utilized as starting materials using a previously described method [17]. Acetylacetone **1**, ethyl cyanoacetate **2**, and malononitrile **3** were the reagents that refluxed with **3a-c** for 4 hours. Each while exposed to acetic acid and catalytic drops from hydrochloric acid. The corresponding new 1*H*-pyrrolo[2,3-*b*]pyridines **4a-c**, **5a-c**, and **6a-c** were generated. By using silica gel column chromatography, the raw components are purified.

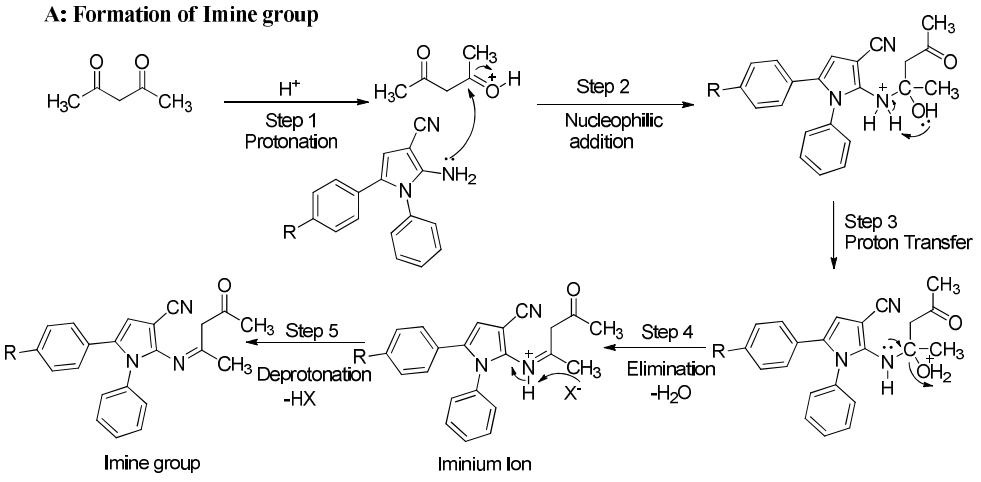


Scheme 1. Synthesis of compounds **4a-c**, **5a-c** and **6a-c**. Reaction conditions: Acetic acid (10 mL), conc. HCl (5 drops), reflux 4 h. (10 mmol) from (i) acetyl acetone, (ii) ethylcyanoacetate, (iii) melononitrile, compounds **3a-c** (10 mmol).

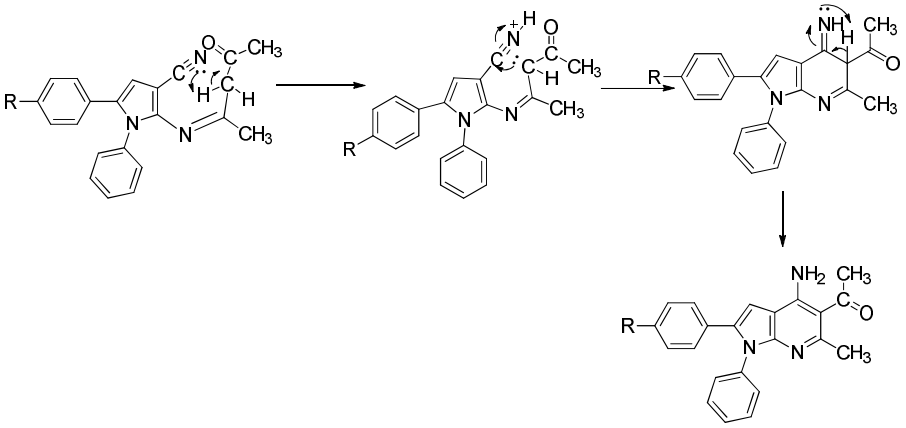
Based on analytical and spectral data, the structures were verified. The designs **4a–c**'s IR assignments revealed recognizable absorption bands around 3440 cm^{-1} for (NH_2 amine), 1675 cm^{-1} due to the C=O group, and 1595 cm^{-1} corresponding to (imine group C=N), as well as the disappearance of a band for (nitrile group CN), which elucidated the structures. The **4a–c** NMR spectra for ^1H and ^{13}C indicated a single signal at δ 11.97 ppm (s, 2H, NH_2 amine). In contrast, ^{13}C NMR spectra showed δ 159 ppm for C=O and 153 ppm due to imine group C=N that elucidated the structures. The absence of a band at 114 ppm for nitrile group CN also proves the target compounds. Compounds **5a–c** IR's spectra generally showed absorption bands for the NH and NH_2 groups in the range of 3346 cm^{-1} and 3018 cm^{-1}. In addition, a peak at 1710 cm^{-1} for the C=O group and 2196 cm^{-1} for the nitrile group CN revealed the structures. The title compounds' ^1H NMR demonstrated a singlet peak at δ 12 ppm (s, 2H, NH_2 amine), also a singlet signal at δ 8 ppm (s, 1H, NH). Furthermore, ^{13}C NMR showed signals at 171 and 114 attributed to C=O and CN, respectively. On the contrary, for compounds **6a-c**, the IR spectra showed two peaks at 3432 cm^{-1} and 3117 cm^{-1} due to NH_2 groups. The peak at 2361 cm^{-1} also corresponds to the CN nitrile group. Moreover, the ^1H and ^{13}C NMR spectra revealed the presence of signals at δ 12.01, 3.55 (s, 2H, NH_2), and 158, 153, and 120 ppm due to imine group C=N, C=C-NH_2, and CN nitrile group. The mass spectrum of the compounds confirmed the expected structures.

The potential pathway leading to the 1-(4-amino-6-methyl-1,2-diphenyl-1*H*-pyrrolo[2,3-*b*]pyridin-5-yl)ethanone derivatives **4a-c** is demonstrated in (Scheme 3). The initial phase entails the formulation of C=N. Catalytic acid increases the electrophilicity of carbonyl carbon, binds to carbonyl oxygen, and weakens the C=O bond. Nucleophilic 1,2-addition is the outcome of the amino nitrogen of pyrrole's attack on the electrophile carbonyl. The subsequent step is a proton transfer, which results in the protonation of OH to yield a superior leaving group. Second, the lone pair on the amine nitrogen becomes free once more due to proton transfer. The remaining step is deprotonating the positively charged imine (iminium) to obtain the neutral imine. Subsequently, the cyclization with the cyano group yields the targeted molecules.

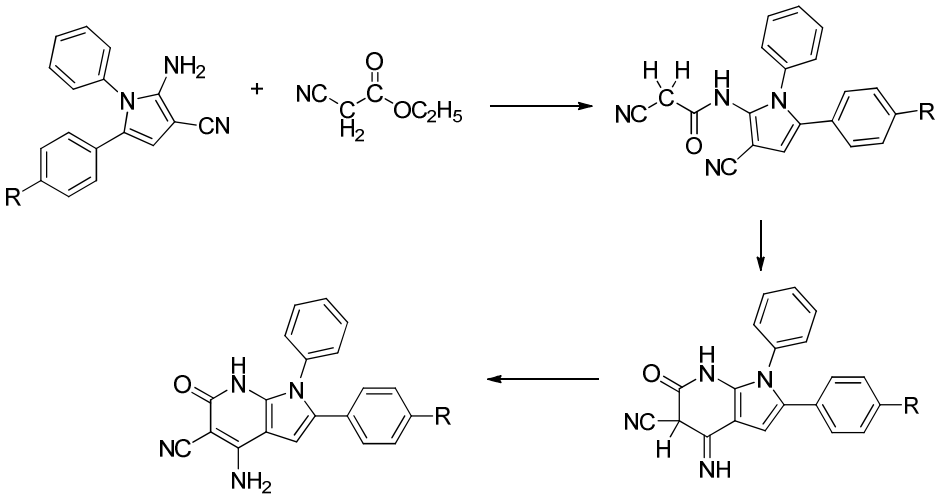
The target compounds **5a–c** were generated as shown in (Scheme 4). According to the plausible mechanism, the reaction was carried out in the ethoxy group, which was left as a good leaving group, which led to the exit of a small molecule of ethyl alcohol away from the carbonyl group supported by spectral analytical data. Providing active methylene protons to the pyrrole nitrile group results in forming of a new substituent amino group via cyclization.



B: Cyclization

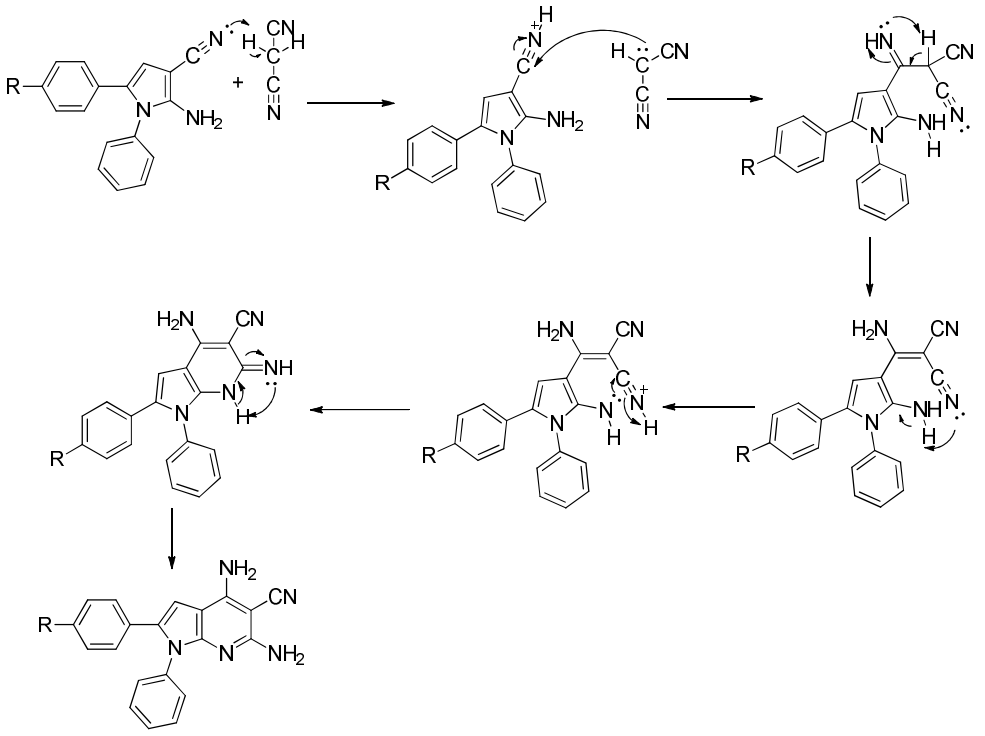


Scheme 3. Plausible mechanism for compounds **4a-c**.



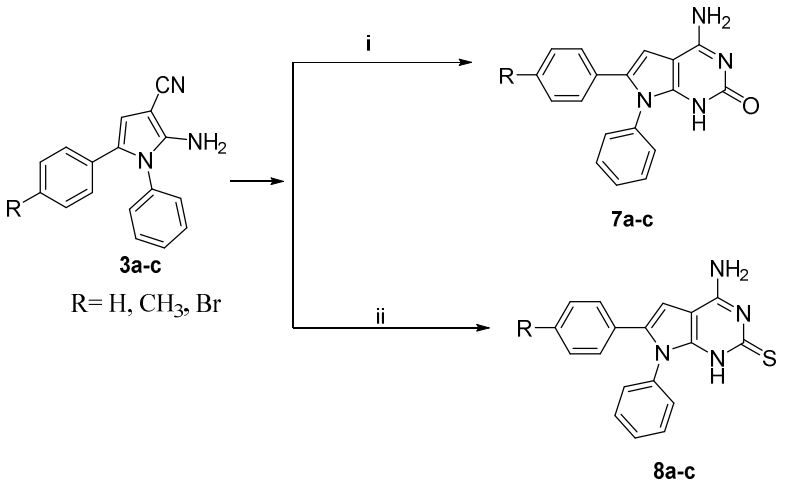
Scheme 4. Plausible mechanism for compounds **5a-c**.

The mechanism of the reaction of **3a-c** derivatives with malononitrile compounds **6a-c** is shown in (Scheme 5). It also results from adding the pyrrole amino group onto the cyano group of malononitrile, forming a new function group imine group C=N and the amino group as a further substituent demonstrated by spectral data.



Scheme 5. Plausible mechanism for compounds **6a-c**.

The general synthetic method for the preparation of the fused bicyclic compounds 4-amino-6,7-diphenyl-1*H*-pyrrolo[2,3-*d*]pyrimidin-2(7*H*)-one as well as 4-amino-6,7-diphenyl-1*H*-pyrrolo[2,3-*d*]pyrimidine-2(7*H*)-thione derivatives **7a-c** and **8a-c** is shown in (Scheme 2). The fusion of starting compounds **3a-c** with urea and thiourea afforded the target compounds **7a-c** and **8a-c**, respectively, a high yield. Based on analytical and spectral data, the structures were verified. The IR assignments of designs **7a-c** and **8a-c** revealed identifiable absorption bands at 3414 cm^{-1} and 3204 cm^{-1} due to NH and NH_2 groups. Additionally, the C=O, C=N, and C=S characteristic bands are at 1661 cm^{-1}, 1580 cm^{-1}, as well as 1318 cm^{-1}. The disappearance of the cyano group also proved the structures. For compounds **7a-c**, ^{1}H NMR showed characteristic bands at 11.15 ppm (s, 1H, NH), 4.45 ppm (s, 2H, NH_2), and 6.66 ppm for *H*-pyrrole, which proved the resulting compounds. Furthermore, ^{13}C NMR showed around 157 and 155 ppm corresponding to C=O and C=N. The ^{1}H and ^{13}C NMR spectra for compounds **8a-c** also demonstrated the existence of signals at 8.04, 5.97 ppm due to (s, 1H, NH), (s, 2H, NH_2), 157, and 154 ppm attributed to the C=S, and imine group C=N. The synthesized compounds' structures were examined utilizing MS analysis.



Scheme 2. Synthesis of compounds **7a-c** and **8a-c**. Reaction conditions: Fusion 15 min, (2 mmol) from (i) urea, (ii) thiourea, compounds **3a-c** (1 mmol).

EXPERIMENTAL

Chemicals and apparatus

In the current research, all solvents and reagents are of analytical grade purity and obtained from Merck and Sigma Aldrich. Utilizing an electrothermal 9100 digital melting apparatus (Büchi, Switzerland), melting points were determined and were uncorrected. On a Bruker DPX spectrum analyzer, KBr IR spectra were recorded (Faculty of Science, Menoufia University). ^{13}C NMR and ^{1}H NMR spectra were determined in DMSO-d_6 solvent on a Bruker DPX 400 MHz or JEOL, ECA 500 MHz NMR spectrometer. Additionally, chemical shifts (δ) were reported in parts per million (ppm) in terms of TMS as an internal standard. Mass spectra were run on DI Analysis Shimadzu QP -2010, in addition to mass spectrometer and HP MODEL MS-5988 at 70 eV. An elemental analysis (C, H, N) was carried out utilizing a Vario III CHN analyzer (Germany) (Faculty of Science, Micro analytical Center, Cairo University). Moreover, obtained results from the TLC MS Xcalibur data SM: 15G (El-Azhar University's Regional Center for Mycology and Biotechnology). Compounds' purity, and reaction progress, were determined by column chromatography silica gel 200-400 mesh and TLC analytical silica gel plates 60 F_{254} utilizing CH_2Cl_2/methanol (39:1), illustrated in (Supplementary material).

*General procedure for synthesizing compounds **4a-c**, **5a-c**, and **6a-c***

A mixture of 2-amino-1,5-diphenyl-1*H*-pyrrole-3-carbonitrile **3a-c** (10 mmol) with acetylacetone, ethyl cyanoacetate and malononitrile (10 mmol) in acetic acid (15 mL) containing few drops from conc. HCl was refluxed for 4 h. TLC monitored the reaction. After cooling at room temperature, the resulting precipitate was collected by filtration, washed from ethanol, and dried to afford **4a-c**, **5a-c**, and **6a-c**. The target products were purified by column chromatography CH_2Cl_2/CH_3OH (39:1).

1-(4-Amino-6-methyl-1,2-diphenyl-1H-pyrrolo[2,3-b]pyridin-5-yl)ethanone (4a). White powder; yield (88%); mp 334-336 ºC; IR (KBr) ν_{max} 3122-3260 (NH_2), 1671 (C=O) 1588 (C=N) cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, δ ppm): 2.26 (s, 3H, CH_3), 2.49 (s, 3H, CH_3-C=O), 6.77 (1*H*-pyrrole), 7.14-7.44 (m, 10H, Ar-H), 12.02 (s, 2H, NH_2, D_2O exchangeable); ^{13}C NMR (500 MHz, DMSO-d_6, δ ppm): 21.14, 23.26, 102.49, 106.13, 127.37-129.02, 153.65, 172.02; EIMS m/z: 341.41 [M^+, 30.23%]; anal. calcd. for $C_{22}H_{19}N_3O$: C, 77.40; H, 5.61; N, 12.31. Found: C, 77.38; H, 5.59; N, 12.29.

1-(4-Amino-6-methyl-1-phenyl-2-(p-tolyl)-1H-pyrrolo[2,3-b]989yridine-5-yl)ethanone (4b). White solid; yield (86%); mp 340-344 ºC; IR (KBr) ν_{max} 3440 (NH_2), 1675 (C=O), 1595 (C=N) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, δ ppm): 1.98 (s, 3H, CH_3), 2.23 (s, 3H, CH_3), 2.26 (s, 3H, CH_3-C=O), 6.71 (1*H*-pyrrole), 7.04-7.44 (m, 9H, Ar-H), 11.97 (s, 2H, NH_2, D_2O exchangeable); ^{13}C NMR (400 MHz, DMSO-d_6, δ ppm): 20.95, 21.35, 21.38, 102.18, 106.25, 128.41-129.36, 135.79-137.27, 153.80, 159.49; EIMS m/z 357.72 [M^+, 100%]; anal. calcd. for $C_{23}H_{21}N_3O$: C, 77.72; H, 5.96; N, 11.82. Found: C, 77.70; H, 5.95; N, 11.80.

1-(4-Amino-2-(4-bromophenyl)-6-methyl-1-phenyl-1H-pyrrolo[2,3-b]989yridine-5-yl)ethanone (4c). White solid; yield (87%); mp 352-353 ºC; IR (KBr) ν_{max} 3435 (NH_2), 1674 (C=O), 1593 (C=N) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, δ ppm): 2.26 (s, 3H, CH_3), 2.49 (s, 3H, CH_3-C=O), 6.83 (1*H*-pyrrole), 7.08-7.44 (m, 9H, Ar-H), 12.01 (s, 2H, NH_2, D_2O exchangeable); ^{13}C NMR (400 MHz, DMSO-d_6, δ ppm): 20.71, 21.14, 101.98, 106.10, 127.99-129.03, 130.05-135.97, 150.00, 153.48, 158.99; EIMS m/z 420.26 [M^+, 37.82%]; anal. calcd. for $C_{22}H_{18}BrN_3O$: C, 62.87; H, 4.32; N, 10.00. Found: C, 62.85; H, 4.30; N, 9.98.

4-Amino-6-oxo-1,2-diphenyl-6,7-dihydro-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (5a). Buff solid; yield (60%); mp 332-334 ºC; IR (KBr) ν_{max} 3300, 3056 (NH, NH_2), 2212 (CN), 1658 (C=O) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, δ ppm): 6.75 (s, 1*H*-pyrrole), 7.05-7.34 (m, 10H, Ar-H), 8.30 (s, 2H, NH_2, D_2O exchangeable), 12.00 (s, 1H, NH, D_2O exchangeable); EIMS m/z 326.67 [M^+, 16.12%]; anal. calcd. for $C_{20}H_{14}N_4O$: C, 73.61; H, 4.32; N, 17.17. Found: C, 73.57; H, 4.30; N, 17.15.

4-Amino-6-oxo-1-phenyl-2-(p-tolyl)-6,7-dihydro-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (5b). White solid; yield (55%); mp 342-344 ºC; IR (KBr) ν_{max} 3346, 3108 (NH, NH_2), 2196 (CN), 1710 (C=O) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, δ ppm): 2.25 (s, 3H, CH_3), 6.84 (s, 1*H*-pyrrole), 7.08-7.31 (m, 9H, Ar-H), 8.40 (s, 2H, NH_2, D_2O exchangeable), 12.01 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (400 MHz, DMSO-d_6, δ ppm): 20.68, 87.07, 114.04, 125.38-138.80, 145.02, 171.99; EIMS m/z 340.04 [M^+, 15.45%]; anal. calcd. for $C_{21}H_{16}N_4O$: C, 74.10; H, 4.74; N, 16.46. Found: C, 74.00; H, 4.70; N, 16.43.

4-Amino-2-(4-bromophenyl)-6-oxo-1-phenyl-6,7-dihydro-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (5c). Buff solid; yield (56%); mp 354-356 ºC; IR (KBr) ν_{max} 3344, 3017 (NH, NH_2), 2194 (CN), 1710 (C=O) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, δ ppm): 6.73 (s, 1*H*-pyrrole), 7.06-7.37 (m, 9H, Ar-H), 8.40 (s, 2H, NH_2, D_2O exchangeable), 12.05 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (400 MHz, DMSO-d_6, δ ppm): 66.34, 103, 106.16, 120.66, 128.08-133.78, 135.96, 150.21, 153.89, 158.83; EIMS m/z 405.88 [M^+, 14.32%]; anal. calcd. for $C_{20}H_{13}BrN_4O$: C, 59.28; H, 3.23; N, 13.83. Found: C, 59.26; H, 3.20; N, 13.80.

4,6-Diamino-1,2-diphenyl-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (6a). Yellowish white solid; yield (50%); mp 330-332 ºC; ^1H NMR (500 MHz, DMSO-d_6, δ ppm): 2.26 (s, 2H, NH_2, D_2O exchangeable), 6.77 (s, 1*H*-pyrrole), 7.14-7.44 (m, 10H, Ar-H), 12.01 (s, 2H, NH_2, D_2O exchangeable); ^{13}C NMR (500 MHz, DMSO-d_6, δ ppm): 66.37, 106.12, 120.01, 127.36-129.27,

153.64, 158.93; EIMS m/z 327.21 [M^+, 44.88%]; anal. calcd. for $C_{20}H_{15}N_5$: C, 73.83; H, 4.65; N, 21.52. Found: C, 73.80; H, 4.63; N, 21.50.

4,6-Diamino-1-phenyl-2-(p-tolyl)-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (6b). Buff solid; yield (56%); mp 355-356 ºC; IR (KBr) ν_{max} 3300, 3113 (NH_2, NH_2), 2212 (CN, nitrile), 1565 (C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.40 (s, 3H, CH_3), 5.40 (s, 2H, NH_2, D_2O exchangeable amine), 6.77 (s, 1*H*-pyrrole), 7.24-7.75 (m, 9H, Ar-H), 12.03 (s, 2H, NH_2, D_2O exchangeable); EIMS m/z 339.39 [M^+, 39.00%]; anal. calcd. for $C_{21}H_{17}N_5$: C, 73.32; H, 5.05; N, 20.63. Found: C, 73.30; H, 5.03; N, 20.61.

4,6-diamino-2-(4-bromophenyl)-1-phenyl-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (6c). Green solid; yield (50%); mp 356-358 ºC; IR (KBr) ν_{max} 3432, 3017 (NH_2, NH_2), 2338-2361 (CN, nitrile), 1593 (C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.27 (s, 2H, NH_2, D_2O exchangeable), 6.83 (s, 1*H*-pyrrole), 7.08-7.46 (m, 9H, Ar-H), 12.01 (s, 2H, NH_2, D_2O exchangeable); ^{13}C NMR (400 MHz, DMSO-d_6, δ ppm): 66.36, 103.01, 106.17, 120.68, 128.11-135.97, 150.23, 153.91, 158.86; EIMS m/z 404.66 [M^+, 32.20%]; anal. calcd. for $C_{20}H_{14}BrN_5$: C, 59.13; H, 3.97; N, 17.24. Found: C, 59.11; H, 3.95; N, 17.22.

General procedure for the synthesis of compounds 7a-c and 8a-c

The fusion of pyrrole derivatives **3a-c** (1 mmol) with either urea or thiourea (2 mmol) for 15 min yielded the corresponding pyrrolopyrimidine derivatives**7a-c** and **8a-c**, respectively.

4-Amino-6,7-diphenyl-1H-pyrrolo[2,3-d]pyrimidin-2(7H)-one (7a). Yellow solid; yield (53%); mp 264-266 ºC; ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm) 3.56 (s, 2H, NH_2, D_2O exchangeable), 6.77 (s, 1*H*-pyrrole), 6.99-7.43 (m, 10H, Ar-H), 10.82 (s, 1H, NH, D_2O exchangeable); EIMS m/z 302.33 [M^+, 23.11%]; anal. calcd. for $C_{18}H_{14}N_4O$: C, 71.51; H, 4.67; N, 18.53. Found: C, 71.50; H, 4.65; N, 18.50.

4-Amino-7-phenyl-6-(p-tolyl)-1H-pyrrolo[2,3-d]pyrimidin-2(7H)-one (7b). Buff solid; yield (55%); mp 310-312 ºC; IR (KBr) ν_{max} 3304, 3067 (NH, NH_2), 1721 (C=O), 1655 (C=N) cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, δ ppm): 2.29 (s, 3H, CH_3), 5.45 (s, 2H, NH_2, D_2O exchangeable), 6.95 (s, 1*H*-pyrrole), 7.00-7.36 (m, 9H, Ar-H), 11.54 (s, 1H, NH, D_2O exchangeable); ^{13}CNMR (500 MHz, DMSO-d_6, δ ppm): 20.29, 106.62, 127.02-128.68, 149.62, 155.10, 159.38; EIMS m/z 316.36 [M^+, 22.17%]; anal. calcd. for $C_{19}H_{16}N_4O$: C, 72.13; H, 5.10; N, 17.71. Found: C, 72.10; H, 5.00; N, 17.69.

4-Amino-6-(4-bromophenyl)-7-phenyl-1H-pyrrolo[2,3-d]pyrimidin-2(7H)-one (7c). Pale green solid; yield (56%); mp 324-326 ° C; IR (KBr) ν_{max} 3414, 3204 (NH, NH_2), 1661 (C=O), 1611 (C=N) cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, δ ppm): 3.50 (s, 2H, NH_2, D_2O exchangeable), 6.99 (s, 1*H*-pyrrole), 7.01-7.43 (m, 9H, Ar-H), 10.87 (s, 1H, NH, D_2O exchangeable); ^{13}CNMR (500 MHz, DMSO-d_6, δ ppm): 101.95, 127.35-134.33, 149.93, 155.33; EIMS m/z 381.53 [M^+, 29.60%]; anal. calcd. for $C_{18}H_{13}BrN_4O$: C, 56.71; H, 3.44; N, 14.70. Found: C, 56.70; H, 3.41; N, 14.68.

4-Amino-6,7-diphenyl-1H-pyrrolo[2,3-d]pyrimidine-2(7H)-thione (8a). Yellow solid; yield (47 %); mp 302-304 ºC; ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 3.50 (s, 2H, NH_2, D_2O exchangeable), 6.91 (s, 1*H*-pyrrole), 7.32-7.84 (m, 10H, Ar-H), 8.04 (s, 1H, NH, D_2O exchangeable); ^{13}CNMR (400 MHz, DMSO-d_6, δ ppm): 101.15, 102.75, 126.88-136.77, 152.18, 154.48, 155.63, 157.48; EIMS m/z 318.32 [M^+, 42.71%]; anal. calcd. for $C_{18}H_{14}N_4S$: C, 67.90; H, 4.43; N, 17.60. Found: C, 67.88; H, 4.40; N, 17.59.

4-Amino-7-phenyl-6-(p-tolyl)-1H-pyrrolo[2,3-d]pyrimidine-2(7H)-thione (8b). Buff solid; yield (45%); mp 320-321 ºC; IR (KBr) ν_{max} 3414, 3300 (NH, NH_2), 1661 (C=N), 1406 (C=S) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, δ ppm): 2.30 (s, 3H, CH_3), 5.486 (s, 2H, NH_2, D_2O exchangeable), 6.13 (s, 1*H*-pyrrole), 6.81-7.28 (m, 9H, Ar-H), 8.40 (s, 1H, NH, D_2O exchangeable); EIMS m/z 332.78 [M^+, 100%]; anal. calcd. for $C_{19}H_{16}N_4S$: C, 68.65; H, 4.85; N, 16.85. Found: C, 68.63; H, 4.83; N, 16.83.

*4-Amino-6-(4-bromophenyl)-7-phenyl-1H-pyrrolo[2,3-d]pyrimidine-2(7H)-thione (**8c**).* Buff solid; yield (48%); mp 330-332 ºC; IR (KBr) ν_{max} 3474, 3180 (NH, NH_2), 1580 (C=N), 1390 (C=S) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, δ ppm): 5.82 (s, 2H, NH_2, D_2O exchangeable), 6.52 (s, 1*H*-pyrrole), 7.20-7.46 (m, 9H, Ar-H), 12.03 (s, 1H, NH, D_2O exchangeable); ^{13}CNMR (400 MHz, DMSO-d_6, δ ppm): 101.95, 127.37-136.37, 149.94, 155.44, 157.82; EIMS m/z 397.29 [M^+, 20.00%]; anal. calcd. for $C_{18}H_{13}BrN_4S$: C, 54.42; H, 3.30; N, 14.10. Found: C, 54.40; H, 3.29; N, 14.08.

CONCLUSION

In conclusion, we have developed a practical synthesis pathway to access novel heterocyclic scaffolds with substituted pyrrolo[2,3-*b*]pyridine and pyrrolo[2,3-*d*]pyrimidine frameworks in a single pot. Furthermore, we illustrated the versatility of this multicomponent reaction by using simple non-cyclic with active methylene, urea, and thiourea substrates to obtain target compounds **4a–c**, **5a–c**, **6a–c**, **7a-c**, and **8a-c**. About 15 new compounds that can be used as organic and medicinal research substrates were synthesized.

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