Synthesis of New Heterocycles from Reactions of 1-Phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonyl Azides

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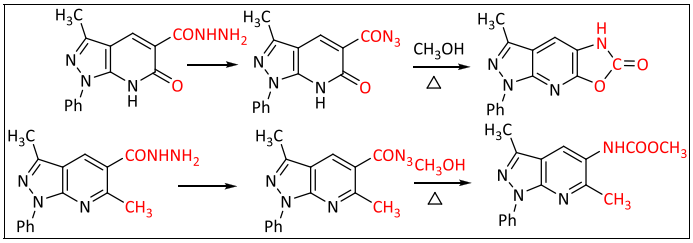

Two individual examples of pyrazolo[3,4-*b*]pyridine-5-carbonyl azides and hydrazides were reacted with various nucleophilic reagents. Different unexpected behaviors was observed. NMR, IR, mass spectra together with elemental analyses and X-ray structure analyses, were used to prove the structure of the obtained products.

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INTRODUCTION

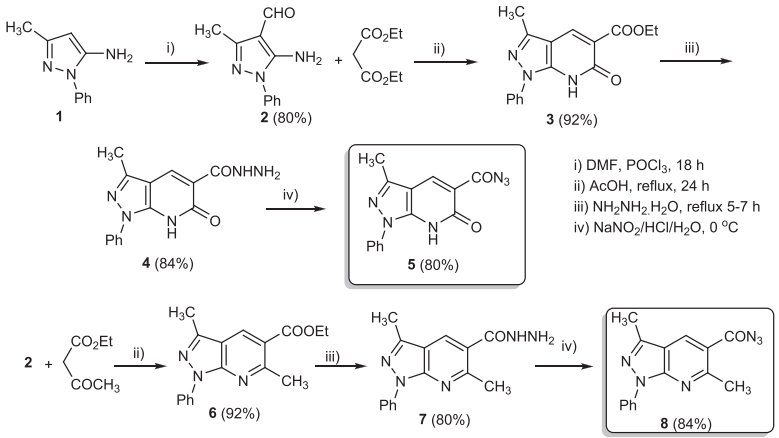
Among the various heterocyclic systems developed over the last centuries, nitrogen-containing heterocyclic compounds play a crucial role in the context of both chemistry and biology. Pyrazolo[3,4-*b*]pyridines belong to this important class of heterocyclic due to their relevance in medicinal chemistry [1,2] displayed by the diverse range of biological and pharmaceutical activities such as antitumor [3,4], antibacterial [5–7], anti-inflammatory [8], inhibitors of protein kinase [9], cyclin-dependent kinase 1 [10], glycogen synthase kinase-3 [11], and human immunodeficiency virus reverse transcriptase [12]. As an example, a rapid and convenient, environmentally benign synthesis of spiro-pyrazolo[3,4-*b*]pyridine derivatives was developed using a three-component coupling of isatin, cyclic-1,3-dione, and pyrazol-5-amine in aqueous ethanol using aluminosilicate nanoparticles as catalyst [13]. Previously, we also prepared various fused pyridine derivatives *via* the reaction of 2,4(1*H*,3*H*)-quinolinediones with diethyl acetylenedicarboxylate. This reaction furnished ethyl 5,6-dihydro-2,5-dioxo-2*H*-pyrano[3,2-*c*]quinoline-4-carboxylates while 2,4(1*H*,3*H*)-quinolinediones afforded dialkyl 2(4-oxo-1,4-dihydroquinolin-3-yl)fumarates in good yields [14]. Quinoline-2,4-diones were reacted with 2-(2-oxo-1,2-dihydroindol-3-ylidene)-malononitrile in pyridine to yield 2′-amino-2,5′-dioxo-5′,6′-dihydrospiro (indoline-3,4′-pyrano[3,2-*c*]quinoline)-3′-carbonitriles in good to excellent yields [15]. In continuation of our work on pyrazolo[3,4-*b*]pyridines [16–21], we aim in this work to synthesize fused heterocyclic systems containing pyrazolo[3,4-*b*]pyridine.

RESULTS AND DISCUSSION

The pyrazolo[3,4-*b*]pyridines **5** and **8** were prepared by the following sequences: The available 5-aminopyrazole **1** was formulated by the procedure described Häufel *et al.* [22] to give compound **2** (Scheme 1). The spectral data of **2** were reported earlier [23]. Synthesis of pyrazolo[3,4-*b*]pyridine-5-carboxylate (**3**) [23] was also achieved by its reaction with diethyl malonate in glacial acetic acid (Scheme 1).

The reaction of **3** with hydrazine hydrate produced the new compound **4** (Scheme 1). The elemental analysis and mass spectrum of **4** proved its molecular formula as $C_{14}H_{13}N_5O_2$. The ^{1}H NMR spectrum of **4** showed the NH_2, NH, and CH-pyridine protons at δ = 6.50, 9.40, and 8.10 ppm, respectively. In ^{13}C NMR spectrum of **4**, the carbonyl-carbons appeared δ = 165.0 and 164.2 ppm, respectively. Reaction of **4** with HNO_2 produced the corresponding 3-methyl-6-oxo-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonyl azide (**5**) (Scheme 1). Analogously, the new compound **8** was established *via* the reaction of **2** with ethyl acetoacetate to give compound **6** [22] in 92% yield (Scheme 1). The elemental analysis and mass spectrum of compound **6** corroborated its gross molecular formula as $C_{17}H_{17}N_3O_2$. The ester protons of **6**

Scheme 1. Strategy of the synthesis of pyrazolo[3,4-*b*]pyridines **5** and **8**.

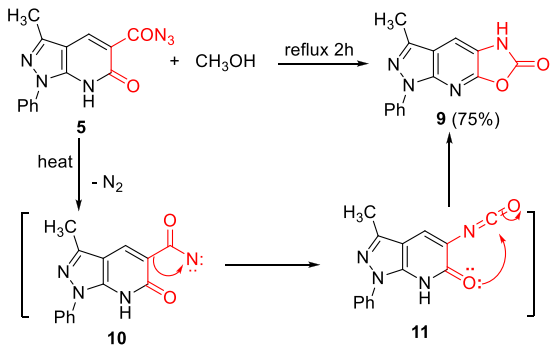


appeared in the ^{1}H NMR as a triplet (3H) and quartet (CH_2) at δ = 1.50 and 4.30 ppm, respectively. The carbonyl ester group resonated in the ^{13}C NMR of **6** at δ = 165.0, whereas the three methyl carbon signals were resonated in the ^{13}C NMR of **6** at δ = 12.4, 14.3, and 20.1 ppm for the methyl-ester, methyl-pyrazole, and methyl-pyridine carbon signals, respectively.

On subjecting compound **6** to the reaction with hydrazine hydrate, compound **7** was obtained in 80% yield (Scheme 1). The mass spectrum and elemental analysis of **7** indicated its molecular formula as $C_{15}H_{15}N_5O$, which is supported by the disappearance of ester carbon signals, and the appearance of the NH and NH_2 in the IR and ^{1}H NMR spectra was a further support of its structure. When compound **7** was reacted with nitrous acid, the target azide **8** was obtained in a good yield (Scheme 1). IR spectra of both carbonyl azides of pyrazolo[3,4-*b*] pyridines **5** and **8** showed resonances at ν = 2147 and 2140 cm^{-1}, respectively, which are characteristic for CON_3 groups. Besides, the disappearance of the bands characteristic for NH and NH_2 groups (see Experimental section) was observed.

Surprisingly, refluxing **5** with methanol for 2 h, a new compound, namely, **9**, was obtained (Scheme 2).

Scheme 2. Suggested mechanism describes the formation of **9**. [Color figure can be viewed at wileyonlinelibrary.com]



Elemental analysis and mass spectrum proved the molecular formula of **9** as $C_{14}H_{10}N_4O_2$. The ^{1}H NMR spectrum of **9** showed two singlets: one for NH at δ = 12.10 and the other for CH-4 at δ = 7.90. Figure 1 shows distinctive carbon atoms of compound **9**. ^{13}C NMR reveals the carbonyl carbon signal (C-6) at δ = 165.0, whereas CH-pyridine and methyl carbon signal were absorbed at δ = 132.0 (CH-4) and 12.4 (C-a), respectively (for detailed spectral data, see Experimental section). The structure of **9** was confirmed by X-ray structure analysis as shown in Figure 2. The mechanism that describes the formation of **9** was based upon elimination of N_2 molecule to give intermediate **10**, which was followed by Curtius rearrangement to give the isocyanate **11** (Scheme 2). Nucleophilic addition of the oxygen lone pair of the carbonyl group would form compound **9** (Scheme 2).

In a different manner, reaction of **8** with CH_3OH gave pyrazolo[3,4-*b*]pyridine-5-yl carbamate (**12**) in 80% yield (Scheme 3). The structure of **12** was confirmed by elemental and spectral data. The IR spectrum showed absorption band at *v* = 1684 cm^{-1} for the carbonyl-ester. Elemental analysis and mass spectrum proved the molecular formula of **12** as $C_{16}H_{16}N_4O_2$. The methyl protons of ester group appeared in the ^{1}H NMR of **12** as a singlet at δ = 3.40 ppm, whereas the carbonyl of the ester group appeared in the ^{13}C NMR spectrum at δ = 162.0 ppm. On reacting compound **8** with hydrazine hydrate in refluxing xylene, the reaction produced compound **13** (Scheme 3). The same compound **13** was

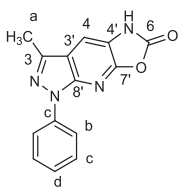


Figure 1. Distinctive carbon atoms of compound **9**.

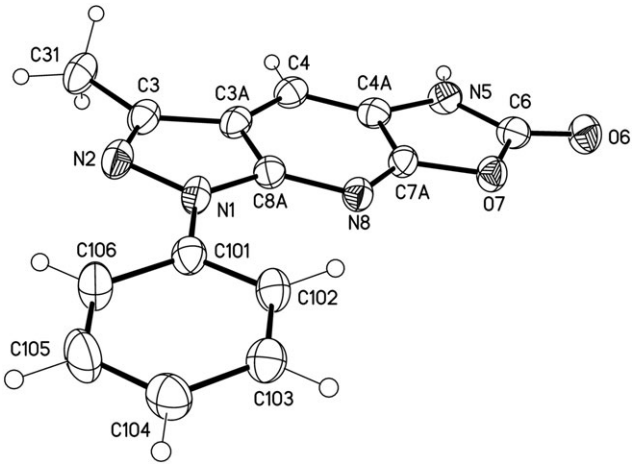
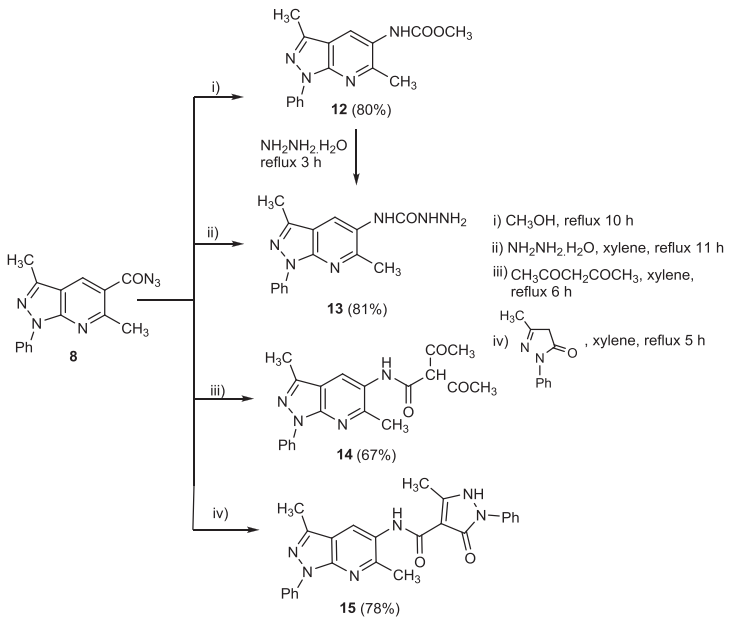


Figure 2. Molecular structure of one of the independent molecules of 3-methyl-1-phenyl-1,5-dihydro-6*H*-oxazolo[5,4-*b*]pyrazolo[4,3-*e*]pyridin-6-one (**9**). Displacement parameters are drawn at 50% probability level).

Scheme 3. Reactions of pyrazolo[3,4-*b*]pyridine **8** with various reagents.



obtained during reaction of **12** with hydrazine hydrate. The ^{1}H NMR spectrum of **13** revealed the two NH protons at δ = 9.10 and 8.20 ppm. The NH_2-hydrazine protons appeared together with the aromatic protons at δ = 7.24–7.18 ppm. The two methyl protons appeared at δ = 2.75 and 2.50 ppm. Reaction of **8** with acetylacetone yielded 2-acetyl-*N*-(3,6-dimethyl-1-phenyl-1*H*-pyrazolo[3,4-*b*] pyridin-5-yl)-3-oxobutanamide (**14**). The elemental analysis and mass spectrum of **14** indicated a molecular formula as $C_{20}H_{20}N_4O_3$. The ^{1}H NMR of compound **14** revealed the CH-proton at δ = 4.40 ppm, whereas the two acetyl protons appeared as one singlet for 6H at δ = 2.25 ppm. In ^{13}C NMR spectrum, the carbonyl of the acetyl group appeared at δ = 209.0, whereas the carbonyl of amide carbon appeared at δ = 163.0 ppm. Besides, the aliphatic-CH carbon resonates at δ = 96.0 ppm. On the other site, reaction of carboazide **8** with pyrazolone in boiling xylene gave the pyrazole-4-carboxamide **15** (Scheme 3). Compound **15** was verified by its IR, MS, ^{1}H NMR, ^{13}C NMR spectra, and elemental analysis. Thus, the IR spectrum showed absorption bands at δ = 3282 cm^{-1} for NH, 2919 cm^{-1} CH aliphatic, and 1685–1680 cm^{-1} for CO groups, respectively. The ^{1}H NMR spectrum showed three signals at δ = 2.20, 2.60, and 3.40 ppm characteristic for CH_3 pyrazole (A), CH_3 pyrazolone (B), and CH_3 pyridine (C). The $(CH_3)C{=}N$ carbon signal resonated in the ^{13}C NMR spectrum of **15** at δ = 155.2, whereas the carbonyl carbon signal of

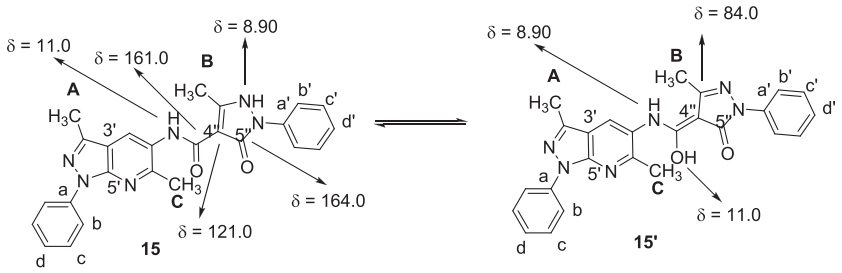


Figure 3. Distinctive protons and carbons of tautomerism forms of **15** and **15′**.

pyrazolone at δ = 164.0 ppm (see Experimental section). The tautomerism of compound **15** (Fig. 3) was confirmed by the appearance C-4″ by two values at δ = 84.0 in **15′** and at δ = 121.0 in **15** (Fig. 3). The carbon signal assigned to carbonyl amide in **15** appeared at δ = 161.0. In ^{1}H NMR spectrum, the tautomerism with the NH and OH protons were appeared at δ = 8.90 and 11.00 (Fig. 3). The three methyl carbon signals appeared at 17.8, 15.4, and 14.0 assigned to (CH_3-C), (CH_3-B), and CH_3-A), respectively.

CONCLUSION

That work reported the reactions of pyrazolo[3,4-*b*] pyridine-5-carbonyl azides and hydrazides with some nucleophilic reagents. It was observed that of carbonyl azide derivative of pyrazolo[3,4-*b*]pyridine-5-carbonyl azide undergo different reaction pathways—a Curtius rearrangement [24,25]—compared with related compounds. Different substituents could be prepared *via* functional groups manipulation.

EXPERIMENTAL

General. Melting points were determined using an APP Digital ST 15 melting point apparatus. Thin-layer chromatography analyses were performed on analytical Merck 9385 silica aluminum sheets (Kieselgel 60) with PF_{254} indicator. The IR spectra were recorded as KBr disks on Shimadzu-408 infrared spectrophotometer, Faculty of Science, Minia University. The NMR spectra were measured using a Bruker AV-400 spectrometer at the Karlsruhe Institut für Technologie, Institute of Organic Chemistry, Karlsruhe, Germany. Chemical shifts were expressed as δ (ppm) with tetramethylsilane as internal reference. The samples were dissolved in DMSO-d_6, s = singlet, d = doublet, dd = doublet of doublet, and t = triplet. Mass spectrometry were recorded on a Varian MAT 312 instrument in EI mode (70 eV) at the Karlsruhe Institut für Technologie, Institute of Organic Chemistry, Karlsruhe, Germany. Elemental analyses were carried out using Varian Elementary device in National Research Center, Giza, Egypt.

Starting materials. Compound **1** was bought from Aldrich. Compounds **2** and **3** were prepared according to literature procedures [22,23].

Compound **2** was obtained as pale yellow crystals in 70%; mp 98°C (lit. [23] 97.5°C); IR (KBr): ν_{max} 3350 (NH_2), 3090 (Ar—CH), 1660 (CO), 1615 (C=N), 1590 cm^{-1} (C=C); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.60 (s, 1H, CHO), 7.60–7.50 (m, 5H, Ph—H), 5.80 (bs, 2H, NH_2), 2.30 (s, 3H, CH_3).

On applying the same procedure mentioned in the literature [23], compound **3** was obtained in 75% yield; mp 286–288°C (lit. [23] 285°C); IR (KBr): ν_{max} 3320 (NH_2), 3080 (Ar—CH), 1660 (CO_2Et), 1615 (C=N), 1590 cm^{-1} (C=C); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.20 (s, 1H, NH), 8.20 (s, 1H, pyridine—H), 8.00–7.90 (t, 2H, *J* = 7 Hz, Ph—H), 7.42–7.30 (m, 3H, Ph—H), 4.40 (q, 2H, CH_2), 2.60 (s, 3H, CH_3), 1.40 (t, 3H, *J* = 7.0 Hz, CH_3).

6,7-Dihydro-3-methyl-6-oxo-1-phenyl-1H-pyrazolo[3,4-b] pyridine-5-carbohydrazide (4). A mixture of compound **3** (0.5 g, 1.68 mmol) in hydrazine hydrate (5 mL) was heated under reflux for 5 h. The solution was cooled, poured onto ice-cold water containing a few drops of acetic acid, filtered, washed with water, dried, and recrystallized from ethanol to give **4** as a yellow powder (0.40 g, 84%); mp 210–212°C; IR (KBr): ν_{max} 3340–3315 ($NHNH_2$), 3070 (Ar—CH), 2970 (Aliph—CH), 1680, 1650 (2CO), 1605 (CvN), 1580 cm^{-1} (C=C); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11:15 (s, 1H, NH—pyridine), 9.40 (s, 1H, NH), 8.10 (s, 1H, pyridine—H), 7.05–6.96 (m, 5H, Ph—H), 6.50 ppm (s, 2H, NH_2), 2.48 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.0, 164.2 (C=O), 160.3 (C=N), 139.6, 137.0 (Ar—C), 133.0 (pyridine—CH), 129.8, 126.0 (Ar—C), 127.9, 126.9 (Ar—2CH), 124.0 (Ar—H), 14.4 (CH_3) ppm. MS (70 eV, %): *m/z* 283 (M^+, 100), 161 (55), 77 (66). *Anal*. Calcd for $C_{14}H_{13}N_5O_2$ (283.29): C, 59.36; H, 4.63; N, 24.72. Found: C, 59.40; H, 4.60; N, 24.90%.

5-(Azidocarbonyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b] pyridin-6(7H)-one (5). A cold solution (0–5°C) of sodium

nitrite (0.319 g, 45 mmol) in 15 mL water was added to a suspension of **4** (0.952 g, 4 mmol) in 1M HCl (2 mL) in an ice bath (0–5°C) over a period of 30 min. The reaction mixture was left to stir for 1 h at the same temperature and then poured into excess water. The yellow precipitate was filtered off and washed thoroughly with water then dried and left without crystallization to give yellow powder **5** (0.90 g, 80%); mp 110–111°C; IR (KBr): ν_{max} 3100 (Ar—CH), 2950 (Aliph—CH), 2147 (CON_3), and 1632 (C=N) cm^{-1}.

Ethyl 3,6-dimethyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate (6). A mixture of **2** (0.5 g, 2.48 mmol) and ethyl acetoacetate (0.32 g, 2.48 mmol) in acetic acid (20 mL) was heated under reflux for 24 h. The solution was cooled, poured onto ice-cold water, filtered, washed with water, dried, and recrystallized from ethanol to give white powder **6** (0.67 g, 92%); mp 100–101°C (lit. [22] 101–103°C); IR (KBr): ν_{max} 2921 (Aliph—CH), 1712 cm^{-1} (CO-ester); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.30 (s, 1H, pyridine—H), 7.15–6.95 (m, 5H, Ph—H), 4.30 (q, 2H, J = 7.0 Hz, CH_2), 2.60 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 1.50 (t, 3H, J = 7.0, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.0 (C=O), 163.3, 161.0 (C=N), 139.0, 138.4 (Ar—C), 133.0 (pyridine—CH), 129.8, 126.0 (Ar—C), 127.9, 126.9 (Ar—2CH), 124.0 (Ar—CH), 62.0 (CH_2-ester), 20.1, 14.3, 12.4 (CH_3) ppm. MS (70 eV, %): *m/z* 295 (M^+, 100), 161 (55), 77 (66). *Anal*. Calcd for $C_{17}H_{17}N_3O_2$ (295.34): C, 69.14; H, 5.80; N, 14.23. Found: C, 69.30; H, 5.65; N, 14.10%.

3,6-Dimethyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbohydrazide (7). A mixture of the ester **6** (5.90 g, 20 mmol) and hydrazine hydrate (15 mL) was heated under reflux for 7 h. The product that formed was then poured into cold water, filtered, washed with water, dried, and crystallized from ethanol to give buff crystals of **7** (6.09 g, 80%); mp: 170–2°C; IR (KBr): ν_{max} 3428, 3288 (NH_2), 2970 (Aliph—CH), 1680 (CO); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 60 (bs, 1H, NH—hydrazine), 8.30 (s, 1H, pyridine—H), 7.40–7.30 (m, 5H, Ph—H), 5.90 (bs, 2H, NH_2—hydrazine), 2.56 (s, 3H, CH_3), 2.10 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3 (C=O), 160.6, 160.0 (C=N), 138.4, 138.0 (Ar—C), 132.6 (pyridine—CH), 129.4, 126.4 (Ar—C), 128.0, 126.7 (Ar—2CH), 124.2 (Ar—CH), 20.4, 16.1 (CH_3) ppm. MS (70 eV, %): *m/z* 281 (M^+, 100), 160 (45), 77 (60). *Anal*. Calcd for $C_{15}H_{15}N_5O$ (281.32): C, 64.04; H, 5.37; N, 24.90. Found: C, 63.90; H, 5.45; N, 25.00%.

Azido (3,6-dimethyl-1-phenyl-1H-pyrazolo[3,4-b]pyridin-5-yl)methanone (8). A cold solution (0–5°C) of sodium nitrite (0.32 g, 45 mmol) in 15 mL water was added to a suspension of carbohydrazide **7** (1.1 g, 4 mmol) in 1M HCl (2 mL) in an ice bath (0–5°C) over a period of 30 min. The reaction mixture was left to stir for 1 h at the same temperature and then poured into excess water. The yellow product was filtered off, washed with water, dried, and left without recrystallization to give **8** (0.95 g, 84%); mp 110–111°C; IR (KBr): ν = 2140 (CON_3) and 1699 cm^{-1} (CO).

3-Methyl-1-phenyl-1,5-dihydro-6H-oxazolo[5,4-b]pyrazolo[4,3-e]pyridin-6-one (9). A mixture of **5** (0.5 g, 1.7 mmol) and methanol (15 mL) was heated under gentle reflux for 2 h. The solution cooled, poured onto ice cold water, filtered, washed with water (100 mL), dried, and recrystallized from ethanol to give **9** (0.33 g, 75%) as yellow crystals; mp 270–272°C; IR (KBr): ν_{max} 3184 (NH), 3184 (Ar—CH), 2990 (Aliph—CH), 1680 (CO) cm^{-1}; ^{1}H NMR: (400 MHz, DMSO-d_6): δ = 12.10 (s, 1H, NH), 8.10 (dd, 2H, J = 7.2, 1.0 Hz, H-c), 7.90 (s, 1H, H-4), 7.30–7.28 (m, 2H, H-b), 7.20 (m, 1H, H-d), 2.50 (s, 3H, CH_3—pyrazole); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.0 (CO), 164.1 (C-7′), 150.2 (C-8′), 143.0 (C-4′), 141.0 (C-e), 138.2 (C-3), 132.0 (C-4), 127.8 (2CH-c), 123.4 (CH-d), 122.0 (2CH-b), 115.0 (C-3′), 12.4 (CH_3-a). MS (70 eV, %): *m/z* 266 (100%). *Anal*. Calcd for $C_{14}H_{10}N_4O_2$ (266.26): C, 63.15; H, 3.79; N, 21.04. Found: C, 63.00; H, 3.70; N, 21.20%.

Crystal structure determination of 9. The single-crystal X-ray diffraction study was carried out on a Bruker D8 Venture diffractometer with Photon100 detector at 123(2) K using Cu–Kα radiation (λ = 1.54178 Å). Dual space methods (SHELXT) [26] were used for structure solution, and refinement was carried out using SHELXL-2014 (full-matrix least-squares on F^2) [27]. Hydrogen atoms were refined using a riding model (H(N). A semi-empirical absorption correction was applied. Refinement with the listed atoms shows residual electron density due to a heavily disordered ethanol solvent that could not be refined with split atom model. In addition, there are traces of water. Therefore, the option "SQUEEZE" of the program package PLATON [28] was used to create an hkl file taking into account the residual electron density in the void areas.

9: Colorless crystals, $C_{14}H_{10}N_2O_4 \cdot 1/3(C_2H_6O)$, M_r = 281.61, crystal size 0.20 × 0.18 × 0.08 mm, triclinic, space group *P-1* (No. 2), a = 10.6979(3) Å, b = 14.3577(4) Å, c = 14.5395(4) Å, α = 68.818(1)°, β = 84.428(1)°, γ = 72.303(1)°, V = 1983.60(10) Å^3, Z = 6, ρ = 1.414 Mg/m^{-3}, μ (Cu–K$_\alpha$) = 0.825 mm^{-1}, F(000) = 880, $2\theta_{max}$ = 144.6°, 30117 reflections, of which 7760 were independent (R_{int} = 0.032), 553 parameters, 3 restraints, R_1 = 0.041 (for 6663 $I > 2\sigma(I)$), wR_2 = 0.108 (all data), S = 1.03, largest diff. peak/hole = 0.384/−0.218 e Å^{-3}.

CCDC 1840903 (**9**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge

Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Methyl 3,6-dimethyl-1-phenyl-1H-pyrazolo[3,4-b]pyridin-5-yl-carbamate (12). A mixture of **8** (0.29 g, 1 mmol) in methanol (50 mL) was heated under reflux for 10 h. The solution was cooled, poured onto ice-cold water, filtered, washed with water, dried, and recrystallized from ethanol/water (1:1) to give brown crystals of **12** (0.23 g, 80%); mp 180–181°C; IR (KBr): ν_{max} 3251 (NH), 3050 (Ar—CH), 2917 (Aliph—CH), 1684 (CO) cm^{-1}; IR (KBr): 3180 (NH), 3180 (Ar—CH), 2890 (Aliph—CH), 1684 (CO) cm^{-1}; ^{1}H NMR: (400 MHz, DMSO-d_6): δ = 9.10 (s, 1H, NH), 7.92 (s, 1H, H-4), 7.30–7.19 (m, 5H, Ar—H), 3.40 (s, 3H, CH_3-ester), 2.60 (s, 3H, CH_3), 2.30 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.0 (CO), 152.1, 151.20 (C═N), 138.0, 135.0, 133.1, 131.0, 130.0 (Ar—C), 128.2, 127.2 (Ar—2CH), 123.0 (Ar—CH-*p*), 25.4, 20.4, 15.9 ppm (CH_3). MS (70 eV, %): *m/z* 296 (100). *Anal*. Calcd for $C_{16}H_{16}N_4O_2$ (296.33): C, 64.85; H, 5.44; N, 18.91. Found: C, 64.80; H, 5.40; N, 19.00%.

N-(3,6-Dimethyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-yl) hydrazinecarboxamide (13). A mixture of methyl carboazide **8** (0.5 g, 1.7 mmol) and hydrazine hydrate (0.85 mL, 1.7 mmol) in xylene (50 mL) was heated under reflux for 11 h. The reaction mixture was poured onto petroleum ether, filtered, and washed with petroleum ether, recrystallized from DMF : water (4:1) to give buff crystals of **13** (0.50 g, 81%); mp 310–312°C; IR (KBr): ν_{max} 3230–2150 ($NHNH_2$), 3020 (Ar—CH), 2860 (Aliph—CH), 1680 (CO) cm^{-1}; ^{1}H NMR: (400 MHz, DMSO-d_6): δ = 9.10 (s, 1H, *N*H—hydrazine), 8.20 (s, 1H, NH), 8.00 (s, 1H, H-4), 7.48–7.44 (m, 2H, Ar—H), 7.24–7.18 (m, 5H, Ar—H, NH_2—hydrazine), 2.75 (s, 3H, CH_3), 2.60 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.0 (CO), 152.4, 151.5 (C═N), 143.0, 140.0 (Ar—C), 133.0 (CH-4), 130.0 (Ar—2CH), 128.8 (Ar—C), 124.0 (Ar—CH), 122.0 (Ar—2CH), 115.4 (Ar—CH-*p*), 25.0, 14.0 ppm (CH_3). MS (70 eV, %): 296 (100). *Anal*. Calcd for $C_{15}H_{16}N_6O$ (296.33): C, 60.80; H, 5.44; N, 28.36. Found: C, 60.70; H, 5.40; N, 28.40%.

Reaction of 8 with acetyl acetone: preparation of 2-acetyl-N-(3,6-dimethyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-yl-3-oxobutanamide (14). A mixture of carboazide **8** (0.5 g, 1.7 mmol) and acetylacetone (1.7 mmol) was heated under reflux for 6 h in xylene (20 mL). The reaction mixture was poured onto petroleum ether, filtered, and washed with petroleum ether. A buff precipitate was recrystallized from DMF : water (4:1) of **14** (0.32 g, 67%); mp 310–312°C; IR (KBr): ν_{max} 3230 (NH), 3010 (Ar—CH), 2870 (Aliph—CH), 1710–1680 (CO) cm^{-1}; ^{1}H NMR: (400 MHz, DMSO-d_6): δ = 8.90 (s, 1H, NH), 8.10 (s, 1H, H-4), 7.40–7.25 (m, 5H, Ar—H), 4.40 (s, 1H, CH—), 2.50 (s, 3H, CH_3), 2.25 (s, 6H, CH_3), 2.18 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 209.0 (2CO), 163.0 (CO), 153.0, 152.0 (C═N), 142.0, 138.0 (Ar—C), 129.7 (Ar—2CH), 128.4 (CH-4), 127.0, 126.0 (Ar—C), 119.0 (Ar—2CH), 115.4 (Ar—CH-*p*), 96.0 (CH), 22.4 ($2CH_3$), 13.2, 12.2 ppm (CH_3). MS (70 eV, %): *m/z* = 364 (100), 263 (65), 237 (80). *Anal*. Calcd for $C_{20}H_{20}N_4O_3$ (364.40): C, 65.92; H, 5.53; N, 15.38. Found: C, 65.90; H, 5.50; N, 15.43%.

N-(3,6-Dimethyl-1-phenyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazole-4-carboxamide (15). A mixture of carboazide **8** (0.25 g, 0.85 mmol) and 1-phenyl-3-methyl-5-pyrazolone (0.15 g, 0.86 mmol) was heated in xylene under reflux for 5 h. The reaction mixture was then poured onto petroleum ether, filtered, and recrystallized from dioxane to give buff powder **15** (0.28 g, 78%); mp 330–332°C; IR (KBr): ν_{max} 3450 (OH), 3282 (NH), 3030 (Ar—CH), 2919 (Aliph—CH), 1680 (CO) cm^{-1}; ^{1}H NMR: (400 MHz, DMSO-d_6): δ = 11.0 (s, 1H, OH (NH)), 8.90 (s, 1H, NH (OH)), 8.10 (s, 1H, H-4), 7.50–7.30 (m, 6H, Ar—H), 7.40–7.25 (m, 4H, Ar—H), 3.40 (s, 3H, CH_3—pyrazolone), 2.60 (s, 3H, CH_3—pyrazole), 2.20 (s, 3H, CH_3—pyridine); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.0 (CO—pyrazolone), 161.0 (CO—amide), 153.4, 151.2, 150.0 (C═N), 137.7, 135.0, 133.2 (Ar—C), 132.8 (CH-4), 130.6, 130.0 (Ar—C), 128.6, 128.0, 127.6, 126.7 (Ar—2CH), 122.4, 122.2 (Ar—CH-*p*), 121.0 (C-4″), 80.0 (C-4′-pyrazolone), 17.8 (CH_3-C), 15.4 (CH_3-B), 14.0 (CH_3-A) ppm (CH_3). MS (70 eV, %): *m/z* 438 (100), 397 (43), 345 (75), 306 (80), 288 (40). *Anal*. Calcd for $C_{25}H_{22}N_6O_2$ (438.49): C, 68.48; H, 5.06; N, 19.17. Found: C, 68.60; H, 5.16; N, 19.30%.

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