ACS OMEGA

Article

Cite This: ACS Omega 2018, 3, 18783−18790

http://pubs.acs.org/journal/acsodf

Unanticipated Cleavage of 2-Nitrophenyl-Substituted *N*-Formyl Pyrazolines under Bechamp Conditions: Unveiling the Synthesis of 2-Aryl Quinolines and Their Mechanistic Exploration via DFT Studies

Gaurav Joshi,[†] Aabid Abdullah Wani,[‡] Sahil Sharma,[§] Priyadeep Bhutani,[∥,⊥] Prasad V. Bharatam,[‡] Atish T. Paul,[∥] and Raj Kumar*[,†,§]

[†]Department of Pharmaceutical Sciences and Natural Products, Central University of Punjab, Bathinda 151001, Punjab, India

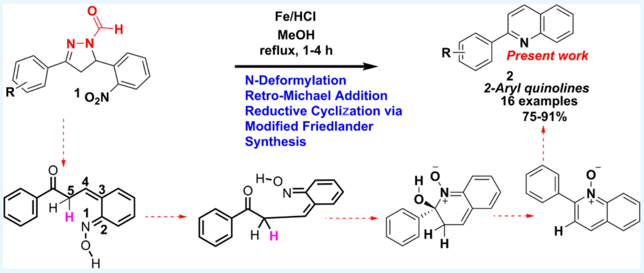
[‡]Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), S.A.S. Nagar, Mohali 160062, India

[§]Department of Pharmaceutical Chemistry, ISF College of Pharmacy, Moga 142001, India

[∥]Laboratory of Natural Product Chemistry, Department of Pharmacy, Birla Institute of Technology and Science, Pilani (BITS Pilani), Pilani Campus, Pilani 333031, Rajasthan, India

Supporting Information

ABSTRACT: We herein report for the first time an unusual decomposition of 2-nitrophenyl-substituted *N*-formyl pyrazolines under Bechamp reduction condition employed to yield 2-aryl quinolines exclusively instead of pyrazolo[1,5-*c*]-quinazolines. The reaction investigation suggests acid-mediated cleavage of **1** followed by a retro-Michael addition, and a subsequent in situ intramolecular reductive cyclization through a modified Friedlander mechanism afforded 2-aryl quinolines (**2**) in good yields. The proposed mechanistic pathways were supported via experimental evidence and density functional theory studies. B3LYP/6-31+G(d) analysis indicated the involvement of trans-2-hydroxyaminochalcone as a key intermediate and its isomerization and cyclization, leading to unusual product formation.



INTRODUCTION

2-Pyrazoline and its derivatives such as *N*-alkanoyl/aroylpyrazolines find wide applications[1] as medicinal agents,[2] possess optical properties,[3] act as chemosensors in bioimaging,[4] and serve as synthetic intermediates.[5] A few literature reports are available on decomposition of 1-pyrazoline[6] (**a**) under thermal and photochemical conditions, which leads to the formation of (Scheme 1i) cyclopropane (**c**) via 1,3-biradical[6a] (**b**) and the formation and extrusion of nitrogen gas (Scheme 1ii).[6b] Bicyclic divinyl-1-pyrazoline (**d**) underwent ring cleavage under similar conditions into a mixture of products (**e**−**g**) via a common diradical intermediate (Scheme 1iii).[7] Thermal decomposition of spiro-1-pyrazolines (**h**) afforded *S*-methylbenxylidenes (**i** and **j**) and spiro-cyclopropanes (**k** and **l**) (Scheme 1iv).[8] Although 2-pyrazoline unlike its isomer 1-pyrazoline is quite stable, it has been found to undergo ring cleavage under thermal condition, e.g., decomposition (Scheme 1v) of 3-aroyl-4-aryl-2-pyrazolines (**m**) yielded 3-alkylchalcone (**n**) along with the formation of cyclopropane (**c**).[9]

Recently, we have reported the one-pot synthesis of pyrazolo[1,5-*c*]quinazoline **3** by reductive cyclocondensation of 2-nitrophenyl-substituted *N*-formyl pyrazolines (**1**) under basic conditions[10] (Scheme 2). To the best of our knowledge, metal-promoted ring cleavage of *N*-formyl-2-pyrazolines under acidic condition is not previously described. We herein for the first time disclose iron-catalyzed, acid-mediated cleavage of *N*-formyl pyrazolines leading to the synthesis of 2-aryl quinolines via retro-Michael addition and subsequent in situ reductive cyclocondensation via the modified Friedlander mechanism (Scheme 2).

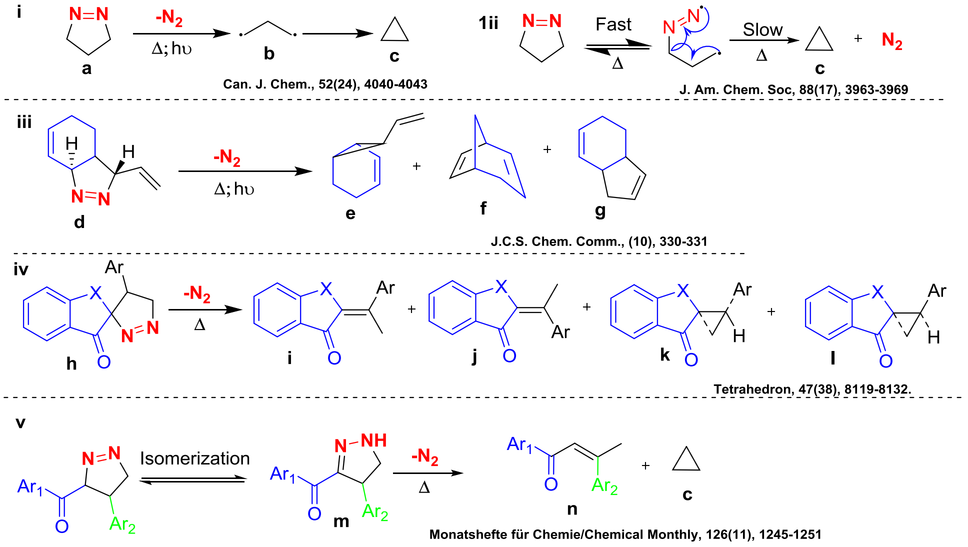
RESULTS AND DISCUSSION

As metals under acidic conditions are very frequently employed to reduce the aromatic nitro group,[11] we selected **1a** as the model substrate (Scheme 3) and carried out the reaction in MeOH at reflux for 2 h under Bechamp reduction condition[12] involving Fe (3 equiv)/HCl (0.5 equiv). To our surprise, the reaction ended with the synthesis of 2-aryl quinoline as major product (isolated yield of **2a**: 91%). Further to get better insight into metal and acidic conditions under Bechamp conditions, we treated **1a** with permutation and combination of various metals and Brønsted acids (Fe, Sn, Zn, Pd in HCl, H_2SO_4, CH_3COOH, trifluroacetic acid (TFA))

Received: October 7, 2018
Accepted: December 19, 2018
Published: December 28, 2018

DOI: 10.1021/acsomega.8b02682
ACS Omega 2018, 3, 18783−18790

Scheme 1. Reported Literature on Ring Cleavage of Pyrazolines



Can. J. Chem., 52(24), 4040-4043

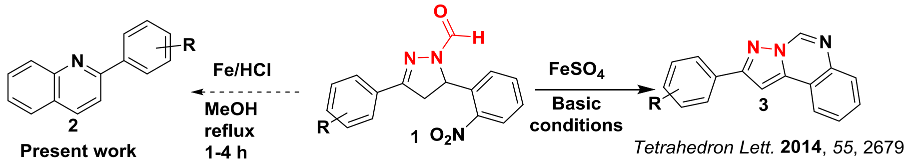
J. Am. Chem. Soc, 88(17), 3963-3969

J.C.S. Chem. Comm., (10), 330-331

Tetrahedron, 47(38), 8119-8132.

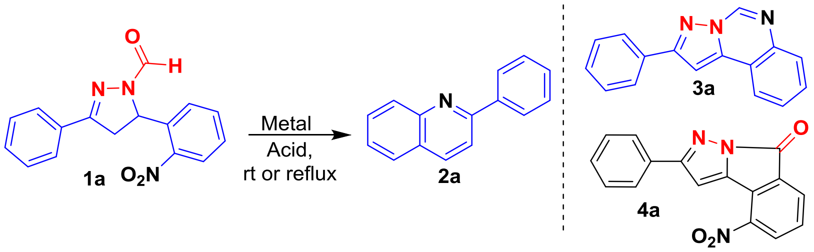
Monatshefte für Chemie/Chemical Monthly, 126(11), 1245-1251

Scheme 2. Synthetic Route of 2-Aryl Quinolines (2) and Previous Reported Work for the Synthesis of Pyrazolo[1,5-*c*]quinazoline (3)



Tetrahedron Lett. **2014**, *55*, 2679

Scheme 3. Synthesis of 2a under Various Conditions

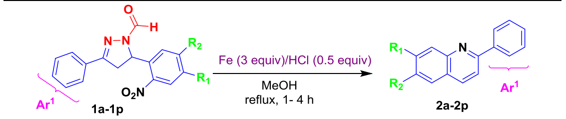


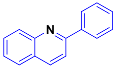
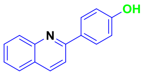
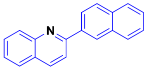
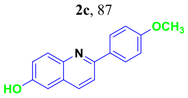
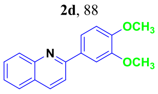
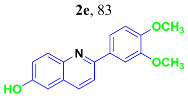
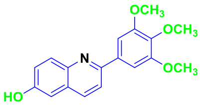
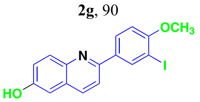
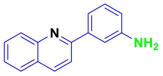
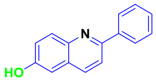
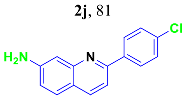
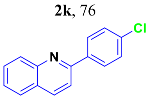
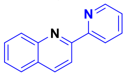
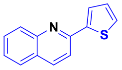
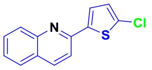
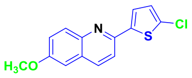
under different reaction conditions, such as dichloromethane, dichloroethane, toluene, tetrahydrofuran, MeOH, and MeCN at room temperature (rt) or under reflux (see Table S1). Interestingly, neither intramolecular Friedel–Crafts acylated product[13] (**4a**) (in TFA with or without metal) nor pyrazolo[1,5-*c*]quinazoline (**3a**)[10,14] (except in Pd/CH_3COOH; 5%) was obtained. All of the reactions yielded **2a** as major component. The best results in terms of yield and cleanliness (less to no side products) were obtained under Bechamp conditions.

To further reconnoiter and prove the generality of this unexpected synthesis, we performed reaction with a variety of 2-nitrophenyl-substituted *N*-formyl pyrazolines having various groups at the aromatic ring(s) and were treated under optimized conditions that yielded 2-aryl quinolines in good yields (Table 1). The reaction progression was observed to be influenced by the electronic nature of the ring substituents. Heteroaromatic rings like pyridine and thiophene (entries 13–16) were tolerant to reaction conditions. The dinitro-substituted substrate **1k** yielded **2k** exclusively (entry 11).

We conducted few control experiments to understand the sequential steps and possible intermediates involved in the mechanism of formation of **2** from **1** (Scheme 4). Treatment of **1a** with acid at rt led to cleavage of *N*-formyl group (**5**), which on addition of metal yielded 2-nitrochalcone **6** as major product through retro-Michael addition along with some minor products: 2-nitrophenyl pyrazole **7** and 2-aminophenyl pyrazole **8**. The formation of 2-pyrazoline **5** indicates that the reaction does not undergo oxidative deformylation.[15] Likewise, in another example, liquid chromatography–mass spectrometry (LC–MS) analysis of reaction mixture containing **1h** and Fe/HCl for 30 min showed the presence of the corresponding deformylated pyrazoline, 2-nitrochalcones, and 2-aryl quinolines (see Scheme S1, Figure S1, and Table S2). A single case on such ring cleavage of 2-pyrazoline leading to an *α*,*β*-unsaturated carbonyl compound is reported to produce nitrogen gas by treating 2-pyrazoline with benzeneseleninic anhydride.[5] Further refluxing of **6** in MeOH under Bechamp reduction condition afforded **2a** in quantitative yield (88%) via proposed intermediate *trans*-2-hydroxyaminochalcone[16] **9**, which we could not isolate (Scheme 4A). However, we

Table 1. Scope of Reaction for the Synthesis of 2-Aryl Quinolines (2a−2p)



entry	(1a-1p); Ar^1; R$_1$, R$_2$	time (h)	yield of 2 (%)^a
1.	**1a**, Ph; $R_1 = R_2 = H$	2	 **2a**, 91
2.	**1b**, Ph; $R_1 = H$, $R_2 = OH$	2.5	 **2b**, 82
3.	**1c**, 2-Napthyl; $R_1 = R_2 = H$	2	 **2c**, 87
4.	**1d**,4-OMeC$_6$H$_4$; $R_1 = H$, $R_2 = OH$	1.5	 **2d**, 88
5.	**1e**, 3,4-OMeC$_6$H$_3$; $R_1 = R_2 = H$	1.5	 **2e**, 83
6.	**1f**, 3,4-OMeC$_6$H$_3$; $R_1 = H$, $R_2 = OH$	2	 **2f**, 90
7.	**1g**, 3,4,5-OMeC$_6$H$_2$; $R_1 = H$, $R_2 = OH$	1	 **2g**, 90
8.	**1h**, 3-I,4-OMeC$_6$H$_3$; $R_1 = H$, $R_2 = OH$	1	 **2h**, 79
9.	**1i**, 4-NH$_2$C$_6$H$_4$; $R_1 = R_2 = H$	2.5	 **2i**, 83
10.	**1j**, 4-OHC$_6$H$_4$;$R_1 = R_2 = H$	3	 **2j**, 81
11.	**1k**, 4-ClC$_6$H$_4$; $R_1 = NO_2$, $R_2 = H$	2	 **2k**, 76
12.	**1l**, 4-Cl C$_6$H$_4$; $R_1 = R_2 = H$	3	 **2l**, 84
13.	**1m**, 2-pyridyl; $R_1 = R_2 = H$	3	 **2m**, 75
14.	**1n**, 2-thienyl; $R_1 = R_2 = H$	4	 **2n**, 77
15.	**1o**, 5-Cl-2-thienyl; $R_1 = R_2 = H$	4	 **2o**, 79
16.	**1p**, 5-Cl-2-thienyl; $R_1 = H$, $R_2 = OMe$	4	 **2p**, 82

^{a}Isolated yield.

obtained **10** and **11**, the corresponding *trans*-2-aminochalcones[17] of **1e** and **1c**, when refluxed for 30 min under Fe/HCl condition along with 2-aryl quinolines (Scheme 4B). No chlorination[12b] was observed in the aromatic ring under Bechamp reduction condition.

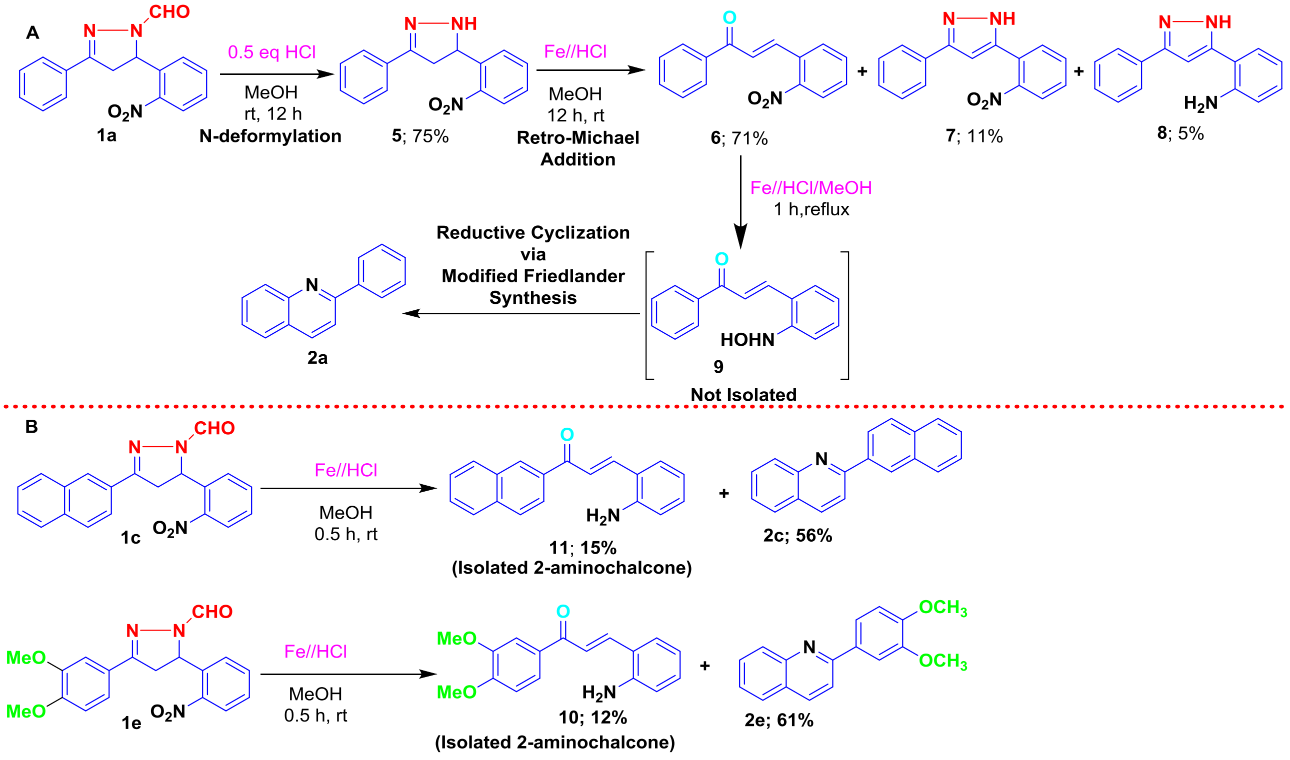
From these observations, we envisage that N-deformylation takes place in the first step of the reaction.[18] To explore this further, an independent experiment was set up, where an equimolar mixture of **1a** and aniline was refluxed under Bechamp reduction in MeOH to yield formanilide along with **2a** (Scheme 5). The formation of formanilide could be justified by the reaction of aniline with in situ generated methyl formate as the rate of reaction was low when the reaction was carried out without methanol. Interestingly, the reaction was found to be general in case of *N*-acetylpyrazolines, leading to 2-aryl quinolines but not with *N*-phenylpyrazoline, where a mixture was obtained, which could not be separated (see Schemes S2 and S3). The second step involves retro-Michael addition, which is generally catalyzed by Lewis/Brønsted acids, and in the present case, it is facilitated by Lewis acid (Fe^{2+})[12b] as no **6** was formed until metal was added. In the third step, reductive cyclization of *trans*-2-nitrochalcone involving a facile isomerization of double bond of **9**[16,17,19] takes place to yield 2-aryl quinoline in a manner not exactly similar to the Friedlander synthesis of quinolines.[20]

The pathways of this step were explicated by using the B3LYP/6-31+G(d) level of quantum chemical analysis (Scheme 6). This reaction may involve three steps. In the first step, **9** can undergo 1,5-Hshift (endergonic by 8.2 kcal/mol) to give a tautomer **12**. Tautomer **12** from tautomer **9** can either be obtained through a neutral pathway, in which the activation barrier for 1,5-Hshift was estimated to be 39 kcal/mol, or involve 1,5-Hshift via radical cation of **9** having an activation barrier of 22.36 kcal/mol (see Scheme S4A,B). Tautomer **12** has a C−C single bond about which rotation is comparatively easier to give the isomer **13**. During the cyclization (step c) of **13**, simultaneous proton transfer from OH to carbonyl oxygen and nucleophilic attack of nitrogen on the electrophilic carbonyl carbon takes place, leading to C−N bond formation (**TS**; activation energy required, 24.77 kcal/mol). The cyclization step gives rise to an intermediate **14**, which is found to be exergonic by 23.8 kcal/mol. The available reaction conditions allow **14** to give the final product **2a**. Density functional theory (DFT) calculations also suggested that isomerization and intramolecular cyclization of *trans*-2-aminochalcone are difficult due to the high activation energy barrier (see Figure S2, path B); however, it is possible under blue light-emitting diode.[19] This was further evidenced when no corresponding 2-aryl quinoline was formed even after refluxing **10** or **11** under Bechamp reduction condition for 12 h. The characterization of final synthetics was carried out using mp, IR, NMR, and high-resolution mass spectrometry (HRMS) techniques.

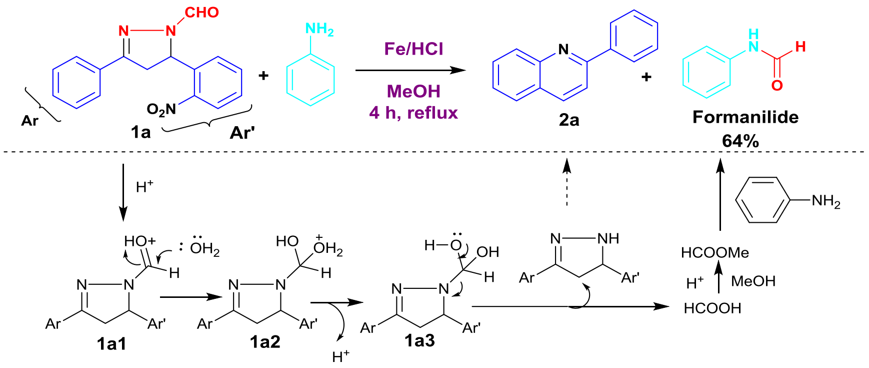
■ CONCLUSIONS

In conclusion, we have studied an unreported breakdown of 2-nitrophenyl substituted *N*-formyl pyrazolines under the influence of Bechamp reduction condition that yielded 2-aryl quinolines exclusively instead of pyrazolo[1,5-*c*]quinazolines or Friedel−Crafts acylated product. The acid and metal played role in deformylation, retro-Michael addition, and intramolecular reductive cyclization in a modified Friedlander manner to afford 2-aryl quinolines. The proposed mechanistic

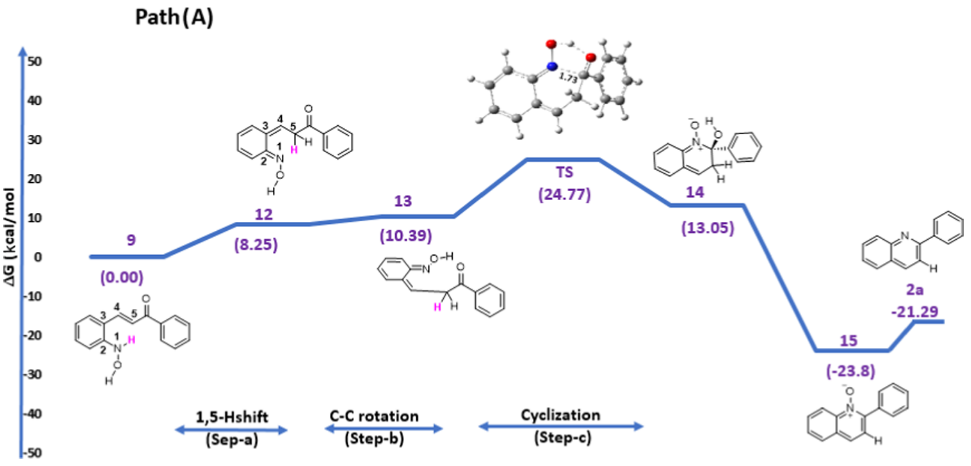
Scheme 4. (A) Control Experiments Conducted Using 1a; (B) Control Experiments Conducted Using 1c and 1e



Scheme 5. Reaction of 1a with Aniline under Bechamp Reduction and the Proposed Mechanism



Scheme 6. Energy Profile Diagrams for the Proposed Reaction Pathway (Path A) during the Formation of 2a[a]



[a]Overall barrier for the reaction is 24.77 kcal/mol, and the energy released is 21.29 kcal/mol in path A.

pathways are supported by experimental evidences and density functional theory (DFT) studies. Quinolines are reported to find a wide variety of applications as antimalarial,[21] anticancer,[22] antitubercular,[23] and anti-inflammatory substances[24] and act as a precursor for C−H activation.[25] Therefore, a straightforward and easy synthetic route for quinoline is still warranted.

■ EXPERIMENTAL SECTION

General Materials and Methods. The reagents of AR/GR quality for synthesis were procured from Sigma-Aldrich, Sisco Research Laboratory, Loba-Chemie Pvt. Ltd., India, and were not further refined for purification. For weighing purpose, a Sartorius analytical balance (BSA224S-CW) was used. Heating was done using a JSGW heating mantle. Solvent was concentrated using an ILMVAC rotary evaporator. Monitoring of reaction progress was done using thin-layer chromatography (TLC) (precoated Merck TLC plates) using gradient concentration of hexane/ethyl acetate or chloroform/methanol as the mobile phase, and detection was performed in the UV/fluorescent analysis cabinet. Stuart melting point apparatus (SMP-30) was used for analyzing the melting points of final synthetics, and a Bruker Fourier transform infrared spectrophotometer was used for obtaining the IR spectra of compounds. NMR and HRMS images were outsourced and recorded at SAIF, Panjab University, Chandigarh, and IIT Ropar, Punjab, respectively, in using CDCl$_3$/dimethyl sulfoxide (DMSO)-d_6 as solvent on 400 MHz (^{1}H) and 100 MHz (^{13}C) Bruker Avance NMR spectrometers.[26]

Illustrative Methodology for Synthesis of *N*-Formyl Pyrazolines (1a−p). In a 100 mL round-bottom flask, a mixture of an appropriate chalcone (1 mmol), formic acid (1.5 mmol), and hydrazine hydrate (80%, 1.5 mmol) was added. The mixture was further subjected under refluxing conditions for 1−4 h. After the completion of reaction as indicated by TLC, cold water was added to the reaction mixture, which resulted in the formation of precipitates. The precipitates were washed thoroughly with excess water and dried before crystallization using ethyl acetate to obtain the pure product.

5-(2-Nitrophenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carbaldehyde (1). Yield: 89%, dull orange solid, mp: 83−85 °C. IR (KBr, cm^{-1}): 3318 (C−OH), 1656 (C═O), 1510 (N═O), 1451 (N═O); ^{1}H NMR (CDCl$_3$, 400 MHz, δ with tetramethylsilane (TMS) = 0): 9.00 (1H, s), 8.13 (1H, d *J* = 1.22 Hz), 7.74-7.71 (2H, m), 7.59 (1H, m), 7.46−7.41 (4H, m), 7.32 (1H, d, *J* = 1.22 Hz), 6.13−6.09 (1H, dd = 4.88 Hz), 4.14−4.07 (1H, dd, *J* = 8.6 Hz), 3.22−3.16 (1H, dd, *J* = 4.88 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz, δ with TMS = 0): 160.18, 156.47, 147.07, 135.73 134.66, 131.07, 130.81, 129.25, 128.99, 126.84, 126.65 125.75, 56.23, 42.95.

General Procedure for Synthesis of 2a−p. For the synthesis of appropriate N-substituted quinolines (**2a−p**), respective formylated pyrazolines (**1a−p**) were refluxed in MeOH for 1−4 h, using catalyst Fe (3 equiv) and HCl (40%, 0.5 equiv). The reaction progress was monitored by TLC. After completion of the reaction, the mixture was passed through celite under pressure to remove Fe. Methanol was further concentrated using a rotary evaporator to obtain a solid crude. The crude was then neutralized with a bicarbonate solution and extracted using ethyl acetate (10 mL × 3). The ethyl acetate layer was further washed with brine solution, moisture-removed by passing it over anhydrous sodium sulfate, and concentrated using a rotary evaporator under reduced pressure to obtain the crude product. The crude purification was carried out by flash chromatography (silica gel # 60−120; petroleum ether/ethyl acetate 60:40).

Physical data of compounds are given below.

2-Phenylquinoline (2a). Yield: 91%, color: light brown solid, mp: 83−85 °C. IR (KBr, cm^{-1}): 3090 (═C−H stretch), 1640 (C═C stretch), 1320 (C−N stretch) ^{1}H NMR (CDCl$_3$, 400 MHz, δ with TMS = 0): 8.22 (1H, d, *J* = 8.52 Hz), 8.17−8.14 (3H, m), 7.88 (1H, d, *J* = 8.56 Hz), 7.82 (1H, m), 7.74−7.70 (1H, m), 7.54−7.52 (3H, m), 7.50−7.45 (1H, m); ^{13}C NMR (CDCl$_3$, 100 MHz, δ with TMS = 0): 157.49, 148.35, 139.77, 136.90, 129.81, 129.77, 129.42, 128.95, 127.67, 127.57, 127.26, 126.39, 119.14.[27]

4-(Quinolin-2-yl)phenol (2b). Yield: 82%, color: creamy white solid, mp: 102−104 °C. IR (KBr, cm^{-1}): 3320 (OH), 1658 (C═N), 1449 (C═N); ^{1}H NMR (CDCl$_3$, DMSO-d_6, 400 MHz, δ with TMS = 0): 9.61 (H−C═N, 1H, s), 8.21 (1H, d, *J* = 8.64 Hz), 8.06 (2H, d, *J* = 8.6 Hz), 7.99 (1H, d, *J* = 8.44 Hz), 7.88 (1H, d, *J* = 8.68 Hz), 7.82 (1H, d, *J* = 8 Hz), 7.66 (1H, t, *J* = 7.20 Hz), 7.46 (1H, t, *J* = 7.20 Hz), 6.91 (2H, d, *J* = 8.64 Hz); ^{13}C NMR (CDCl$_3$, DMSO-d_6, 100 MHz, δ with TMS = 0): 158.06, 156.06, 147.52, 136.27, 129.58, 129.15, 128.68, 128.37, 127.24, 126.27, 125.34, 117.17, 115.38. HRMS (time-of-flight electrospray ionization (TOF-ESI)) Calcd for $C_{15}H_{11}NO$: 221.0841 [M]$^+$; observed: 222.6226 [M + H]$^+$.

2-(Naphthalen-2-yl)quinoline (2c). Yield: 87%, color: white solid, mp: 124−126 °C. IR (KBr, cm^{-1}): 2943 (C−H stretch), 2831 (═C−H stretch), 1453 (−C−H bending), 1019 (C−N stretch) ^{1}H NMR (DMSO-d_6, 400 MHz, δ with TMS = 0): 8.84 (1H, s), 8.50 (2H, m), 8.34 (1H, d, *J* = 8.56 Hz), 8.14−8.08 (3H, m), 8.04−7.98 (2H, m), 7.81 (1H, m), 7.62−7.58 (3H, m); ^{13}C NMR (100 MHz, DMSO-d_6, TMS = 0): 156.45, 148.14, 137.76, 136.53, 134.02, 133.61, 130.53, 129.64, 129.31, 128.89, 128.38, 128.12, 127.54, 127.37, 127.09, 125.21, 119.50. HRMS (TOF-ESI) Calcd for $C_{19}H_{13}N$: 255.1048 [M]$^+$; observed: 256.1085 [M + H]$^+$.

2-(4-Methoxyphenyl)quinolin-6-ol (2d). Yield: 88%, color: yellowish solid, mp: 99−101 °C. IR (KBr, cm^{-1}): 3319 (−OH stretch), 2945 (C−H stretch), 2833 (═C−H stretch), 1656 (C═C stretch), 1449 (−C−H bending), 1019 (C−O stretch); ^{1}H NMR (DMSO-d_6, 400 MHz, δ with TMS = 0): 9.76 (1H, s), 8.10−8.03 (3H, m), 7.82 (2H, m), 7.27−7.24 (1H, dd, *J* = 2.52 Hz), 7.07 (1H, d, *J* = 2.44 Hz), 6.99 (2H, d, *J* = 8.72 Hz), 3.82 (3H, s); ^{13}C NMR (CDCl$_3$, DMSO-d_6, 100 MHz, δ with TMS = 0): 159.96, 155.14, 152.65, 142.75, 134.74, 131.55, 130.19, 127.91, 127.76, 121.88, 117.96, 113.78, 108.07, 78.22, 54.96, 40.18; MS (EI): 291.02 [M$^+$]. HRMS (TOF-ESI) Calcd for $C_{16}H_{13}NO_2$: 251.0946 [M]$^+$; observed: 252.0992 [M + H]$^+$.

2-(3,4-Dimethoxyphenyl)quinoline (2e). Yield: 83%, color: off-white solid, mp: 112−114 °C. ^{1}H NMR (DMSO-d_6, 400 MHz, δ with TMS = 0): 8.35 (1H, d, *J* = 4.8 Hz), 8.10 (1H, d, *J* = 8.4 Hz), 8.01 (1H, d, *J* = 8.4 Hz), 7.92 (1H, d, *J* = 8 Hz), 7.87 (1H, m), 7.80 (1H, dd, *J* = 1.6 Hz) 7.69 (1H, t, *J* = 7.2 Hz), 7.52 (1H, t, *J* = 7.2 Hz), 7.06 (1H, d, *J* = 8.4 Hz), 3.87 (3H, s), 3.80 (3H, s); ^{13}C NMR (DMSO-d_6, 100 MHz, δ with TMS = 0): δ 156.25, 150.95, 149.41, 148.02, 137.39, 131.95, 130.46, 129.65, 128.14, 127.32, 126.54, 120.70, 119.00, 112.28, 110.84, 56.14, 40.25. HRMS (TOF-ESI) Calcd for $C_{17}H_{15}NO_2$: 265.1103 [M]$^+$; observed: 266.1140 [M + H]$^+$.

2-(3,4-Dimethoxyphenyl)quinolin-6-ol (2f). Yield: 90%, color: off-white/yellowish solid, mp: 108−110 °C. IR (KBr, cm^{-1}): 3479 (−OH stretch), 2922 (C−H stretch), 2856 (=C−H stretch), 1598 (C=C stretch), 1436 (−C−H bending), 1226 (C−O stretch); ^{1}H NMR ($CDCl_3$, 400 MHz, δ with TMS = 0): 8.02 (1H, d, J = 2.08 Hz), 7.96 (1H, d, J = 8.44 Hz), 7.74−7.72 (2H, m), 7.54 (1H, d, J = 8.16 Hz), 7.26 (1H, s), 7.05 (1H, s), 6.95 (1H, d, J = 8.36 Hz), 3.94 (3H, s), 3.90 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz, δ with TMS = 0): 154.81, 154.58, 150.06, 149.29, 143.19, 135.73, 132.36, 130.13, 128.28, 122.22, 120.22, 119.57, 111.07, 110.45, 109.06, 55.94. HRMS (TOF-ESI) Calcd for $C_{17}H_{15}NO_3$: 281.1052 $[M]^+$; observed: 282.1504 $[M + H]^+$.

2-(3,4,5-Trimethoxyphenyl)quinolin-6-ol (2g). Yield: 90%, color: bright yellow solid, mp: 119−121 °C. IR (KBr, cm^{-1}): 3318 (−OH stretch), 2947 (C−H stretch), 2835 (=C−H stretch), 1651 (C=C stretch), 1061 (C−O stretch); ^{1}H NMR (DMSO-d_6, 400 MHz, δ with TMS = 0): 10.89 (1H, s), 8.79 (1H, s), 8.62 (1H, s), 8.32 (1H, s), 7.57−7.45 (4H, m), 3.95 (6H, s), 3.76 (3H, s); ^{13}C NMR (100 MHz, DMSO-d_6, δ with TMS = 0): 157.92, 153.73, 151.31, 150. 45, 142.28, 140.92, 135.61, 129.62, 128.28, 126.16, 124.93, 121.61, 109.55, 107.17, 60.83, 57.01. HRMS (TOF-ESI) Calcd for $C_{18}H_{17}NO_4$: 311.1158 $[M]^+$; observed: 312.1596 $[M + H]^+$.

2-(3-Iodo-4-methoxyphenyl)quinolin-6-ol (2h). Yield: 79%, color: cream white solid, mp: 93−95 °C. IR (KBr, cm^{-1}): 3319 (−OH stretch), 2945 (C−H stretch), 2833 (=C−H stretch), 1552 (C=C stretch), 1346 (−C−H bending), 1019 (C−O stretch), 560 (C−I stretch); ^{1}H NMR ($CDCl_3$, DMSO-d_6, 400 MHz, δ with TMS = 0): 9.80 (1H, s), 8.61 (1H, d, J = 2 Hz), 7.82 (2H, t, J = 2 Hz), 8.14−8.11 (1H, dd, J = 2.08 Hz), 8.07 (1H, m), 7.89 (1H, d, J = 9.04 Hz), 7.83 (1H, d, J = 8.68 Hz), 7.32−7.29 (1H, dd, J = 2.60 Hz), 7.10 (1H, d, J = 2.52 Hz), 7.03 (1H, d, J = 8.64 Hz), 3.90 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$, DMSO-d_6 δ with TMS = 0): 163.48, 160.62, 156.29, 147.96, 142.51, 140.15, 138.71, 135.51, 133.21, 133.17, 127.31, 123.08, 120.71, 116.11, 113.30, 91.47, 61.47, 45.47. HRMS (TOF-ESI) Calcd for $C_{16}H_{12}INO_2$: 376.9913 $[M]^+$; observed: 377.9966 $[M + H]^+$.

3-(Quinolin-2-yl)aniline (2i). Yield: 83%, color: pale yellow solid, mp:103−106 °C. IR (KBr, cm^{-1}): 3428 (N−H stretch), 2923 (C−H stretch), 2856 (=C−H stretch), 1609 (C=C stretch), 1528 (−C−H bending); ^{1}H NMR ($CDCl_3$, 400 MHz, δ with TMS = 0): 8.19 (2H, t, J = 8.52 Hz), 7.82−7.79 (2H, m), 7.69 (1H, t, J = 7.32 Hz), 7.54−7.44 (3H, m), 7.29 (1H, t, J = 7.96 Hz), 6.78 (1H, d, J = 7.96 Hz), 3.8 (2H, s); ^{13}C NMR (100 MHz, DMSO-d_6, δ with TMS = 0): 174.00, 156.51, 147.03, 145.85, 139.63, 135.67, 128.66, 128.58, 128.47, 126.40, 126.16, 125.17, 118.21, 116.95, 115.18, 113.15. HRMS (TOF-ESI) Calcd for $C_{15}H_{12}N_2$: 220.1000 $[M]^+$; observed: 221.1051 [M + H].

2-Phenylquinolin-6-ol (2j). Yield: 81%, color: brown solid, mp: 96−98 °C. IR (KBr, cm^{-1}): 3317 (−OH stretch), 2947 (C−H stretch), 2835 (=C−H stretch), 1650 (C=C stretch), 1451 (−C−H bending), 1017 (C−O stretch); ^{1}H NMR ($CDCl_3$, DMSO-d_6 400 MHz, δ with TMS = 0): 9.74 (1H, s), 8.12 (2H, m), 8.05 (1H, d, J = 8.6 Hz), 7.90 (1H, d, J = 9.08 Hz), 7.82 (1H, d, J = 8.68), 7.45 (2H, t, J = 7.2 Hz) 7.39−7.36 (1H, m), 7.31−7.29(1H, m), 7.10 (1H, d, J = 2.36 Hz), 6.92 (1H, d, J = 8.28 Hz); ^{13}C NMR ($CDCl_3$, DMSO-d_6, 100 MHz, δ with TMS = 0): 158.06, 151.06, 147.52, 136.27, 129.58, 129.15, 129.68, 129.37, 127.24, 126.27, 125.34, 117.77, 115.38. HRMS (TOF-ESI) Calcd for $C_{15}H_{11}NO$: 221.0841 $[M]^+$; observed: 222.0899 $[M + H]^+$.

2-(4-Chlorophenyl)quinolin-7-amine (2k). Yield: 76%, color: orange solid, mp: 145−147 °C. IR (KBr, cm^{-1}): 3424 (−NH_2 stretch), 2929 (C−H stretch), 1596 (C=C stretch), 1463 (−C−H bending), 1323 (C−O stretch), 774 (C−I); ^{1}H NMR (DMSO-d_6, 400 MHz, δ with TMS = 0): 8.21 (2H, d, J = 8.56 Hz), 8.11 (1H, d, J = 8.56 Hz), 7.69 (1H, d, J = 8.56 Hz), 7.56 (1H, d, J = 8.56 Hz), 5.80 (2H, s); ^{13}C NMR (100 MHz, DMSO-d_6, δ with TMS = 0): 154.80, 151.07, 150.39, 138.69, 137.07, 134.41, 129.19, 128.84, 128.96, 120.30, 119.45, 113.96, 107.00. HRMS (TOF-ESI) Calcd for $C_{15}H_{11}ClN_2$: 254.0611 $[M]^+$; observed: 255.0661 $[M + H]^+$.

2-(4-Chlorophenyl)quinoline (2l). Yield: 84%, color: light yellow solid, mp: 109−111 °C. IR (KBr, cm^{-1}): 2949 (C−H stretch), 2866 (=C−H stretch), 1646 (C=C stretch), 1013 (C−O stretch), 815 (C−Cl stretch); ^{1}H NMR (DMSO-d_6, 400 MHz, δ with TMS = 0): 8.44 (1H, d, J = 8.56 Hz), 8.27 (2H, m), 8.13 (1H, m), 8.03 (1H, m), 7.97 (1H, m), 7.77−7.73 (1H, m), 7.58−7.56 (3H, m); ^{13}C NMR (100 MHz, DMSO-d_6, δ with TMS = 0): 155.33, 147.98, 137.94, 135.05, 130.61, 129.60, 129.49, 129.42, 129.37, 128.36, 127.59, 127.20, 119.10. HRMS (TOF-ESI) Calcd for $C_{15}H_{10}ClN$: 239.0502 $[M]^+$; observed: 240.0546 $[M + H]^+$.

2-(Pyridin-2-yl)quinoline (2m). Yield: 75%, color: greenish semisolid, mp: 106−108 °C. IR (KBr, cm^{-1}): 2977 (C−H stretch), 2851 (=C−H stretch), 1598 (C=N stretch), 1137 (C−C stretch), 1226 (C−O stretch); ^{1}H NMR ($CDCl_3$, 400 MHz, δ with TMS = 0): 9.34 (1H, d, J = 1.92), 8.71−8.70 (1H, dd, J = 1.6 Hz), 8.54 (1H, q), 8.29 (1H, d, J = 8.56 Hz), 8.18 (1H, d, J = 8.44 Hz), 7.19−7.86 (2H, m), 7.77 (1H, t, J = 1.36 Hz), 7.57 (1H, m), 7.49−7.46 (1H, m). HRMS (TOF-ESI) Calcd for $C_{14}H_{10}N_2$: 206.0844 $[M]^+$; observed: 207.1143 $[M + H]^+$.

2-(Thiophen-2-yl)quinoline (2n). Yield: 77%, color: light brown solid, mp: 120−122 °C. IR (KBr, cm^{-1}): 1660 (C=C stretch), 1456 (−C−H bending); ^{1}H NMR (DMSO-d_6, 400 MHz, δ with TMS = 0): 8.35 (1H, d, J = 8.56 Hz), 8.07 (1H, d, J = 8.56), 7.96−7.90 (3H, m), 7.72−7.68 (2H, m), 7.53−7.50 (1H, m), 7.19−7.17 (1H, m); ^{13}C NMR (100 MHz, DMSO-d_6, δ with TMS = 0): 152.46, 147.81, 145.30, 137.55, 130.66, 130.18, 129.04, 128.90, 128.43, 127.61, 127.46, 126.74, 118.26. HRMS (TOF-ESI) Calcd for $C_{13}H_9NS$: 211.0456 $[M]^+$; observed: 212.0502 $[M + H]^+$.

2-(5-Chlorothiophen-2-yl)quinoline (2o). Yield: 79%, color: pale yellow solid, mp: 89−91 °C. IR (KBr, cm^{-1}): 2920 (C−H stretch), 2852 (=C−H stretch), 2355 (C−S stretch), 1594 (C=C stretch), 1429 (−C−H bending), 785 (C−Cl stretch); ^{1}H NMR ($CDCl_3$, 400 MHz, δ with TMS = 0): 8.03−7.95 (2H, dd, J = 8.04), 7.68−7.59 (3H, m), 7.42−7.37 (2H, m), 6.87 (1H, s); ^{13}C NMR ($CDCl_3$, 100 MHz, δ with TMS = 0): 151.44, 147.96, 144.09, 136.74, 133.54, 130.02, 129.15, 127.53, 127.25, 126.32, 124.83, 116.62. HRMS (TOF-ESI) Calcd for $C_{13}H_8ClNS$: 245.0066 $[M]^+$; observed: 246.0458 $[M + H]^+$.

2-(5-Chlorothiophen-2-yl)-6-methoxyquinoline (2p). Yield: 82%, color: white solid, mp: 96−98 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, δ with TMS = 0): 8.12 (1H, d, J = 7.44), 7.73 (1H, d, J = 7.52 Hz), 7.49−7.28 (3H, m), 7.08−6.97 (2H, m), 4.11 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz, δ with TMS = 0): 155.18, 150.43, 144.11, 139.80, 136.83, 133.31, 128.37, 127.24, 126.59, 124.73, 119.45, 117.26, 108.75, 56.31. HRMS (TOF-ESI) Calcd for $C_{14}H_{10}ClNOS$: 275.0172 $[M]^+$; observed: 276.0607 $[M + H]^+$.

5-(2-Nitrophenyl)-3-phenyl-1H-pyrazole (7). Yield: 11%, color: brownish solid, mp: 137−139 °C. IR (KBr, cm^{-1}): 3456 (N−H), 1664 (C=N), 1524 and 1348 (N=O), 1217 (C−N); ^1H NMR ($CDCl_3$, 400 MHz, δ with TMS = 0): 7.67−7.76 (3H, m), 7.56−7.63 (3H, m), 7.33−7.51 (5H, m); ^{13}C NMR ($CDCl_3$, 100 MHz, δ with TMS = 0): 149.02, 146.37, 146.16, 132.09, 130.97, 129.04, 128.74, 128.04, 126.47, 125.62, 124.56, 123.82, 02.59. MS (ESI): m/z = 265 $[M]^+$.

2-(3-Phenyl-1H-pyrazol-5-yl)aniline (8). Yield: 5%, color: yellow solid, mp: 125−127 °C. IR (KBr, cm^{-1}): 3360 (N−H), 3285 (N−H), 1613 (C=N), 1579 (C=C), 1248 (C−N); ^1H NMR ($CDCl_3$, 400 MHz, δ with TMS = 0): 13.23 (D_2O exchangeable NH, 1H, bs), 7.81 (1H, s), 7.79 (1H, s), 7.31−7.54 (4H, m), 7.00 (2H, s), 6.75 (1H, d, J = 7.91 Hz), 6.61 (1H, t, J = 7.32 Hz), 6.22 (D_2O exchangeable NH_2, 2H, bs). MS (ESI): m/z = 236.1 $[M]^+$.

(E)-3-(2-Aminophenyl)-1-(3,4-dimethoxyphenyl)prop-2-en-1-one (10). Yield: 12%, color: yellow solid, mp: 132−134 °C. IR (KBr, cm^{-1}): 3420 ($-NH_2$ stretch), 2929 (C−H stretch), 2826 (=C−H stretch), 1642 (−C=O), 1509 (−C−H bending), 1125 (C−N stretch); ^1H NMR (DMSO-d_6, 400 MHz, δ with TMS = 0): 7.95 (1H, d, J = 15.2 Hz), 7.81 (1H, d, J = 8 Hz), 7.69−7.63 (2H, m), 7.55 (1H, s), 7.08−7.04 (2H, m), 6.67 (1H, d, J = 8 Hz), 6.54 (1H, d, J = 8 Hz), 5.65 (2H, s, D_2O exchangeable NH_2), 3.81 (6H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 187.74, 153.38, 149.44, 149.21, 140.03, 132.00, 131.51, 128.26, 123.50, 119.88, 118.87, 116.98, 116.82, 111.36, 111.15, 56.07. HRMS (TOF-ESI) Calcd for $C_{17}H_{17}NO_3$, 283.1208 $[M]^+$; observed 284.1259 $[M + H]^+$.

(E)-3-(2-Aminophenyl)-1-(naphthalen-2-yl)prop-2-en-1-one (11). Yield: 15%, color: white solid, mp: 141−143 °C; ^1H NMR (DMSO-d_6, 400 MHz, δ with TMS = 0): 8.86 (1H, s), 8.14−7.95 (5H, m), 7.84 (1H, d, J = 15.2 Hz), 7.74 (1H, d, J = 7.75 Hz), 7.65−7.58 (2H, m), 7.09 (1H, t, J = 8 Hz), 6.70 (1H, d, J = 8 Hz), 6.57 (1H, t, J = 8 Hz), 5.74 (2H, s, D_2O exchangeable NH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 189.28, 149.71, 140.89, 135.93, 135.42, 132.90, 132.31, 130.53, 130.10, 129.23, 128.88, 128.28, 127.58, 124.75, 119.86, 118.70, 117.07, 116.81. HRMS (TOF-ESI) Calcd for $C_{19}H_{15}NO$, 273.1154 $[M]^+$; observed 274.1188 $[M + H]^+$.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.8b02682.

Gibbs free-energy calculations; LC−MS data; and copies of ^1H, ^{13}C NMR, and HRMS images of the products (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: raj.khunger@gmail.com, rajcps@cup.ac.in.

ORCID

Prasad V. Bharatam: 0000-0002-7064-8561
Raj Kumar: 0000-0001-5113-6627

Present Address

⊥Pharmaceutical Candidate Optimization, Biocon Bristol Myers-Squibb R&D Center (BBRC), Syngene International Limited, Biocon Park, Plot 2 & 3, Bommasandra IV Phase, Bangalore 560099, India (P.B.).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank Vice Chancellor and Dean, Academic Affairs, for providing the funds to support the present work. They acknowledge CIL, CUPB, for data analysis. G.J. acknowledges CSIR, New Delhi (Grant no. 05/1051(0011)/2018-EMR-I), for providing SRF. P.B. acknowledges Arbro Pharmaceuticals Pvt. Ltd. (Analytical Division), New Delhi, India, for LC−MS analysis.

■ REFERENCES

(1) Varghese, B.; Al-Busafi, S. N.; Suliman, F. O.; Al-Kindy, S. M. Unveiling a versatile heterocycle: pyrazoline—a review. *RSC Adv.* **2017**, *7*, 46999−47016.

(2) (a) Alex, J. M.; Kumar, R. 4,5-Dihydro-1 H-pyrazole: an indispensable scaffold. *J. Enzyme Inhib. Med. Chem.* **2014**, *29*, 427−442. (b) Marella, A.; Ali, R.; Alam, T.; Saha, R.; Tanwar, O.; Akhter, M.; Shaquiquzzaman, M.; Alam, M. M. Pyrazolines: a biological review. *Mini-Rev. Med. Chem.* **2013**, *13*, 921−931. (c) Alex, J. M.; Singh, S.; Kumar, R. 1-Acetyl-3,5-diaryl-4,5-dihydro (1H) pyrazoles: exhibiting anticancer activity through intracellular ROS scavenging and the mitochondria-dependent death pathway. *Arch. Pharm.* **2014**, *347*, 717−727.

(3) (a) Fu, H.; Xiao, D.; Yao, J.; Yang, G. Nanofibers of 1,3-Diphenyl-2-pyrazoline Induced by Cetyltrimethylammonium Bromide Micelles. *Angew. Chem., Int. Ed.* **2003**, *42*, 2883−2886. (b) Arshad, M. N.; Birinji, A. S.; Khalid, M.; Asiri, A. M.; Al-Amry, K. A.; Aqlan, F. M.; Braga, A. A. Synthesis, spectroscopic, single crystal diffraction and potential nonlinear optical properties of novel pyrazoline derivatives: Interplay of experimental and computational analyses. *Spectrochim. Acta, Part A* **2018**, 146.

(4) (a) Rangasamy, M.; Palaninathan, K. Pyrazoline based fluorescent chemosensor for Al3+ ion detection and live cell imaging. *New J. Chem.* **2018**, 10891. (b) Bozkurt, E.; Gul, H. I. A novel pyrazoline-based fluorometric "turn-off" sensing for Hg^{2+}. *Sens. Actuators, B* **2018**, *255*, 814−825.

(5) Tuloup, R.; Danion-Bougot, R.; Danion, D.; Pradere, J. Oxidative ring opening of 2-pyrazolines. Application to lactamisation and formylation of 1,3-6h-thiazines. *Tetrahedron Lett.* **1988**, *29*, 6249−6252.

(6) (a) Engel, P. S.; Shen, L. Photochemical and thermal decomposition of 1-pyrazolines. *Can. J. Chem.* **1974**, *52*, 4040−4043. (b) Crawford, R. J.; Mishra, A. The Mechanism of the Thermal Decomposition of 1-Pyrazolines and Its Relationship to Cyclopropane Isomerizations1. *J. Am. Chem. Soc.* **1966**, *88*, 3963−3969. (c) Bryce-Smith, D.; Gilbert, A. The organic photochemistry of benzene—I. *Tetrahedron* **1976**, *32*, 1309−1326.

(7) Schneider, M. P.; Csacsko, B. Thermal decomposition of bicyclic divinyl-Δ1-pyrazolines and divinylcyclopropanes. *J. Chem. Soc.* **1977**, *10*, 330−331.

(8) Tóth, G.; Lévai, A.; Dinya, Z.; Snatzke, G. Thermal, decomposition of some new spiro-1-pyrazolines. *Tetrahedron* **1991**, *47*, 8119−8132.

(9) (a) Lévai, A. Synthesis and thermal decomposition of 3-aroyl-4-aryl-2-pyrazolines. *Monatsh. Chem.* **1995**, *126*, 1245−1251. (b) Jones, W. Pyrazolines. III. The Stereochemistry of the Decomposition of 2-Pyrazolines1. *J. Am. Chem. Soc.* **1959**, *81*, 5153−5156.

(10) Kumar, D.; Kumar, R. Microwave-assisted synthesis of pyrazolo [1, 5-c] quinazolines and their derivatives. *Tetrahedron Lett.* **2014**, *55*, 2679−2683.

(11) Kadam, H. K.; Tilve, S. G. Advancement in methodologies for reduction of nitroarenes. *RSC Adv.* **2015**, *5*, 83391−83407.

(12) (a) Béchamp, A. J. Bechamp Reduction. *Ann. Chim. Phys.* **1854**, *42*, 186. (b) Popat, V.; Padhiyar, N. Kinetic study of bechamp process for p-nitrotoluene reduction to p-toluidine. *Int. J. Chem. Eng. Appl.* **2013**, *4*, 401.

(13) Ahmed, N.; Dev, D. Alternate Synthesis Route of 2-(Substituted Phenyl)-3, 3a-dihydro-8H-pyrazolo [5, 1-a] isoindol-8-ones via Chalcone-Based N-Formyl-pyrazolines. *Synth. Commun.* **2013**, *43*, 689−704.

(14) Sawant, D. M.; Sharma, S.; Pathare, R. S.; Joshi, G.; Kalra, S.; Sukanya, S.; Maurya, A. K.; Metre, R. K.; Agnihotri, V. K.; Khan, S.; et al. Relay tricyclic Pd (ii)/Ag (i) catalysis: design of a four-component reaction driven by nitrene-transfer on isocyanide yields inhibitors of EGFR. *Chem. Commun.* **2018**, 11530.

(15) Kumar, K.; Perumal, P. A novel one-pot oxidative deformylation of N-formyldihydroquinolines employing ferric chloride hexahydrate. Synthesis of 4-chloro-2-phenylquinolines and 4-chloro-2-(1,3-diphenyl-1*H*-pyrazol-4-yl) quinolines. *J. Heterocycl. Chem.* **2008**, *45*, 597−599.

(16) Barros, A. I.; Silva, A. M. One-pot synthesis of 2-(2-hydroxyaryl) quinolines: reductive coupling reactions of 2′-hydroxy-2-nitrochalcones. *Tetrahedron Lett.* **2003**, *44*, 5893−5896.

(17) Bharadwaj, K. C. Acrylamide in Rauhut-Currier reaction; intramolecular isomerization of activated alkenes for quinolone synthesis. *Tetrahedron* **2017**, *73*, 5690−5699.

(18) Olah, G. A.; Ohannesian, L.; Arvanaghi, M. Formylating agents. *Chem. Rev.* **1987**, *87*, 671−686.

(19) (a) Chen, X.; Qiu, S.; Wang, S.; Wang, H.; Zhai, H. Blue-light-promoted carbon−carbon double bond isomerization and its application in the syntheses of quinolines. *Org. Biomol. Chem.* **2017**, *15*, 6349−6352. (b) **Note:** The estimated barrier for cis−trans isomerization of nitro radical anion was calculated to be 37 kcal/mol, which was 5 kcal/mol less than that of cis−trans isomerization observed in Path B thus supporting the path A (see Supporting Information, Scheme S5).

(20) Marco-Contelles, J.; Pérez-Mayoral, E.; Samadi, A.; do Carmo Carreiras, M.; Soriano, E. Recent advances in the Friedlander reaction. *Chem. Rev.* **2009**, *109*, 2652−2671.

(21) Kaur, K.; Jain, M.; Reddy, R. P.; Jain, R. Quinolines and structurally related heterocycles as antimalarials. *Eur. J. Med. Chem.* **2010**, *45*, 3245−3264.

(22) Jain, S.; Chandra, V.; Jain, P. K.; Pathak, K.; Pathak, D.; Vaidya, A. Comprehensive review on current developments of quinoline-based anticancer agents. *Arabian J. Chem.* **2016**, DOI: 10.1016/j.arabjc.2016.10.009.

(23) Keri, R. S.; Patil, S. A. Quinoline: a promising antitubercular target. *Biomed. Pharmacother.* **2014**, *68*, 1161−1175.

(24) Kumar, S.; Bawa, S.; Gupta, H. Biological activities of quinoline derivatives. *Mini-Rev. Med. Chem.* **2009**, *9*, 1648−1654.

(25) (a) Dong, J.; Long, Z.; Song, F.; Wu, N.; Guo, Q.; Lan, J.; You, J. Rhodium or Ruthenium-Catalyzed Oxidative C-H/C-H Cross-Coupling: Direct Access to Extended π-Conjugated Systems. *Angew. Chem.* **2013**, *125*, 608−612. (b) Yang, L.; Qian, B.; Huang, H. Brønsted Acid Enhanced Rhodium-Catalyzed Conjugate Addition of Aryl C-H Bonds to α,β-Unsaturated Ketones under Mild Conditions. *Chem. − Eur. J.* **2012**, *18*, 9511−9515. (c) Zhang, X. S.; Zhu, Q. L.; Luo, F. X.; Chen, G.; Wang, X.; Shi, Z. J. Aromatic C−H addition to ketones: the effect of directing groups. *Eur. J. Org. Chem.* **2013**, *2013*, 6530−6534.

(26) Chauhan, M.; Rana, A.; Alex, J. M.; Negi, A.; Singh, S.; Kumar, R. Design, microwave-mediated synthesis and biological evaluation of novel 4-aryl (alkyl) amino-3-nitroquinoline and 2,4-diaryl (dialkyl) amino-3-nitroquinolines as anticancer agents. *Bioorg. Chem.* **2015**, *58*, 1−10.

(27) Khusnutdinov, R.; Bayguzina, A.; Aminov, R.; Dzhemilev, U. Synthesis of 2-Phenylquinoline and its Derivatives by Multi-component Reaction of Aniline, Benzylamine, Alcohols, and CCl_4 Catalyzed by $FeCl_3 \cdot 6H_2O$. *J. Heterocycl. Chem.* **2016**, *53*, 144−146.