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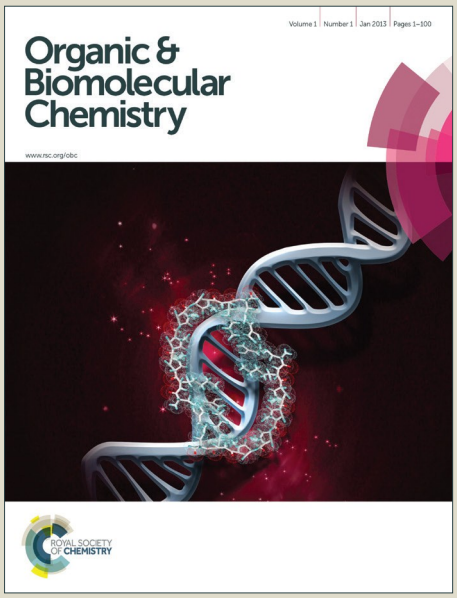

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ARTICLE

Tandem copper (Cu) catalysed *N*-arylation—vinylogous nitroaldol condensation of 3,5-disubstituted 4-nitropyrazoles†‡

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Owk Obulesu,[a,b] Jagadeesh Babu Nanubolu,[c] and Surisetti Suresh[a,b]*

A tandem process involving copper catalysed *N*-arylation and vinylogous nitroaldol condensation is described. The reaction of 3,5-dialkylsubstituted 4-nitropyrazoles and *ortho*-halo substituted (hetero)aryl aldehyes or ketones furnished 3-nitropyrazolo[1,5-*a*]quinoline and heteroaryl-fused 3-nitropyrazolo[1,5-*a*]pyridine derivatives in moderate to high yields.

Introduction

Tandem reactions have attracted greater attention in organic synthesis in recent years.[1] Indeed, Robinson's seminal work, about a century ago, on the total synthesis of tropinone describes the power of tandem reaction processes in organic synthesis.[2] These processes offer the construction of complex molecules in an efficient manner.[3] Transition metals and catalysts thereof have been used extensively to perform tandem reactions.[4] Among the transition metal catalysts, copper catalysts have received a great deal of attention due to their availability and inexpensiveness.[5] *N*-arylation reaction catalysed by copper[6] has attracted significant interest due to the reason that *N*-aryl linkage is an integral part of several therapeutic molecules.[7] Tandem reactions triggered by copper catalysed *N*-arylation followed by condensations offer the synthesis of a variety of *N*-heterocycles[8] which are potential compounds for applications in biology and medicine. The condensation reactions in these processes include imine or aldol or Knoevenagel condensations wherein nucleophile that participates in the condensation being a primary amine group[8a-l] or an active α-methylene group.[8a,8m-q]

We envisaged to develop a tandem process involving copper catalysed *N*-arylation—vinylogous nitroaldol[9] condensation[9b] using substrates of type **A** and *ortho*-halo (hetero)aryl carbonyl compounds **B** (Figure 1). The model substrate **A** contains the essential functionalities like *NH* for *N*-arylation and an active γ-methylene group, activated by a nitro group through conjugation, to participate in the vinylogous nitroaldol condensation reaction.

Figure 1 Strategy for tandem copper catalysed *N*-arylation—vinylogous nitroaldol condensation process.

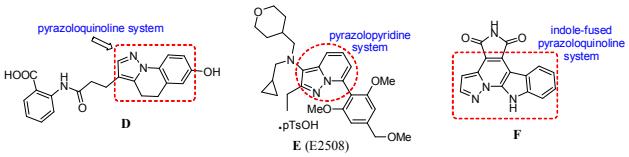

Figure 2 Biologically active *N*-fused pyrazoloquinoline and pyrazolopyridine derivatives.

This process would furnish the corresponding quinoline or heteroaryl-fused pyridine systems **C** containing the nitro group that could be useful for further functional group transformation. Employment of suitable *NH*-heterocycles such as pyrazoles in this process would lead to the synthesis of *N*-fused pyrazoloquinoline or heteroaryl- and *N*-fused pyrazolopyridine derivatives that are valuable compounds in medicinal chemistry.[10] For instance, *N*-fused pyrazoloquinoline derivative **D** act as GPR109A agonist agent.[10h] Pyrazolo[1,5-*a*]pyridine **E** has been proved to possess excellent drug properties and advanced into clinical trials for the treatment of stress related disorders.[10j] Indole-fused pyrazolopyridine derivative **F** was shown to be potent anticancer agent (Figure 2).[10k]

Results and Discussion

We have identified readily available *NH*-heterocycle such as 3,5-dimethyl-4-nitropyrazole **1a** as a suitable substrate to test the proposed tandem copper catalysed *N*-arylation—vinylogous nitroaldol condensation (Table 1). The substrate **1a** contains the required *NH* group for *N*-arylation and an active 5-methyl group, activated by 4-nitro group through conjugation, for the vinylogous nitroaldol condensation.

[a] *Organic and Biomolecular Chemistry Division, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad, 500007, India. E-mail: surisetti@iict.res.in*
[b] *Academy of Scientific and Innovative Research (AcSIR), CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad, 500007, India.*
[c] *Center for X-ray Crystallography, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad, 500007, India.*

† This work is dedicated to Professor Mariappan Periasamy

‡ Electronic Supplementary Information (ESI) available: Experimental procedures, spectral data, copies of NMR spectra for products, CIF of **3a** (CCDC 1052135) and **5a** (CCDC 1057420), see DOI: 10.1039/x0xx00000x

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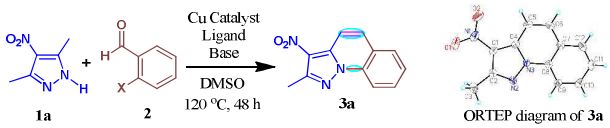
Table 1 Optimization survey for the reaction of **1a** and **2**[a]



Entry	X	Catalyst	Ligand	Base	Yield **3a**[b]
1	Br	CuI	Ethylenediamine	K_2CO_3	40
2	Br	CuI	(L)-Proline	K_2CO_3	33
3	Br	CuI	BINOL	K_2CO_3	17
4	**Br**	**CuI**	**Neocuproine**	**K_2CO_3**	**91 (84)**[c]
5	Br	CuBr	Neocuproine	K_2CO_3	18
6	Br	$Cu(OTf)_2$	Neocuproine	K_2CO_3	29
7	Br	CuI	Neocuproine	$NaHCO_3$	85
8	Br	CuI	Neocuproine	K_3PO_4	22
9	Cl	CuI	Neocuproine	K_2CO_3	17
10	I	CuI	Neocuproine	K_2CO_3	49

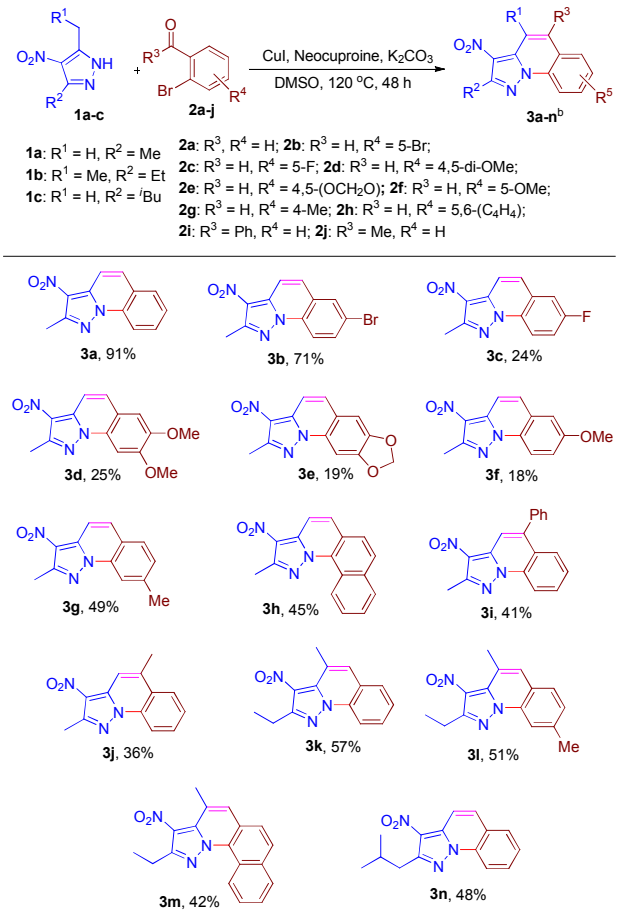
a. Reaction conditions: **1a** (0.5 mmol), **2** (0.5 mmol), Cu catalyst (0.05 mmol), ligand (0.1 mmol), base (1.65 mmol), DMSO (2 mL); b. Yields are for isolated products; c. Reaction was run at 10 mmol scale.

Initially, we have performed the reaction of **1a** and 2-bromobenzaldehyde **2a** in DMSO using CuI as a catalyst, ethylenediamine as a ligand and K_2CO_3 as a base. Gratifyingly, this reaction has resulted in the formation of the expected 2-methyl-3-nitropyrazolo[1,5-*a*]quinoline **3a** in 40% isolated yield (Table 1, entry 1). The X-ray crystallographic analysis of the product **3a** confirmed its structure (for an ORTEP diagram, see Table 1).[11] We have then screened several copper catalysts, ligands, bases and solvents (Table 1, entries 1-8) for this reaction—it turned out that the combination of CuI-neocuproine-K_2CO_3 in DMSO proved the best to provide the compound **3a** in excellent yield (Table 1, entry 4). *It is noteworthy that this combination enabled to scale up the reaction to a gram scale (1.9 g, 84%, Table 1, entry 4)*. It was also observed that either copper catalyst-base combination or base alone did give the product **3a** albeit in significantly lower yields. In the presence of CuI-ligand and in the absence of base the formation of the product **3a** was not observed (see supporting information for a detailed optimization survey). Among the *ortho*-halobenzaldehydes, 2-bromobenzaldehyde gave the best isolated yield of product **3a** (Table 1, entries 4, 9 and 10).

Having the set of optimized conditions in hand, we next turned to extend the scope of this tandem process with respect to 3,5-disubstituted 4-nitropyrazoles and *ortho*-bromo substituted aryl aldehydes or ketones. The results are summarized in Scheme 1.

The reaction of **1a** and 2,5-dibromobenzaldehyde **2b** gave good yield of the corresponding pyrazolo[1,5-*a*]quinoline product **3b**. Whereas the reaction of **1a** and 2-bromo-5-fluorobenzaldehyde **2c** gave low yield of the corresponding pyrazolo[1,5-*a*]quinoline product **3c**. The reaction of **1a** and 2-bromobenzaldehydes **2d-g**, bearing electron donating substituents, gave low to moderate yields of the corresponding pyrazolo[1,5-*a*]quinoline products **3d-3g**.

Scheme 1 Reaction scope for the synthesis of pyrazolo[1,5-*a*]quinoline derivatives[a]



a. Reaction conditions: **1** (0.5 mmol), **2** (0.5 mmol), CuI (0.05 mmol), neocuproine (0.1 mmol), K_2CO_3 (1.65 mmol), DMSO (2 mL); b. Yields are for isolated products.

The reaction of **1a** and 2-bromo-1-naphtaldehyde **2h** furnished benzo-fused pyrazolo[1,5-*a*]quinoline product **3h** in moderate yield. Use of sterically hindered *ortho*-bromo carbonyl compounds **2i-j** afforded the corresponding pyrazoloquinolines **3i-j** in reasonable yields. 3,5-Dialkyl substituted 4-nitropyrazoles **1b-c** were employed in this copper catalyzed tandem *N*-arylation-vinylogous nitroaldol condensation process to give the corresponding pyrazolo[1,5-*a*]quinoline products **3k**-**3n**.

We then turned our focus to subject *ortho*-halo heteroaryl carbonyl compounds and 3,5-dialkyl substituted 4-nitropyrazoles in the tandem copper catalysed *N*-arylation—vinylogous nitroaldol condensation process that would deliver heteroaryl-fused 3-nitropyrazolo[1,5-*a*]pyridine derivatives. The results are summarized in Table 2.

The reactions of **1a-c** with 2-chloro-1-methyl-1*H*-indole-3-carbaldehyde **4a** afforded the corresponding tetracyclic indole-fused pyrazolo[1,5-*a*]pyridine systems **5a-c** in high yields (Table 2, entries 1-3). The structure of the product **5a** was revealed by X-ray crystallographic analysis (for an ORTEP diagram, see Table 2).[12]

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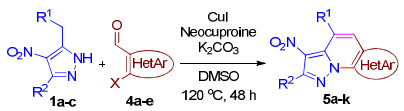
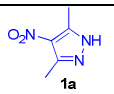
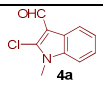
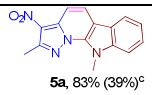
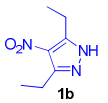
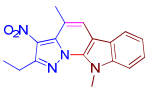
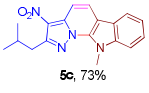
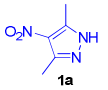
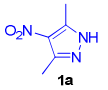
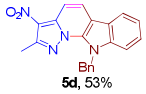
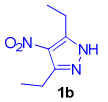
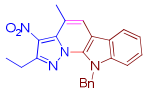
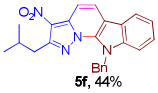
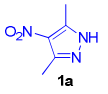
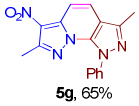
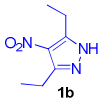
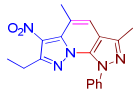
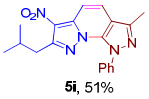
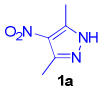
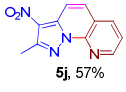
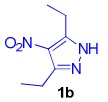
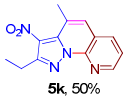
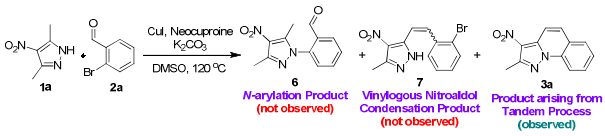
Table 2 Reaction of 3,5-dialkyl substituted 4-nitropyrazoles **1a-c** and *ortho*-halo heteroaryl aldehydes **4a-e**[a]

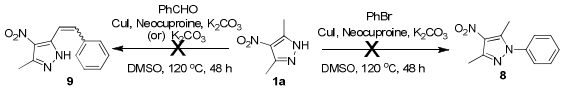


Entry	Substrate **1**	Substrate **4**	Product **5**, yield[b]
1			 **5a**, 83% (39%)[c]
2			 **5b**, 77%
3			 **5c**, 73%
4			—
5			 **5d**, 53%
6			 **5e**, 46%
7			 **5f**, 44%
8			 **5g**, 65%
9			 **5h**, 63%
10			 **5i**, 51%
11			 **5j**, 57%
12			 **5k**, 50%

a. Reaction conditions: **1** (0.5 mmol), **4** (0.5 mmol), CuI (0.05 mmol), neocuproine (0.1 mmol), K_2CO_3 (1.65 mmol), DMSO (2 mL); b. Yields are for isolated products; c. The reaction was performed using only K_2CO_3.



Scheme 2 Control experiments



Scheme 3 Attempted individual *N*-arylation and vinylogous nitroaldol condensation of **1a**

It is important to note that the reaction of **1a** and **4a** in the absence of copper catalyst provided the corresponding adduct **5a** in 39% yield only. This reaction may be explained by a nucleophilic aromatic substitution (S_NAr) reaction via an addition-elimination process.[6q,r] However, the reaction of **1a** and **4b** did not give the desired product by using the combination of CuI-neocuproine-K_2CO_3. The *N*-arylation—vinylogous nitroaldol condensation of **1a-c** with benzyl substituted 2-chloro-1*H*-indole-3-carbaldehyde **4c** furnished the corresponding indole-fused pyrazolo[1,5-*a*]pyridine derivatives **5d-f** in moderate yields (Table 2, entries 5-7). The reactions of **1a-c** and 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde **4d** provided the corresponding dipyrazole-fused pyridine derivatives **5g-i** in good yields (Table 2, entries 8-10). The reactions of 2-bromo-3-pyridinecarbaldehyde **4e** and **1a-1b** afforded the corresponding pyridine-fused pyrazolo[1,5-*a*]pyridine derivatives **5j-5k** in good yields (Table 2, entries 11-12).

It was thought that the present tandem copper catalysed *N*-arylation—vinylogous nitroaldol condensation reaction would involve the intermediates **6** or **7** that could result from the sole *N*-arylation or sole vinylogous nitroaldol condensation, respectively (Scheme 2). We have monitored the reaction of 3,5-dimethyl-4-nitropyrazole **1a** and 2-bromobenzaldehyde **2a** by TLC and ESI-MS at different intervals under the reaction conditions to find out whether the formation of intermediates **6** or **7** takes place or not. It was observed that the formation of product **3a** only occurred in this reaction. But no mass peaks (ESI-MS) were observed that correspond to either of the products **6** or **7**.

We have also conducted few experiments to perform *N*-arylation and vinylogous nitroaldol condensation separately using **1a** with suitable substrates. It is important to note that simple *N*-aylation of **1a** using bromobenzene did not give the corresponding *N*-arylated product **8** under the reaction conditions (Scheme 3).[6j,k] The unsuccessful *N*-arylation may be due to the reasons that (i) 3,5-dimethyl-4-nitropyrazole is a weak *N*-nucleophile due to the conjugation of *NH* with 4-nitro group, and or (ii) lack of *ortho*-coordinating group in the bromobenzene. The reaction of **1a** and benzaldehyde did not give the expected condensation product **9** (Scheme 3). In this case 5-methyl group of **1a** may not be enough acidic, due to the presence of *NH* group, to undergo vinylogous nitroaldol condensation with benzaldehyde. Hence it may be noted that the present tandem process is triggered by copper-catalysed *N*-arylation of **1** with the assistance of carbonyl group of **2** (or **4**) and the carbonyl group would participate in the vinylogous nitroaldol condensation to culminate the process.

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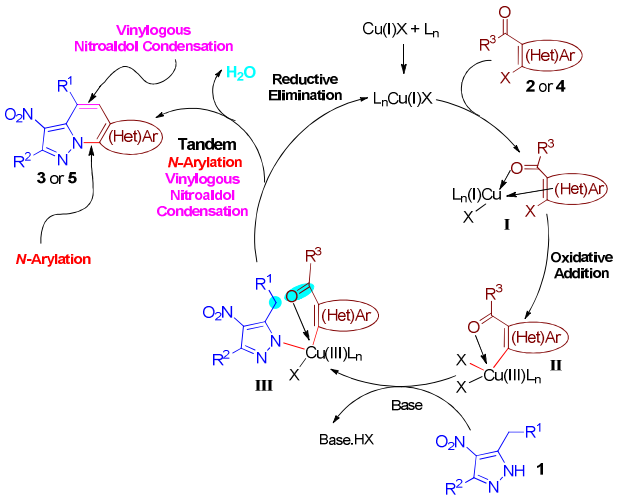
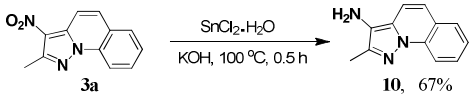


Scheme 4 Plausible mechanism



Scheme 5 Reduction of nitro group of **3a**

Considering the above control experiments and literature reports, a plausible mechanism can be proposed for the formation of **3** or **5** in the present tandem copper catalysed *N*-arylation—vinylogous nitroaldol condensation. It has been reported that suitable *ortho*-substituents promote copper-catalysed *N*-arylations.[8h,l,n] Initially, coordination of *ortho*-halo (hetero)aryl carbonyl compound (**2** or **4**) with copper catalyst would give intermediate **I**. Oxidative addition of the intermediate **I** lead to the formation of intermediate **II**. Complexation of **II** with **1** may provide intermediate **III**, in the presence of base. The ensuing intermediate **III** on reductive elimination would give the products **3** or **5** via tandem *N*-arylation—vinylogous nitroaldol condensation (Scheme 4).

The reduction of nitro group of **3a** using $SnCl_2$ afforded the corresponding 2-methylpyrazolo[1,5-a]quinolin-3-amine**10** in 67% yield (Scheme 5).

Conclusions

In summary, we have developed and demonstrated a new tandem reaction process involving copper catalysed *N*-arylation—vinylogous nitroaldol condensation between 3,5-dialkylsubstituted 4-nitropyrazoles and *ortho*-halo substituted (hetero)aryl aldehydes or ketones. This process furnished 3-nitropyrazolo[1,5-*a*]quinoline and heteroaryl-fused 3-nitropyrazolo[1,5-*a*]pyridine derivatives in moderate to high yields. Further studies on the exploration and exploitation of tandem processes involving arylation/addition—cyclisation is an ongoing research work in our laboratory.

Experimental

General

Reactions were carried out in oven dried reaction flasks or screw-cap vials. Solvents and reagents were transferred by oven-dried syringes at ambient temperature. Analytical thin layer chromatography (TLC) was performed on Merck glass or aluminium sheets pre-coated with silica gel 60 F_{254} by using UV as a visualizing agent (or) a 0.5% aqueous potassium permanganate solution—heat (or) iodine as developing agents. Solvents were removed under reduced pressure. Column chromatography was performed using silica gel (60-120 or 100-200 or 230-400 mesh). The elution was assisted by applying pressure with an air pump. Melting points reported in this work are uncorrected and were determined using a Superfit capillary point apparatus. The IR spectra were recorded on a Bruker FT-IR spectrophotometer by dissolving the sample in chloroform. IR (KBr) spectra were recorded on a Thermo Nicolet NEXUS 670 FT-IR instrument. ^{1}HNMR spectra were recorded on 300 and 500 MHz spectrometers in appropriate solvents and chemical shifts are referenced to TMS via residual solvent signals. The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet. ^{13}C NMR spectra were recorded on 75 and 125 MHz spectrometers. The mass spectral analyses were carried out using Electrospray Ionization (ESI) techniques. Mass spectra were obtained on a Shimadzu LCMS-2020 mass spectrometer and high resolution mass spectra (HRMS) were recorded on a Thermo Scientific Exactive™ Orbitrap Mass Spectrometer or QSTAR XL Hybrid MS/MS mass spectrometer. X-ray data for compounds **3a** and **5a** were collected at room temperature using the Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα radiation (λ=0.71073Å) with ω-scan method. All reactions were performed using freshly distilled and dried solvents wherever it was necessary. All solvents were distilled using standard procedures. Unless otherwise noted, starting materials, catalysts, ligands and reagents were obtained from commercial suppliers (Aldrich, Alfa Aesar, and TCI) and those were used without further purification.

Synthesis of pyrazoles 1a-c

Pyrazoles **1a-c** were prepared by following literature reports.[13]

ortho-Halo heteroaryl aldehydes 4a-d

5-Chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde **4d** was prepared according to the reported procedure.[14] 2-Chloro-1*H*-indole-3-carbaldehyde **4b** was prepared following the same procedure as for **4d** by using indolin-2-one. The compound **4b** was subjected to alkylation using methyl iodide and benzyl bromide in the presence of sodium hydride in DMF to obtain 2-chloro-1-methyl-1*H*-indole-3-carbaldehyde **4a** and 1-benzyl-2-chloro-1*H*-indole-3-carbaldehyde **4c**, respectively.

General procedure for the synthesis of 3a-n

3,5-Dialkyl-4-nitro-1*H*-pyrazole **1a-c** (0.5 mmol), CuI (9.5 mg, 0.05 mmol), K_2CO_3 (227 mg, 1.65 mmol), neocuprione (21 mg, 0.1 mmol) and dimethyl sulfoxide (2 mL) were added into a 10 mL screw cap vial. The reaction mixture was stirred at room temperature for 30 min, followed by the addition of *o*-halo aryl aldehyde or ketone **2a-j**

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(0.5 mmol). The reaction mixture was stirred at 120 ^{o}C for 48 h. The reaction mixture was cooled to room temperature, diluted with water, extracted with ethyl acetate (2 x 20 mL), dried over anhydrous Na_2SO_4 and filtered. The solvent was removed in vacuo to afford a crude residue. The residue was purified by flash column chromatography (hexane/EtOAc) on silica gel to obtain pyrazolo[1,5-*a*]quinoline derivatives **3a-n**.

2-Methyl-3-nitropyrazolo[1,5-*a*]quinoline 3a:- yellow solid, 103 mg, 91%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 192-194 ^{o}C; IR ($CHCl_3$) 742, 1214, 1431, 1515, 3019 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 2.85 (s, 3H), 7.60-7.63 (m, 1H), 7.81-7.84 (m, 1H), 7.90-7.94 (m, 2H), 8.26 (d, *J* = 9.5 Hz, 1H), 8.64 (d, *J* = 8.5 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 14.7, 115.6, 116.1, 123.9, 126.4, 128.7, 131.2, 131.3, 133.2, 133.4, 135.7, 149.9; MS (ESI) m/z 228 $[M+H]^+$ 250 $[M+Na]^+$; HRMS (ESI, m/z): calcd for $C_{12}H_{10}N_3O_2$ $[M+H]^+$ 228.07635, found 228.07675.

7-Bromo-2-methyl-3-nitropyrazolo[1,5-*a*]quinoline 3b:- light green solid, 109 mg, 71%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 3:97); MP 220-222 ^{o}C; IR ($CHCl_3$) 668, 771, 1463, 1514, 2921, 3015 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 2.84 (s, 3H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.89-7.90 (dd,J_1 = 2.0 Hz, J_2 = 9 0 Hz, 1H), 8.06 (d, *J* = 2.0 Hz, 1H), 8.29 (d, *J* = 9.5 Hz, 1H), 8.52 (d, *J* = 9.0 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 14.6, 116.9, 117.9, 119.9, 125.2, 125.8, 129.9, 130.8, 132.2, 134.3, 135.5, 150.2; MS (ESI) m/z 305 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{12}H_9O_2N_3Br$ $[M+H]^+$ 305.9799, found 305.98784.

7-Fluoro-2-methyl-3-nitropyrazolo[1,5-a]quinoline 3c:- yellow solid 29 mg, 24%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 180-182 ^{o}C; IR ($CHCl_3$) 742, 1214, 1531, 1693, 3019 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 2.84 (s, 3H), 7.54-7.61 (m, 2H), 7.86 (d, *J* = 9.0 Hz, 1H), 8.30 (d, *J* =9.0 Hz, 1H), 8.62-8.67 (m, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 14.6, 113.1, 113.2, 116.9, 118.4 (9.0 Hz), 120.0 (25.2 Hz), 125.0, 130.0, 130.3, 149.9; MS (ESI) m/z 246 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{12}H_9O_2N_3F$ $[M+H]^+$ 246.06757, found 246.06005.

7,8-Dimethoxy-2-methyl-3-nitropyrazolo[1,5-*a*]quinoline 3d:- yellow solid, 36 mg, 25%, R_f = 0.3 (EtOAc/hexane, 50:50) Column Chromatography (EtOAc/hexane, 25:75); MP 232-234 ^{o}C; IR ($CHCl_3$) 772, 1218, 1514, 2852, 2922 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 2.84 (s, 3H), 4.04 (s, 3H), 4.15 (s, 3H), 7.21 (s, 1H), 7.84 (d, *J* = 9.0 Hz, 1H), 8.02 (s, 1H), 8.16 (d, *J* = 9.3 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 14.7, 56.3, 56.7, 97.2, 107.6, 113.6, 118.4, 129.1, 130.3, 131.6, 135.2, 149.0, 150.0, 153.3; MS (ESI) m/z 288 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{14}H_{14}O_4N_3$ $[M+H]^+$ 288.09061, found 288.09722.

2-Methyl-3-nitro-[1,3]dioxolo[4,5-*g*]pyrazolo[1,5-*a*]quinoline 3e:- yellow solid, 26 mg, 19%, R_f = 0.5 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 212-214 ^{o}C; IR ($CHCl_3$) 752, 1215, 1467, 1514, 2852, 2921 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 2.82 (s, 3H), 6.19 (s, 2H), 7.19 (s, 1H), 7.79 (d, *J* = 9.3 Hz, 1H), 8.03 (s, 1H), 8.14 (d, *J* = 9.0 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 14.7, 95.9, 102.5, 105.2, 113.6, 119.8, 130.6, 135.4, 147.4, 150.1, 151.6; MS (ESI) m/z 272 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{13}H_{10}O_4N_3$ $[M+H]^+$ 272.05931, found 272.06648.

7-Methoxy-2-methyl-3-nitropyrazolo[1,5-a]quinoline 3f:- yellow solid 23 mg, 18%, R_f = 0.3 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 198-200 ^{o}C; IR ($CHCl_3$) 741, 1215, 1420, 1516, 3019 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 2.82 (s, 3H), 3.96 (s, 3H), 7.23 (d, *J* = 2.5 Hz, 1H), 7.42 (dd, J_1 = 2.5 Hz, J_2 = 9.5 Hz, 1H), 7.84 (d, *J* = 9.5 Hz, 1H), 8.22 (d, *J* = 9.5 Hz, 1H), 8.52 (d, *J* = 9.0 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 14.6, 55.8, 108.5, 116.1, 117.6, 121.5, 125.2, 128.3, 130.7, 134.7, 149.7, 157.9; MS (ESI) m/z 258 $[M+H]^+$ HRMS (ESI, m/z): calcd for $C_{13}H_{12}O_3N_3$ $[M+H]^+$ 258.08732, found 258.08783.

2,8-Dimethyl-3-nitropyrazolo[1,5-*a*]quinoline 3g:- yellow solid, 59 mg, 49%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 198-200 ^{o}C; IR ($CHCl_3$) 772, 1219, 1499, 1510, 2852, 2922 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 2.63 (s, 3H), 2.83 (s, 3H), 7.42 (d, *J* =8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 9.0 Hz, 1H), 8.17 (d, *J* =9.5 Hz, 1H), 8.42 (s, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 14.7, 22.2, 114.5, 115.6, 121.8, 128.1, 128.4, 131.2, 133.3, 135.8, 142.5, 149.8; MS (ESI) m/z 242 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{13}H_{12}O_2N_3$ $[M+H]^+$ 242.08513 found 242.09259.

2-Methyl-3-nitrobenzo[*h*]pyrazolo[1,5-*a*]quinoline 3h:- yellow solid, 62 mg, 45%, R_f = 0.5 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 222-224 ^{o}C; IR ($CHCl_3$) 772, 1218, 1511, 2852, 2921 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 2.98 (s, 3H), 7.80-7.90 (m, 3H), 7.98 (d, *J* = 9.0 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 8.09 (d, *J* = 9.0 Hz, 1H), 8.53 (d, *J* = 9.0 Hz, 1H), 10.71 (d, *J* = 8.5 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 14.9, 115.7, 123.1, 124.0, 125.4, 127.7, 128.1, 128.3, 128.5, 128.6, 130.2, 131.8, 134.9, 137.7, 149.6; MS (ESI) m/z 278 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{16}H_{12}O_2N_3$ $[M+H]^+$ 278.09240, found 278.09254.

2-Methyl-3-nitro-5-phenylpyrazolo[1,5-*a*]quinoline 3i:- white solid, 62 mg, 41%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 220-222 ^{o}C; IR ($CHCl_3$) 772, 1219, 1498, 1677 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 2.87(s, 3H), 7.53-7.58 (m, 6H), 7.81-7.85 (m, IH), 7.91 (d, *J* = 8.5 Hz, 1H), 8.22 (s, 1H), 8.73 (d, *J* = 8.5 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 14.8, 115.5, 116.3, 123.3, 126.2, 127.7, 128.8, 128.9, 129.6, 131.1, 133.5, 135.2, 137.4, 144.2, 150.1; MS (ESI) m/z 304 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{18}H_{14}O_2N_3$ $[M+H]^+$ 304.10078, found 304.10847.

2,5-Dimethyl-3-nitropyrazolo[1,5-*a*]quinoline 3j:- white solid, 43 mg, 36%, R_f = 0.7 (EtOAc/hexane, 0.5:9.5) Column Chromatography (EtOAc/hexane, 2:98); MP 208-210 ^{o}C; IR ($CHCl_3$) 772, 1219, 1515, 1709, 3019 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 2.77 (s, 3H), 2.82 (s, 3H), 7.61-7.64 (m, 1H), 7.79-7.85 (m, 1H), 8.01 (d, *J* = 8.1 Hz, 1H), 8.12 (s, 1H), 8.65 (d, *J* = 8.4 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 14.7, 19.6, 115.0, 116.3, 124.1, 124.8, 125.3, 126.2, 130.9, 132.9, 135.4, 139.8, 149.8; MS (ESI) m/z 242 $[M+H]^+$ HRMS (ESI, m/z): calcd for $C_{13}H_{12}O_2N_3$ $[M+H]^+$ 242.09240, found 242.09266.

2-Ethyl-4-methyl-3-nitropyrazolo[1,5-*a*]quinoline 3k:- yellow solid, 73 mg, 57%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography

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(EtOAc/hexane, 5:95); MP 196-198 °C; IR ($CHCl_3$) 743, 1214, 1420, 1531, 3019 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 1.44 (t, *J* = 7.5 Hz, 3H), 2.76 (s, 3H), 3.17 (q, *J* = 7.5 Hz, 2H), 7.53-7.56 (m, 1H), 7.59 (s, 1H), 7.71.7.74 (m, 1H), 7.77 (d, *J* =8.0 Hz, 1H), 8.62 (d, *J* =8.5 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 12.4, 21.5, 21.9, 116.2, 123.6, 125.8, 126.2, 127.1, 127.5, 130.0, 130.5, 132.5, 134.9, 154.4; MS (ESI) m/z 256 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{14}H_{14}O_2N_3$ $[M+H]^+$ 256.10805 found, 256.10807.

2-Ethyl-4,8-dimethyl-3-nitropyrazolo[1,5-*a*]quinoline 3l:- yellow solid, 69 mg, 51%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 176-178 °C; IR ($CHCl_3$) 743, 1214, 1420, 1531, 3019 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 1.45 (t, *J* = 7.5 Hz 3H), 2.60 (s, 3H), 2.73 (s, 3H), 3.17 (q, *J* = 7.5 Hz, 2H), 7.35-7.37 (m, 1H), 7.54 (s, 1H), 7.65 (d, *J* =8.0 Hz, 1H), 8.42 (s, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 12.6, 21.4, 21.9, 22.1, 115.7, 121.5, 124.6, 127.3, 127.9, 130.5, 132.5, 135.1, 141.0, 154.4; MS (ESI) m/z 270 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{15}H_{16}O_2N_3$ $[M+H]^+$ 270.12374, found 270.12370.

2-Ethyl-4-methyl-3-nitrobenzo[*h*]pyrazolo[1,5-*a*]quinoline 3m:- yellow solid, 64 mg, 42%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 228-230 °C; IR ($CHCl_3$) 753, 1411, 1645, 2824, 2946, 3329 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 1.58-1.60 (m, 3H), 2.83 (s, 3H), 3.31 (q, *J* = 7.5 Hz, 2H), 7.74-7.78 (m, 3H), 7.85 (t, *J* = 7.5 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 10.69 (d, *J* = 8.5 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 12.2, 21.2, 22.0, 122.6, 124.0, 124.7, 125.8, 127.5, 127.8, 127.9, 128.1, 128.6, 131.7, 134.5, 136.6, 153.7; MS (ESI) m/z 306 $[M+H]^+$ HRMS (ESI, m/z): calcd for $C_{18}H_{16}O_2N_3$ $[M+H]^+$ 306.12370, found 306.12278.

2-Isobutyl-3-nitropyrazolo[1,5-a]quinoline 3n:- light yellow solid, 65 mg, 48%, R_f = 0.6 (EtOAc/hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 178-180 °C; IR ($CHCl_3$) 770, 1214, 2853, 2922, 3019 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.05 (d, *J* = 6.0 Hz, 6H), 2.25-2.34 (m, 1H), 3.13 (d, *J* = 7.5 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.82 (t, *J* = 7.5 Hz, 1H), 7.89-7.94 (m, 2H), 8.28 (d, *J* = 9.3 Hz, 1H), 8.67 (d, *J* = 8.4 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ =22.6, 27.7, 36.8, 115.8, 116.2, 124.0, 126.4, 128.6, 131.2, 133.3, 152.8; MS (ESI) m/z 270 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{15}H_{16}O_2N_3$ $[M+H]^+$ 270.12370, found 270.12320.

General procedure for the synthesis of 5a-k

General procedure for the synthesis of **3a-n** was followed by using 3,5-dialkyl-4-nitro-1*H*-pyrazole **1a-c** and *o*-halo heteroaryl aldehyde **4a-d**.

2,10-Dimethyl-3-nitro-10*H*-pyrazolo[1',5':1,6]pyrido[2,3-*b*]indole 5a:- yellow solid, 116 mg 83%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 258-260 °C; IR ($CHCl_3$) 772, 1219, 1507, 1626, 1644, 2920 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 2.85 (s, 3H), 4.59 (s, 3H), 7.43-7.40 (m, 1H), 7.54-7.58 (m, 2H), 8.05 (d, *J* = 7.5 Hz, 1H), 8.09 (d, *J* = 9.0 Hz, 1H), 8.26 (d, *J* = 9.0 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ =15.0, 32.6, 107.7, 109.9, 119.9, 121.3, 122.0, 125.5, 125.9, 134.7, 137.6, 138.4, 151.4; MS (ESI) m/z 281 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{15}H_{13}O_2N_4$ $[M+H]^+$ 281.10330, found 281.10323.

2-Ethyl-4,10-dimethyl-3-nitro-10*H*-pyrazolo[1',5':1,6]pyrido[2,3-*b*]indole 5b:- yellow solid, 119 mg 77%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 186-188 °C; IR ($CHCl_3$) 771, 1215, 1514, 3019 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 1.46 (t, *J* = 7.5 Hz, 3H), 2.79 (s, 3H), 3.19 (q, *J* = 7.5 Hz, 2H), 4.57 (s, 3H), 7.36-7.39 (m, 1H), 7.52-7.54 (m, 2H), 7.96 (s, 1H), 8.02 (d, *J* = 7.5 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 12.1, 21.2, 22.2, 32.6, 109.2, 109.8, 117.7, 119.8, 121.1, 121.5, 125.5, 126.2, 133.6, 136.5, 138.4, 155.9; MS (ESI) m/z 309 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{17}H_{17}O_2N_4$ $[M+H]^+$309.13460, found 309.13350.

2-Isobutyl-10-methyl-3-nitro-10*H*-pyrazolo[1',5':1,6]pyrido[2,3-*b*]indole 5c:- yellow solid, 118 mg, 73%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 182-184 °C; IR ($CHCl_3$) 771, 1216, 1530, 2853, 2925, 3019 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 1.08 (d, *J* = 6.5 Hz, 6H), 2.31-2.39 (m, 1H), 3.16 (d, *J* = 7.0 Hz, 2H), 4.60 (s, 3H), 7.40-7.43 (m, 1H), 7.56 (d, *J* = 4.0 Hz, 2H), 8.06-8.08 (m, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 8.28 (d, *J* = 9.0 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 22.7, 27.5, 32.6, 37.1, 107.9, 109.9, 110.1, 120.0, 121.1, 121.4, 121.9, 125.5, 125.8, 134.8, 137.9, 138.3, 154.2; MS (ESI) m/z 323 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{18}H_{19}O_2N_4$ $[M+H]^+$ 323.15025, found 323.15094.

10-Benzyl-2-methyl-3-nitro-10*H*-pyrazolo[1',5':1,6]pyrido[2,3-*b*]indole 5d:- yellow solid, 94 mg, 53%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 210-212 °C; IR ($CHCl_3$) 742, 1213, 1408, 1519, 1626, 3019 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 2.81 (s, 3H), 6.40 (s, 2H), 7.21-7.25 (m, 3H), 7.27-7.29 (m, 2H), 7.38-7.42 (m, 1H) 7.46-7.49 (m, 1H), 7.50-7.52 (m, 1H), 8.07 (d, *J* = 7.5 Hz, 1H), 8.15 (d, *J* = 9.0 Hz, 1H), 8.30 (d, *J* = 9.0 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 15.0, 48.8, 108.1, 110.3, 110.9, 112.0, 120.0, 121.6, 122.3, 125.4, 126.0, 126.9, 127.7, 128.8, 134.2, 136.8, 137.8, 151.5; MS (ESI) m/z 357 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{21}H_{17}O_2N_4$ $[M+H]^+$ 357.13460, found 357.13426.

10-Benzyl-2-ethyl-4-methyl-3-nitro-10*H*-pyrazolo[1',5':1,6]pyrido-[2,3-*b*]indole 5e:- yellow solid, 88 mg, 46%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 208-210 °C; IR ($CHCl_3$) 742, 1214, 1517, 3019 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 1.37 (t, *J* = 7.2 Hz, 3H), 2.81 (s, 3H), 3.16 (q, *J* = 7.6 Hz, 2H), 6.36 (s, 2H), 7.18-7.22 (m, 2H), 7.22-7.24 (m, 2H), 7.24-7.26 (m, 1H), 7.35-7.39 (m, 1H), 7.44-7.48 (m, 1H), 7.51-7.54 (m, 1H), 7.99 (s, 1H), 8.03 (d, *J* = 8.0 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 12.0, 21.2, 22.2, 48.8, 109.5, 110.7, 118.2, 119.9, 121.4, 121.7, 125.7, 126.1, 126.9, 127.6, 128.7, 133.2, 136.5, 137.4, 138.1, 155.9; MS (ESI) m/z 385 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{23}H_{21}O_2N_4$ $[M+H]^+$ 385.16590, found 385.16571.

10-Benzyl-2-isobutyl-3-nitro-10*H*-pyrazolo[1',5':1,6]pyrido[2,3-*b*]indole 5f:- yellow solid, 87 mg 44%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 206-208 °C; IR ($CHCl_3$) 771, 1216, 1464, 1713, 2912, 3019 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 0.97 (d, *J* = 6.5 Hz, 6H), 2.22-2.30 (m, 1H), 3.10 (d, *J* = 7.0 Hz, 2H), 6.38 (s, 2H), 7.20-7.25 (m, 5H), 7.39-7.42 (m, 1H), 7.47-7.51

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(m, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 8.18 (d, *J* = 9.0 Hz, 1H), 8.32 (d, *J* = 9.0 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 22.6, 27.3, 37.1, 48.9, 108.6, 110.4, 110.7, 199.9, 121.9, 122.0, 125.4, 126.0, 126.9, 127.7, 128.7, 137.0, 137.9, 154.3; MS (ESI) m/z 399 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{24}H_{23}O_2N_4$ $[M+H]^+$ 399.18155, found 399.18233.

3,7-Dimethyl-6-nitro-1-phenyl-1*H*-dipyrazolo[1,5-a:4',3'-*e*]pyridine 5g:- white solid, 100 mg 65%, R_f = 0.6 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 240-242 °C; IR ($CHCl_3$) 771, 1596, 1622, 2921, cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 2.67 (s, 6H), 7.48-7.57 (m, 3H), 7.60-7.67 (m, 2H), 7.90 (d, *J* = 8.7 Hz, 1H), 8.11 (d, *J* = 9.6 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 12.3, 14.9, 110.5, 113.1, 125.0, 126.7, 128.4, 128.6, 134.3, 138.0, 138.3, 145.4, 150.7; MS (ESI) m/z 308 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{16}H_{14}O_2N_5$ $[M+H]^+$ 308.11420, found 308.11421.

7-Ethyl-3,5-dimethyl-6-nitro-1-phenyl-1H-dipyrazolo[1,5-a:4',3'-*e*]pyridine 5h:- yellow solid, 105 mg 63%, R_f = 0.6 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 178-180 °C; IR ($CHCl_3$) 772, 1219, 1484, 1743, 2923 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.19 (t, *J* = 7.5 Hz, 3H), 2.63 (s, 3H), 2.72 (s, 3H), 3.00 (q, *J* = 7.5 Hz, 2H), 7.46-7.53 (m, 3H), 7.56 (s, 1H), 7.60-7.63 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 11.3, 12.2, 21.1, 21.7, 112.2, 120.5, 124.5, 126.9, 128.1, 128.3, 133.5, 136.6, 138.6, 144.4, 154.9; MS (ESI) m/z 336 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{18}H_{18}O_2N_5$ $[M+H]^+$ 336.14550, found 336.14562.

7-Isobutyl-3-methyl-6-nitro-1-phenyl-1*H*-dipyrazolo[1,5-a:4',3'-*e*]pyridine 5i:- yellow solid, 89 mg, 51%, R_f = 0.5 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 180-182 °C; IR ($CHCl_3$) 771, 1215, 1505, 2852, 2955 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 0.95 (d, *J* = 6.6 Hz, 6H), 2.04-2.16 (m, 1H), 2.68 (s, 3H), 2.96 (d, *J* = 6.9 Hz, 2H), 7.47-7.54 (m, 3H), 7.60-7.66 (m, 2H), 7.90 (d, *J* = 9.3 Hz, 1H), 8.11 (d, *J* = 9.3 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 12.2, 22.5, 26.9, 36.8, 110.6, 112.9, 124.9, 126.8, 128.3, 128.6, 138.0, 138.3, 145.3, 153.3; MS (ESI) m/z 350 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{19}H_{20}O_2N_5$ $[M+H]^+$ 350.16115, found 350.16241.

2-Methyl-3-nitropyrazolo[1,5-*a*][1,8]naphthyridine 5j:- light yellow solid, 65 mg 57%, R_f = 0.4 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 240-242 °C; IR ($CHCl_3$) 774, 1214, 1406, 1516,3019 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 2.93 (s, 3H), 7.66-7.70 (m, 1H), 7.93 (d, *J* = 9.5 Hz, 1H), 8.33 (dd, J_1 =8.0 Hz, J_2 =80 Hz, 1H), 8.36 (d, *J* = 9.5 Hz, 1H), 9.04 (s, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 14.7, 117.0, 118.9, 122.7, 130.2, 137.6, 137.7, 143.2, 151.0, 152.1; MS (ESI) m/z 229 $[M+H]^+$ HRMS (ESI, m/z): calcd for $C_{11}H_9O_2N_4$ $[M+H]^+$ 229.07200, found 229.07190.

2-Ethyl-4-methyl-3-nitropyrazolo[1,5-*a*][1,8]naphthyridine 5k:- yellow solid, 64 mg, 50%, R_f = 0.6 (EtOAc/Hexane, 1:9) Column Chromatography (EtOAc/hexane, 5:95); MP 230-232 °C; IR ($CHCl_3$) 741, 1214, 1432, 1514, 3019 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 1.43 (t, *J* = 7.5 Hz, 3H), 2.76 (s, 3H), 3.21 (q, *J* = 7.0 Hz, 2H), 7.53 (s, 1H), 7.55-7.59 (m, 1H), 8.16 (d, J_1 =8.0 Hz, 1H), 8.92 (m, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 13.1, 21.2, 21.7, 118.5, 122.5, 127.4, 128.2, 128.9, 136.4, 142.4, 151.0, 155.4; MS (ESI) m/z 257 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{13}H_{13}O_2N_4$ $[M+H]^+$ 257.10330, found 257.10302.

Synthesis of 2-Methylpyrazolo[1,5-*a*]quinolin-3-amine 10

Reduction of nitro group[15] of 2-methyl-3-nitropyrazolo[1,5-*a*]quinoline **3a**: Compound **3a** (113 mg, 0.5 mmol) was suspended in water (10 mL) and added a 3.5 M KOH (10 mL) solution. To this mixture, solid $SnCl_2{\cdot}2H_2O$ (0.5 g, 2 mmol) was then added portion-wise. The reaction mixture was stirred at 100 °C and monitored by TLC. After 0.5 h, the compound 3a disappeared (by TLC). The reaction mixture was cooled to room temperature and insoluble material was filtered. The filtrate was extracted with chloroform (2 x 20 mL) and the organic phase was washed with brine (5 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated to get the product, 2-methylpyrazolo[1,5-a]quinolin-3-amine 10 without any further purification.

2-Methylpyrazolo[1,5-*a*]quinolin-3-amine 10:- yellow solid, 66 mg, 67%, R_f = 0.3 (EtOAc/hexane, 50:50) Column Chromatography (EtOAc/hexane, 40:60); MP 164-166 °C; IR (KBr) 764, 1218, 2853, 2923, 3423 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 2.47 (s, 3H), 7.18-7.22 (m, 1H), 7.23-7.25 (m, 1H), 7.31-7.35 (m, 1H), 7.55-7.60 (m, 1H), 7.64-7.67 (m, 1H), 8.40 (d, J_1 = 8.0 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 14.7, 115.7, 116.0, 123.9, 126.4, 128.7, 131.2, 131.3, 133.4, 135.8, 149.9; MS (ESI) m/z 198 $[M+H]^+$; HRMS (ESI, m/z): calcd for $C_{12}H_{12}N_3$ $[M+H]^+$ 198.10257, found 198.10239.

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11 Crystal data for **3a**: $C_{12}H_9N_3O_2$, *M* = 227.22, Pale Yellow Needle, 0.48 x 0.15 x 0.06 mm^3, orthorhombic, space group *Pbca* (No. 61), *a* = 7.4947(11), *b* = 13.0618(18), *c* = 21.098(3) Å, *V* = 2065.4(5) $Å^3$, *Z* = 8, D_c = 1.461 g/cm^3, F_{000} = 944, CCD area detector, MoKα radiation, λ = 0.71073 Å, *T* = 293(2)K, $2\vartheta_{max}$ = 49.9º, 18250 reflections collected, 1809 unique (R_{int} = 0.0403), Final *GooF* = 1.399, *R1* = 0.0840, *wR2* = 0.1622, *R* indices based on 1709 reflections with I >2σ(I) (refinement on F^2), 155 parameters, μ = 0.104 mm^{-1}. CCDC 1052135 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.

12 Crystal data for **5a**: $C_{15}H_{12}N_4O_2$, *M* = 280.29, brown needle, 0.43 x 0.18 x 0.09 mm^3, triclinic, space group $P\bar{1}$ (No. 2), a = 7.1508(10), b = 9.6154(14), c = 10.0654(14) Å, *α* = 82.965(2), *β* = 70.019(2), γ = 87.230(2)°, V = 645.50(16) $Å^3$, *Z* = 2, *Dc* = 1.442 g/cm^3, F_{000} = 292, CCD area detector, MoKα radiation, λ = 0.71073 Å, T = 293(2)K, $2\vartheta_{max}$ = 50.0º, 6234 reflections collected, 2269 unique (R_{int} = 0.0252), Final *GooF* = 1.155, R1 = 0.0568, wR2 = 0.1339, R indices based on 1968 reflections with I >2σ(I) (refinement on F^2), 192 parameters, μ = 0.100 mm^{-1}. CCDC 1057420 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.

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