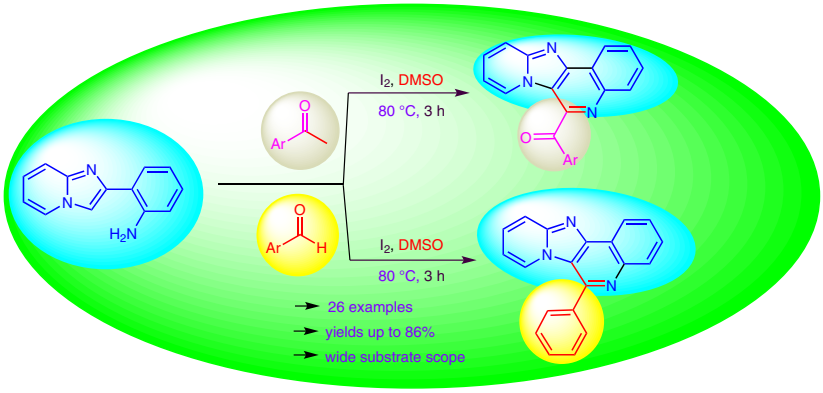
Synthesis A. Kale et al. Paper

# Synthesis of Pyrido-Fused Imidazo[4,5-*c*]quinolines by $I_2$-DMSO Promoted Oxidative Cross Coupling and Intramolecular Cyclization

**Ashok Kale**[a]
**Chiranjeevi Bingi**[a]
**Nagarjuna Chary Ragi**[b]
**Prabhakar Sripadi**[b]
**Prabhakar Rao Tadikamalla**[c]
**Krishnaiah Atmakur***[a,d]

[a] Division of Crop Protection Chemicals, CSIR-Indian Institute of Chemical Technology, Tarnaka, Hyderabad 500 007, India
krishnu@iict.res.in
[b] National Center for Mass Spectrometry, CSIR-Indian Institute of Chemical Technology, Tarnaka, Hyderabad 500 007, India
[c] Centre for NMR & Structural Chemistry, CSIR-Indian Institute of Chemical Technology, Tarnaka, Hyderabad 500 007, India
[d] AcSIR-Indian Institute of Chemical Technology, Tarnaka, Hyderabad 500 007, India



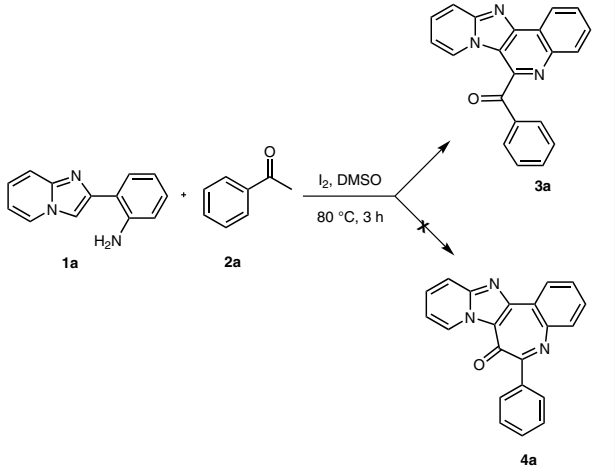

Received: 20.09.2016
Accepted after revision: 08.11.2016
Published online: 07.12.2016
DOI: 10.1055/s-0036-1588366; Art ID: ss-2016-n0655-op

**Abstract** The synthesis of a series of novel quinoline fused imidazo[4,5-*c*]quinolines was accomplished by a simple, efficient, iodine–dimethyl sulfoxide ($I_2$–DMSO) promoted sequential oxidative cross coupling followed by intramolecular cyclization of pyridoimidazole arylamines and carbonyl compounds in a one-pot reaction. Simple reaction conditions, no metal catalyst, no additives, no ligand, selective product formation and high yields are the advantages of this method.

**Key words** benzaldehydes, acetophenones, imidazopyridine, oxidative coupling

Polyheterocycles are vital structural motifs with numerous applications in pharmaceutical and material science.[1] Among them, a wide range of biological activities[2] are associated with nitrogen-rich polycyclic frameworks. Accordingly, the construction of this framework through controlled organic synthesis, and in particular through cascade sequences,[3] is a current goal of organic chemists. To realize these goals, approaches have often been explored that are based on multicomponent reactions. In this context, our attention was drawn to the annulation of imidazo pyridines to synthesize pyrido-fused imidazo[4,5-*c*]quinoline compounds. Imidazo pyridine (IP) compounds are privileged N-fused heterocycles that exhibit diverse biological activities such as antiviral, antibacterial, and anti-inflammatory action, and can function as CXC chemokine receptor type-4 (CXCR 4) antagonists. Furthermore, numerous drugs with an IP core moiety such as Nicopidem and Alpidem have also come on the market.[4] On the other hand, molecules with a quinoline skeleton possess a variety of biological effects including antimicrobial,[5–9] anticancer[10–17] and antiviral[18–20] activities. Quinoline compounds were also reported to inhibit DENV2 RNA expression in Huh-7-DV-Fluc cells.[21] Additionally, annulation of IP compounds has led to the synthesis of compounds that demonstrate a variety of pharmacological properties.[22] Therefore, the synthesis of N-heterocycles having both an IP and a quinoline moiety in a single molecular framework may generate significant levels of activity.[23] With this background, a literature survey was conducted that revealed that surprisingly very few reports are available on the construction of quinoline-fused imidazopyridine compounds. For example, Kundu reported[24] the synthesis of quinoline-fused imidazopyridine compounds starting from pyridazoimidazole, arylamine and carbonyl compounds through Pictet–Springler cyclization. Chauhan also reported[25] on the use of similar reaction conditions involving cyanuric chloride. Very recently, Zhang[26] reported on a synthesis starting from 2-bromophenacylbromide, 2-aminopyridine, and carbonyl compounds. However, these methods use a catalyst together with an additive and/or ligand. Therefore, there remains a need to develop simple methodologies to synthesize the quinoline-fused imidazo pyridine compounds. With this background, and also as a part of our research work on the synthesis of N-rich heterocyclic compounds of biological interest,[27] herein, we report the synthesis of quinoline-fused imidazo pyridine compounds by a simple $I_2$-DMSO promoted reaction of pyridoimidazole arylamines and carbonyl compounds in a one-pot reaction without involving any metal catalyst, additive or ligand.

Initially, 2-(imidazo[1,2-*a*]pyridin-2-yl)aniline (**1a**) was prepared by following a reported method.[25] Thus obtained compound **1a** (1.0 mmol) was reacted with acetophenone **2a** (1.0 mmol) under Kornblum reaction conditions to give quinoline-fused pyridoimidazole **3a** through formation of the C-3 dicarbonylated compound[28] followed by its intramolecular cyclization. To our delight, the reaction proceeded as per our presumption and gave the desired product **3a** exclusively in 46% yield (Scheme 1).




**Scheme 1**

Excited by the exclusive formation of **3a**, experiments were carried out to improve the yields by varying reaction parameters. When the quantity of $I_2$ was increased to 1.2 equivalents, an increase in the yield to 63% was observed. Further increase in the quantity of $I_2$ to 1.5 equivalents raised the yield to 84%. However, no change in the yield was observed upon further increase in iodine quantity. Reactions performed in a range of temperatures revealed that 80 °C was optimal for this reaction. Subsequently, experiments were also carried out by employing iodine along with bases such as piperidine, triethylamine, KOH, DBU or DABCO. However, no significant improvement in the yield of **3a** was observed. Furthermore, when the reaction was carried out with KI, NaI, NIS or CuI rather than with iodine, no product formation was observed.

The structure of **3a** was determined based on the spectral data. The $^1$H NMR spectra showed one doublet signal at δ = 8.98–8.95 ppm (1 H), three multiplets at δ = 8.94–8.91 (1 H), 8.32–8.27 (1 H), and 8.26–8.21 ppm (2 H), a doublet signal at δ = 8.10–8.04 ppm (1 H), followed by three multiplet signals at δ = 7.88–7.83 (2 H), 7.73–7.68 (2 H), and 7.58–7.52 ppm (2 H), and a triplet at δ = 7.12–7.07 ppm (1 H) accounting for all the aromatic protons. Given that this data is equally consistent with compound **4a** (Figure 1), attempts were made to obtain crystals that were suitable for X-ray crystallography studies. However, these attempts were unsuccessful. Therefore, extensive NMR studies were conducted to determine the exact structure of the product.

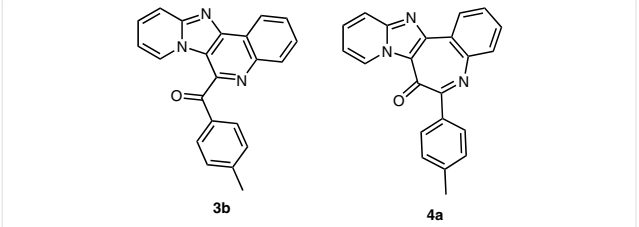



**Figure 1** Structures of **3a** and **4a**

In this instance, compound **3b** was subjected to extensive NMR studies. On the 2D NOESY spectrum, a weak NOE correlation was observed between the proton at δ = 8.13, 8.86 ppm (ca. 4 Å) and δ = 8.13, 8.27 ppm (Figure 2). Furthermore, a strong heteronuclear correlation by HMBC was observed between the carbonyl carbon at δ = 193.5 ppm and aromatic protons at δ = 8.13 ppm (Figure 2), supporting the structure of **3b** (Figure 1). This was further confirmed by the 1D and 2D NMR experiments.

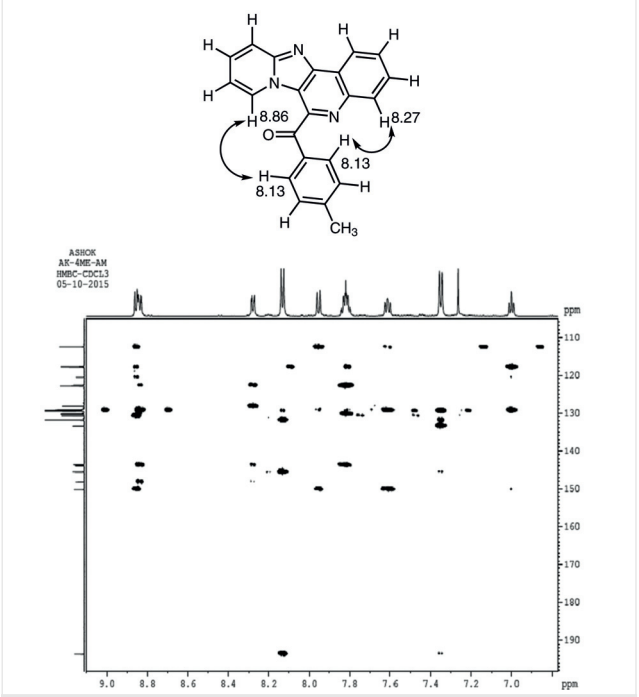



**Figure 2** HMBC spectroscopic analysis of **3b**

The structure of **3b** was unambiguously confirmed by extensive mass spectral analysis.

Positive ion ESI mass spectral analysis of **3b** showed an abundant protonated molecule $[M + H]^+$ ion at *m*/*z* 338 in addition to $[M + H - CO]^+$ (*m*/*z* 310) (Figure 3). The HRMS data confirmed the elemental composition for the ion *m*/*z* 338 as $C_{22}H_{16}N_3O$.

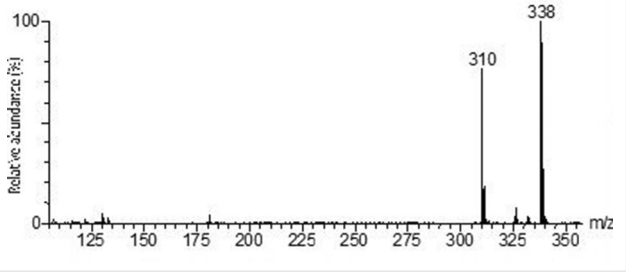



**Figure 3** Positive ion ESI mass spectrum of compound **3b**

We then performed MS/MS experiments on the $[M + H]^+$ ion (*m*/*z* 338).

The ESI-MS/MS spectrum of the $[M + H]^+$ ion of compound **3b** (*m*/*z* 338) is shown in (Figure 4). The spectrum displayed product ions at *m*/*z* 310, 218, 191, 119, 91, and 78. The elemental composition of these ions as obtained from HRMS data is summarized in Table 1. Formation of the product ions at *m*/*z* 310, 191, 91, and 78 can be explained by both the possible structures **3b** and **4a** (Figure 1). However, the major ions at *m*/*z* 218 and 119 can only be explained by structure **3b**. The fragmentation pathway of the $[M + H]^+$ ion is depicted in (Scheme 2). The ion *m*/*z* 119 cannot be explained by structure **4a**, whereas the ion *m*/*z* 218 could be formed from structure **4a** by the loss of $C_8H_{10}N$· radical from the $[M + H]^+$ ion. However, the elemental composition of the ion *m*/*z* 218 ($C_{14}H_8N_3$) reveals that it is formed from $[M + H]^+$ ion by the loss of $C_8H_8O$, which can only be explained by structure **3b**. Thus, the fragmentation pattern confirms the structure of compound as **3b**.

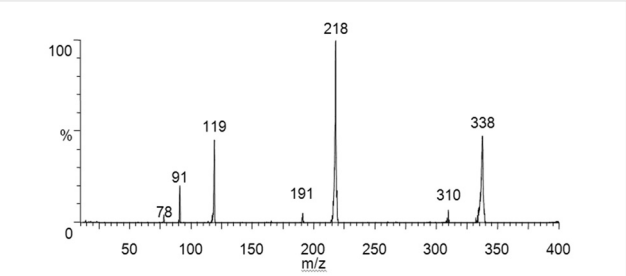


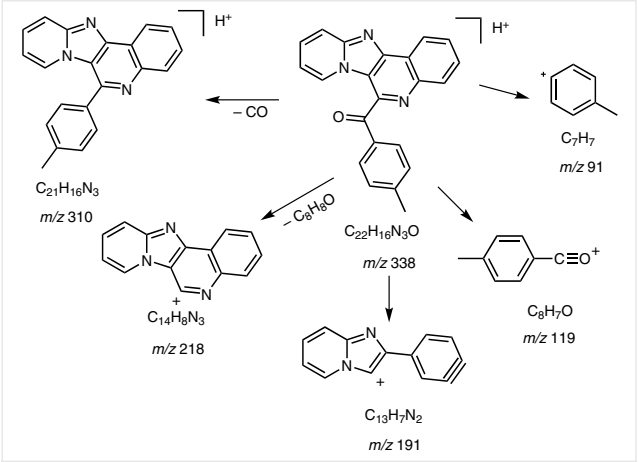

**Figure 4** ESI-MS/MS spectrum of $[M + H]^+$ ion (*m*/*z* 338) of compound **3b**

The reaction pathway for the formation of compound **3a** and the requirement for $I_2$ were then verified by conducting a series of control experiments. Thus, compound **1a** was reacted with phenylglyoxal **2b** under similar reaction conditions to those in Scheme 1. Gratifyingly, this reaction gave **3a** in 84% yield (Scheme 3). Subsequently, same reaction was carried out without $I_2$ under similar reaction conditions and no formation of either **3a** or **3aa** was observed. However, when the reaction was conducted at 110 °C for 6 hours, formation of **3a** was observed in 22% yield along with **3aa** in 62% yield. To verify the yield improvements of **3a** if any, the same reaction was extended to 12 hours and a perceptible improvement in the yield of **3a** (38%) was observed. However, no further improvement in yield was observed after 24 hours heating. Critically, in the presence of $I_2$ in DMSO, compound **3aa** was completely converted into the desire product **3a**. These studies substantiate the formation of **3a** through oxidative coupling product **3aa**, followed by intramolecular cyclization.

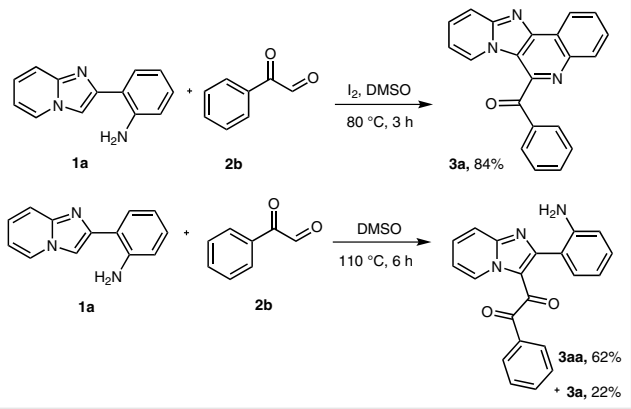
Having confirmed the structure of **3a** and established the reaction conditions, this protocol was generalized by reacting compound **1a** with a range of electron-rich, neutral, and electron-deficient aryl methyl ketones and also with 2-acetyl naphthalene and 2-acetyl furan (Table 2). Electron-rich functional groups such as methyl, 4-methoxy, 2,4-dimethoxy, and 3,4,5-trimethoxy aryl methyl ketones

**Table 1** HRMS Data of **3b** and the Product Ions Formed During MS/MS of the $[M + H]^+$ Ion

| Ion (*m*/*z*) | Molecular formula | Calcd mass | Found mass | Error (ppm) |
|---|---|---|---|---|
| 338 | $C_{22}H_{16}NO$ | 338.13 | 338.128 | 4.7 |
| 310 | $C_{21}H_{16}N_3$ | 310.13 | 310.133 | 4.3 |
| 218 | $C_{14}H_8N_3$ | 218.07 | 218.071 | 4.9 |
| 191 | $C_{13}H_7N_2$ | 191.06 | 191.060 | 5.2 |
| 119 | $C_8H_7O$ | 119.04 | 119.049 | 5.5 |
| 91 | $C_7H_7$ | 91.055 | 91.0548 | 5.7 |

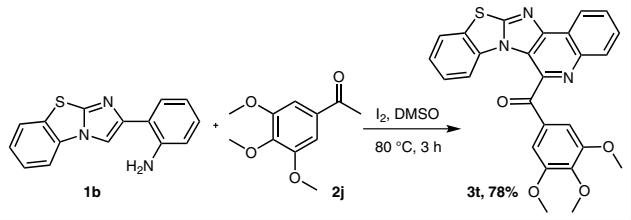



**Scheme 2** Fragmentation pathway for the $[M + H]^+$ ion of compound **3b**




**Scheme 3**

gave better yields than electron-deficient aryl methyl ketones. When the reaction was conducted with different substituents on the benzene ring of the imidazopyridine, **3o–p** were obtained in good yields. Experiments were also carried out with substrates bearing a range of substituents on the imidazo pyridine ring to give the product **3q–s** in good yields. Compound **3t** was also obtained in 78% yield by reacting **1b** with **2j** (Scheme 4).



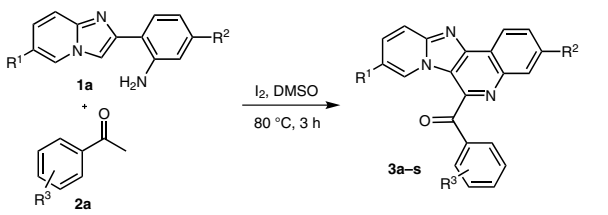

**Scheme 4**

The protocol was also extended to aldehydes and, to our satisfaction, was found to be quite compatible, producing the corresponding products **6** in excellent yields (Table 3).

A plausible mechanism has been proposed for the formation of **3a**, whereby the aryl methyl ketone forms phenylglyoxal under Kornblum reaction conditions (Scheme 5). Nucleophilic attack of the imidazopyridine on the electron-deficient carbonyl carbon of phenylglyoxal, which is activated by iodine, leads to **A**. Further, subsequent intramolecular cyclization reaction gives **3a**.

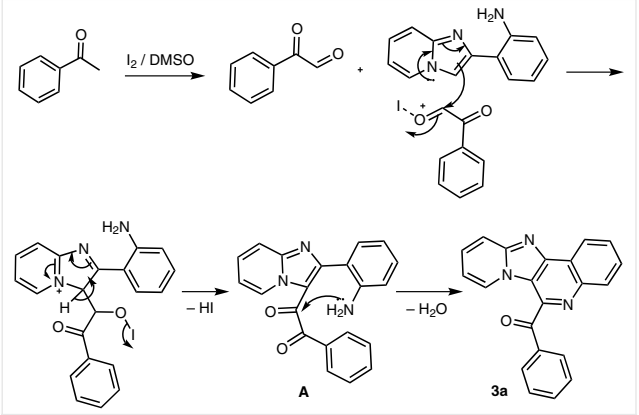
In conclusion, we have developed a simple and highly efficient method for the synthesis of pyrido-fused imidazo[4,5-*c*]quinolines by means of oxidative cross coupling followed by an intramolecular cyclization of pyridoimidazole arylamines and carbonyl compounds promoted by $I_2$/DMSO. Advantageously, this methodology provides a straightforward, one-pot, high yielding approach that does not require prior activation of C($sp^2$)–H or the use of any metal catalyst or base. The conditions can promote mecha-

**Table 2** Synthesis of Phenyl(pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)methanones **3**[a]



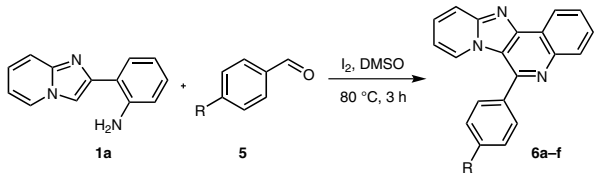

| Entry | Product | $R^1$ | $R^2$ | $R^3$ | Time (h) | Yield (%)[b] |
|---|---|---|---|---|---|---|
| 1 | **3a** | H | H | H | 3 | 84 |
| 2 | **3b** | H | H | 4-Me | 3 | 86 |
| 3 | **3c** | H | H | 4-OMe | 3 | 85 |
| 4 | **3d** | H | H | 4-OEt | 3 | 81 |
| 5 | **3e** | H | H | 4-F | 3 | 81 |
| 6 | **3f** | H | H | 4-Br | 3 | 79 |
| 7 | **3g** | H | H | 4-Cl | 3 | 82 |
| 8 | **3h** | H | H | 4-$NO_2$ | 3 | 80 |
| 9 | **3i** | H | H | 3,5-$(OMe)_2$ | 3 | 84 |
| 10 | **3j** | H | H | 3,4,5-$(OMe)_3$ | 3 | 86 |
| 11 | **3k** | H | H | 4-$CF_3$ | 3 | 82 |
| 12 | **3l** | H | H | 4-OBn | 3 | 80 |
| 13 | **3m** | H | Me | H | 3 | 84 |
| 14 | **3n** | H | Cl | H | 3 | 78 |
| 15 | **3o** | Me | H | H | 3 | 86 |
| 16 | **3p** | Cl | H | H | 3 | 74 |
| 17 | **3q** | Br | H | 4-Me | 3 | 71 |
| 18 | **3r** | H | H | furyl | 3 | 82 |
| 19 | **3s** | H | H | naphthyl | 3 | 78 |

[a] Reaction conditions: i. **2** (1.66 mmol), $I_2$ (2.5 mmol), DMSO (5 mL), r.t., 5 min; ii. **1** (1.66 mmol), 80 °C, ca. 3 h.
[b] Yield of isolated product.




**Scheme 5** Proposed mechanism

**Table 3** Synthesis of 6-Phenylpyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolines **6**[a]




| Entry | Product | R | Time (h) | Yield (%)[b] |
|---|---|---|---|---|
| 1 | **6a** | H | 3 | 80 |
| 2 | **6b** | Me | 3 | 83 |
| 3 | **6c** | F | 3 | 79 |
| 4 | **6d** | Cl | 3 | 78 |
| 5 | **6e** | Br | 3 | 76 |
| 6 | **6f** | CN | 3 | 74 |

[a] Reaction conditions: i. **5** (1.8 mmol), $I_2$ (0.9 mmol), DMSO (5 mL), r.t., 5 min; ii. 2-(imidazo[1,2-*a*]pyridin-2-yl)aniline (**1a**; 1.8 mmol), 80 °C, ca. 3 h.
[b] Yield of isolated product.

nistically distinct reactions and the formation of new C–C and C–N bonds. The scope and utility of this protocol is general and the approach is anticipated to be suitable for a number of applications.

Melting points were measured with a CINTEX programmable melting point apparatus and are uncorrected. $^1$H and $^{13}$C NMR spectra of samples in $CDCl_3$ and DMSO-$d_6$ were recorded with Bruker AVANCE 300, 400 and 500 MHz spectrometers. Chemical shifts (δ) are reported relative to TMS (δ = 0.0 ppm) as the internal standard. Mass spectra were recorded with ESI and EI spectrometers. ESI high-resolution mass spectra were recorded with a QSTAR XL hybrid MS/MS system (Applied Bio systems/MDS sciex, foster city, USA), equipped with an ESI source (IICT, Hyderabad), EI high-resolution mass spectra were recorded with a JEOL-AccuToF mass spectrometer. IR spectra were recorded with a Thermo Nicolet nexus-670 spectrometer with reference to KBr. TLC was performed on Merck 60 F-254 silica gel plates. The chemicals used in this work were obtained from commercial channels and were used without purification.

### Mass Spectrometric Analysis

Positive ESI-MS and MS/MS analyses were performed with a Quattro LC Triple quadrupole mass spectrometer (Micromass, Manchester, UK) under the control of Mass Lynx software (version 4.1). Sample was introduced into the source by using an infusion pump [Harvard Apparatus (Holliston, MA, USA)] at a flow rate of 10 µL/min. Capillary and cone voltages were kept at 3.50 kV and 30 V, respectively. Nitrogen was used as the desolvation gas. The source and desolvation temperatures were kept at 100 °C and 250 °C, respectively. For full-scan experiments, the MS1 was scanned from *m*/*z* 40 to 600. For the MS/MS experiments, keeping MS1 static, the precursor ion of interest was mass selected and the product ions spectrum was obtained by scanning MS2. Argon was used as the collision gas, and the collision gas cell was kept at a pressure of $4.0 \times 10^{-4}$ mbar. The collision energy used was 15–30 eV. The spectra reported were averages of 25 to 30 scans. The HRMS experiments were performed with a Exactive ORBITRAP mass spectrometer (Thermo Scientific, Waltham, MA, USA) equipped with an ESI source. The data was acquired using Xcallibur software (Thermo Scientific). The sample was introduced into the source by flow injection (10 µL loop) using MeOH as the mobile phase at a flow rate of 30 µL/min. The HRMS data for the fragment ions (product ions) was obtained by in-source fragmentation (all ion fragmentation) using a HCD cell and the collision energies used were 10 to 25 eV. Elemental composition for the parent as well as product ions was obtained from the measured accurate mass values by using the software.

### Phenyl(pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)methanone 3a; Typical Procedure

To a two-necked round-bottomed flask equipped with a reflux condenser and a stopper was added acetophenone (**2a**; 200 mg, 1.66 mmol, 1 equiv.), molecular iodine (635 mg, 2.5 mmol, 1.5 equiv.), and DMSO (5 mL) and the reaction mixture was stirred at r.t. for ca. 5 min. To this, 2-(imidazo[1,2-*a*]pyridin-2-yl)aniline (**1a**; 348 mg, 1.66 mmol, 1 equiv.) was added and the reaction mixture was heated to 80 °C for 3 h. The course of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was allowed to cool to r.t., then the iodine was quenched with 1 N aq $Na_2S_2O_3$ solution (10 mL) by stirring the reaction mixture at r.t. for ca. 10 min. The reaction mixture was washed with water and extracted into EtOAc, and the organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was passed through a column silica gel (EtOAc–hexane, 40:60) to give the pure **3a**.

Yield: 450 mg (84%); pale yellow solid; mp 204–206 °C.

IR (KBr): 2925, 1655, 1490, 1357, 1251, 1114, 985, 852, 705 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 8.98–8.95 (d, *J* = 9.0 Hz, 1 H), 8.94–8.91 (m, 1 H), 8.32–8.27 (m, 1 H), 8.26–8.21 (m, 2 H), 8.10–8.04 (m, 1 H ), 7.88–7.83 (m, 2 H), 7.73–7.68 (m, 2 H), 7.58–7.52 (m, 2 H), 7.12–7.07 (t, *J* = 7.2 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 192, 164.2, 149.2, 143.7, 143.9, 134.2, 132.1, 131.4, 130.1, 129.5, 129.3, 128.3, 123.1, 121.8, 120, 117.3, 114.4, 114.1, 113.1.

ESI-MS: *m*/*z* = 324 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{14}N_3O$: 324.1125; found: 324.1124.

### Pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl(p-tolyl)methanone (3b)

Yield: 276 mg (86%); pale yellow solid; mp 221–223 °C.

IR (KBr): 2922, 1654, 1419, 1356, 1252, 1182, 1023, 897, 752 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 8.90–8.80 (m, 2 H), 8.32–8.24 (m, 1 H), 8.16–8.10 (m, 2 H), 7.98–7.92 (m, 1 H), 7.87–7.76 (m, 2 H), 7.64–7.56 (m, 1 H), 7.38–7.32 (m, 2 H), 7.04–6.97 (t, *J* = 6.9 Hz, 1 H), 2.56 (s, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 193.4, 150.6, 148.1, 145.3, 143.7, 143.5, 133.7, 131.7, 130.1, 130.5, 129.4, 129.2, 129.1, 128.0, 122.7, 122.6, 120.5, 117.7, 112.4, 21.8.

ESI-MS: *m*/*z* = 338 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{16}N_3O$: 338.1283; found: 338.1287.

### (4-Methoxyphenyl)(pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)methanone (3c)

Yield: 280 mg (85%); pale yellow solid; mp 216–218 °C.

IR (KBr): 2923, 1644, 1491, 1331, 1261, 1174, 1024, 898, 767 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 8.88–8.78 (m, 2 H), 8.38–8.16 (m, 3 H), 8.05–7.92 (m, 1 H), 7.90–7.73 (m, 2 H), 7.68–7.54 (m, 1 H), 7.12–6.89 (m, 3 H), 3.92 (s, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 191.3, 160.4, 158.1, 148.1, 133.9, 133.2, 131.3, 130.9, 129.6, 129.3, 129.0, 128.3, 128.0, 124.8, 118.6, 117.2, 115.5, 113.2, 55.1.

ESI-MS: *m*/*z* = 354 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{16}N_3O_2$: 354.1236; found: 354.1237.

**(4-Ethoxyphenyl)(pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)methanone (3d)**

Yield: 284 mg (81%); pale yellow solid; mp 227–229 °C.

IR (KBr): 2923, 1608, 1485, 1355, 1253, 1172, 897, 835, 753 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 8.85–8.80 (m, 2 H), 8.23–8.21 (m, 1 H), 8.19–8.12 (m, 2 H), 8.01–7.96 (m, 1 H), 7.78–7.73 (m, 2 H), 7.73–7.58 (m, 1 H), 6.98–6.96 (m, 1 H), 6.91–6.86 (m, 2 H), 4.12–4.05 (q, *J* = 11.0, 14.7 Hz, 2 H), 4.42–4.36 (t, *J* = 7.0 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 191.7, 164.1, 149.1, 143.8, 143.6, 134.1, 132.1, 131.4, 130.0, 129.4, 129.2, 128.3, 123.1, 121.7, 120.1, 117.2, 114.4, 114.0, 113.1, 63.9, 14.6.

ESI-MS: *m*/*z* 368 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{18}N_3O_2$: 368.1012; found: 368.1014.

**(4-Fluorophenyl)(pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)methanone (3e)**

Yield: 256 mg (80%); pale yellow solid; mp 203–205 °C.

IR (KBr): 2924, 1661, 1409, 1327, 1110, 1066, 896, 853, 754 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 9.04–9.00 (d, *J* = 7.0 Hz, 1 H), 8.98–8.93 (m, 1 H), 8.39–8.22 (m, 4 H), 8.16–8.09 (d, *J* = 9.0 Hz, 1 H), 7.91–7.85 (m, 2 H), 7.78–7.71 (m, 1 H), 7.26–7.20 (m, 1 H), 7.18–7.11 (t, *J* = 6.8 Hz, 1 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 192.0, 170.32, 163.27 (d, $^2J$ = 251.6 Hz), 143.8, 143.6, 136.1, 134.1, 132.2, 131.2, 130.0, 128.7, 128.6 (d, $^1J$ = 8.0 Hz), 127.4, 123.0, 120.2, 117.4, 114.8, 114.5, 113.0.

ESI-MS: *m*/*z* = 342 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{13}FN_3O$: 342.1035; found: 342.1037.

**(4-Bromophenyl)(pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)methanone (3f)**

Yield: 300 mg (79%); pale yellow solid; mp 214–216 °C.

IR (KBr): 2923, 1653, 1490, 1322, 1171, 1066, 897, 834, 739 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 9.10–9.06 (d, *J* = 9.0 Hz, 1 H), 8.96–8.91 (m, 1 H), 8.39–8.35 (m, 1 H), 8.23–8.21 (m, 2 H), 8.09–7.99 (m, 1 H), 7.91–7.88 (m, 2 H), 7.84–7.81 (m, 3 H), 7.16–7.10 (t, *J* = 6.5 Hz, 1 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 191.9, 154.4, 148.2, 147.8, 134.6, 133.4, 132.5, 132.2, 131.2, 130.3, 129.9, 129.4, 129.3, 128.6, 128.1, 124.4, 119.1, 117.7, 116.3.

ESI-MS: *m*/*z* = 402 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{13}BrN_3O$: 402.0235; found: 402.0235.

**(4-Chlorophenyl)(pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)methanone (3g)**

Yield: 280 mg (82%); pale yellow solid; mp 218–220 °C.

IR (KBr): 2924, 1654, 1491, 1249, 1087, 1025, 894, 832, 758 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$+DMSO-$d_6$): δ = 9.01–8.96 (m, 1 H), 8.86–8.83 (m, 1 H), 8.26–8.21 (m, 3 H), 8.09–8.01 (m, 1 H), 7.86–7.80 (m, 2 H), 7.71–7.69 (m, 1 H), 7.36–7.31 (m, 2 H), 7.13–7.10 (t, *J* = 6.5 Hz, 1 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$+DMSO-$d_6$): δ = 191.5, 146, 142.7, 139.9, 133.5, 132.4, 131.2, 129.4, 128.9, 128.2, 128.1, 122.3, 121.3, 121.2, 119.7, 116.5, 112.6, 127.9, 124.7.

ESI-MS: *m*/*z* 358 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{13}ClN_3O$: 358.0738; found: 358.0734.

**(4-Nitrophenyl)(pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)methanone (3h)**

Yield: 281 mg (80%); pale yellow solid; mp 225–227 °C.

IR (KBr): 2924, 1617, 1524, 1487, 1361, 1246, 929, 864, 721 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 9.59–9.53 (m, 1 H), 7.86–7.82 (d, *J* = 8.9 Hz, 1 H), 7.57–7.49 (m, 2 H), 7.39–7.29 (m, 2 H), 7.16–7.02 (m, 6 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 193.2, 149.8, 147.9, 145.1, 143.3, 143.5, 133.1, 131.5, 130.3, 129.9, 129.1, 128.9, 128.8, 127.8, 122.5, 122.4, 120.3, 117.5, 112.1.

ESI-MS: *m*/*z* = 369 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{13}N_4O_3$: 369.1652; found: 369.1654.

**(3,5-Dimethoxyphenyl)(pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)methanone (3i)**

Yield: 304 mg (84%); pale yellow solid; mp 208–210 °C.

IR (KBr): 2927, 1648, 1437, 1333, 1186, 1028, 999, 759, 721 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 9.91–9.86 (m, 2 H), 8.46–8.41 (m, 1 H), 8.10–8.06 (m, 1 H), 8.05–8.00 (m, 1 H), 7.93–7.91 (m, 3 H), 7.67–7.61 (m, 1 H), 7.09–7.01 (m, 1 H), 6.96–6.93 (m, 1 H), 3.98 (s, 6 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 192.2, 154.5, 149.9, 149.1, 147.9, 143.8, 130.6, 130.0, 129.1, 129, 128.7, 128.0, 124.1, 122.8, 120.4, 117.7, 112.4, 112.5, 110, 56.2, 56.1.

ESI-MS: *m*/*z* = 384 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{18}N_3O_3$: 384.1345; found: 384.1346.

**Pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl(3,4,5-trimethoxyphenyl)methanone (3j)**

Yield: 330 mg (86%); pale yellow solid; mp 197–199 °C.

IR (KBr): 2930, 1649, 1491, 1334, 1187, 1029, 961, 833, 721 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 8.89–8.83 (m, 1 H), 8.32–8.27 (m, 2 H), 8.02–7.98 (d, *J* = 9.0 Hz, 1 H), 7.86–7.80 (m, 2 H), 7.72–7.63 (m, 2 H), 7.59–7.52 (m, 1 H), 7.51–7.44 (m, 1 H), 7.05–6.99 (t, *J* = 6.8 Hz, 1 H), 3.99 (s, 3 H), 3.88 (s, 6 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 192.3, 152.9, 150.1, 148.2, 143.7, 132.9, 132.1, 131.9, 131.8, 130.65, 130.6, 130.0, 129.1, 128.5, 128.4, 122.8, 117.8, 112.4, 109.2, 61.1, 56.2.

ESI-MS: *m*/*z* = 414 $[M + H]^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{20}N_3O_4$: 414.1442; found 414.1448.

**Pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl[4-(trifluoromethyl)phenyl]methanone (3k)**

Yield: 304 mg (82%); pale yellow solid; mp 221–223 °C.

IR (KBr): 2923, 1667, 1409, 1523, 1175, 1064, 954, 860, 748 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 9.08–9.03 (d, *J* = 7.0 Hz, 1 H), 8.88–8.84 (m, 1 H), 8.37–8.34 (m, 2 H), 8.28–8.23 (m, 2 H), 8.10–8.06 (d, *J* = 9.1 Hz, 1 H), 7.84–7.81 (m, 2 H), 7.76–7.74 (m, 1 H), 7.68–7.63 (m, 1 H), 7.19–7.18 (m, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 192.7, 168.5, 150.1, 147.9, 143.4, 142.4, 139.0, 134.8 (d, $^2J$ = 32.2 Hz), 133.4, 131.9, 131.1, 130.4, 130.2, 129.5, 129.4, 128.8, 125.3, 122.7 (q, $^1J$ = 260.4 Hz), 117.8, 112.8.

ESI-MS: *m*/*z* = 392 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{13}F_3N_3O$: 392.1003; found: 392.1005.

**[4-(Benzyloxy)phenyl](pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)methanone (3l)**

Yield: 80% (330 mg); pale yellow solid; mp 231–233 °C.

IR (KBr): 2933, 1656, 1354, 1247, 1175, 1016, 935, 896, 744 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 9.23–9.21 (d, *J* = 9.0 Hz, 1 H), 8.86–8.81 (m, 1 H), 8.23–8.21 (m, 2 H), 8.13–8.09 (m, 1 H), 8.01–7.99 (m, 2 H), 7.63–7.61 (m, 1 H), 7.34–7.29 (m, 5 H), 7.28–7.27 (m, 1 H), 7.18–7.16 (m, 2 H), 7.09–7.06 (t, *J* = 6.5 Hz, 1 H), 5.21 (s, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 192.0, 163.7, 162.9, 143.6, 136.1, 135.9, 134.1, 132.2, 131.2, 130.1, 129.4, 129.2, 128.7, 128.3, 127.4, 123, 122.1, 121.9, 120.2, 117.4, 114.8, 114.5, 113.0, 70.2.

ESI-MS: *m*/*z* = 430 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{20}N_3O_2$: 430.1544; found: 430.1545.

**(3-Methylpyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)(phenyl)methanone (3m)**

Yield: 252 mg (84%); pale yellow solid; mp 215–217 °C.

IR (KBr): 2922, 1671, 1536, 1446, 1357, 1261, 1039, 926, 809, 724 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 8.15–8.09 (d, *J* = 7.4 Hz, 1 H), 8.02–7.97 (m, 2 H), 7.93–7.87 (m, 2 H), 7.65–7.39 (m, 6 H), 7.04 (m, 1 H), 2.45 (s, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 193.1, 161.7, 153.9, 144.4, 143.1, 134.4, 133.7, 131.4, 129.4, 129.2, 129.1, 128.4, 127.5, 126.4, 124.6, 123.9, 116.8, 114.3, 21.6.

EI-MS: *m*/*z* = 337 [M]$^+$.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{22}H_{15}N_3O$: 337.1215; found: 337.1212.

**(3-Chloropyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)(phenyl)methanone (3n)**

Yield: 227 mg (78%); pale yellow solid; mp 235–237 °C.

IR (KBr): 2924, 1674, 1606, 1571, 1416, 1283, 1177, 1042, 958, 834, 752 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 8.58 (s, 1 H), 8.39 (m, 1 H), 8.99 (m, 1 H), 8.42 (m, 1 H), 8.04 (d, *J* = 7.3 Hz, 1 H), 7.64–7.58 (m, 1 H), 7.57–7.51 (m, 1 H), 7.49–7.44 (t, *J* = 7.7 Hz, 1 H), 7.42–7.37 (m, 1 H), 7.32–7.25 (m, 2 H), 7.09–7.01 (m, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 189.4, 157.4, 147.6, 133.0, 132.6, 132.2, 131.7, 130.0, 129.7, 129.1, 127.9, 125.9, 118.6, 117.2, 116.3, 116.0, 115.8, 115.6, 115.4.

EI-MS: *m*/*z* = 357 [M]$^+$.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{21}H_{12}ClN_3O$: 357.0667; found: 357.0668.

**(9-Methylpyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)(phenyl)methanone (3o)**

Yield: 259 mg (86%); pale yellow solid; mp 210–212 °C.

IR (KBr): 2926, 1654, 1463, 1345, 1234, 1065, 914, 822, 763 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 8.86–8.83 (d, *J* = 9.0 Hz, 1 H), 8.67–8.61 (m, 1 H), 8.39–8.36 (m, 1 H), 8.35–8.31 (m, 2 H), 7.96–7.94 (m, 1 H), 7.82–7.76 (m, 2 H), 7.71–7.69 (m, 1 H), 7.51–7.47 (m, 3 H), 2.49 (s, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 193.7, 148.5, 143.4, 143.3, 135.9, 134.3, 134.1, 131.6, 130.1, 129.9, 129.2, 128.5, 128.3, 126.8, 122.9, 122.8, 122.1, 120.2, 116.7, 18.4.

ESI-MS: *m*/*z* = 338 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{16}N_3O$: 338.1283; found: 338.1287.

**(9-Chloropyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)(phenyl)methanone (3p)**

Yield: 215 mg (74%); pale yellow solid; mp 239–240 °C.

IR (KBr): 2921, 1655, 1568, 1487, 1327, 1254, 1176, 948, 808, 761 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 9.07 (m, 1 H), 8.87–8.84 (m, 1 H), 8.30–8.24 (m, 2 H), 8.14–8.11 (m, 1 H), 8.03–7.99 (m, 1 H), 7.89–7.82 (m, 2 H), 7.74–7.69 (m, 1 H), 7.66–7.61 (m, 1 H), 7.59–7.55 (m, 1 H), 7.50–7.45 (t, *J* = 7.7 Hz, 1 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 193.4, 147.6, 143.4, 143.1, 135.7, 134.2, 133.3, 132.5, 131.7, 130.3, 129.7, 128.9, 128.4, 127.5, 123.0, 122.0, 121.0, 120.5, 117.7.

ESI-MS: *m*/*z* = 358 [M + H]$^+$.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{13}ClN_3O$: 358.0726; found: 358.0741.

**(9-Bromopyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)(*p*-tolyl)methanone (3q)**

Yield: 200 mg (71%); pale yellow solid; mp 223–225 °C.

IR (KBr): 2923, 1689, 1519, 1457, 1315, 1231, 1069, 934, 745 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.83 (d, *J* = 8.8 Hz, 1 H), 7.68–7.66 (m, 1 H), 7.64–7.62 (m, 2 H), 7.32–7.29 (m, 2 H), 7.27–7.23 (m, 1 H), 7.21–7.18 (m, 2 H), 7.13–7.09 (m, 2 H), 2.42 (s, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 190.9, 158.4, 148.2, 145.2, 132.8, 130.9, 130.7, 130.2, 129.9, 129.6, 129.4, 129.3, 129.2, 127.8, 118.8, 117.5, 117.2, 115.6, 21.8.

ESI-MS: *m*/*z* = 416 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{15}BrN_3O$: 416.0391; found: 416.0393.

**Furan-2-yl(pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)methanone (3r)**

Yield: 240 mg (82%); pale yellow solid; mp 198–200 °C.

IR (KBr): 2923, 1643, 1490, 1357, 1259, 1172, 896, 834, 739 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 9.41–9.40 (m, 1 H), 9.16–9.11 (m, 1 H), 8.36–8.32 (m, 1 H), 8.01–7.96 (m, 1 H), 7.92–7.86 (m, 4 H), 7.64–7.61 (m, 1 H), 7.21–7.19 (m, 1 H), 6.98–6.96 (m, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$ + DMSO-$d_6$): δ = 179.3, 150.9, 148.2, 142.8, 142.1, 131.1, 129.8, 129.4, 128.9, 128.1, 125.4, 122.3, 121.6, 116.5, 112.5, 112.4, 119.7, 110.0, 97.5.

ESI-MS: $m/z$ = 314 $[M + H]^+$.

HRMS (ESI): $m/z$ $[M + H]^+$ calcd for $C_{19}H_{12}N_3O_2$: 314.1142; found: 314.1145.

**Naphthalen-2-yl(pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)methanone (3s)**

Yield: 274 mg (78%); pale yellow solid; mp 231–233 °C.

IR (KBr): 2924, 1644, 1489, 1354, 1274, 1097, 952, 828, 745 $cm^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 8.98–8.95 (m, 2 H), 8.70 (s, 1 H), 8.38–8.23 (m, 2 H), 8.21–8.10 (m, 2 H), 8.01–7.88 (m, 4 H), 7.83–7.74 (m, 1 H), 7.71–7.63 (m, 1 H), 7.61–7.53 (m, 1 H), 7.12–7.08 (t, $J$ = 7.1 Hz, 1 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 191.1, 158.2, 148.0, 135.8, 132.5, 132.3, 132.0, 130.9, 130.6, 129.8, 129.6, 129.3, 129.2, 129.0, 128.4, 127.79, 127.0, 126.7, 123.7, 118.7, 117.4, 115.7.

ESI-MS: $m/z$ = 374 $[M + H]^+$.

HRMS (ESI): $m/z$ $[M + H]^+$ calcd for $C_{25}H_{16}N_3O$: 374.1290; found: 374.1287.

**Benzo[4′,5′]thiazolo[2′,3′:2,3]imidazo[4,5-*c*]quinolin-6-yl(3,4,5-trimethoxyphenyl)methanone (3t)**

Yield: 275 mg (78%); pale yellow solid; mp 257–258 °C.

IR (KBr): 2924, 1654, 1577, 1467, 1335, 1233, 1120, 993, 818, 737 $cm^{-1}$.

$^1$H NMR (300 MHz, DMSO-$d_6$ + $CDCl_3$): δ = 9.02 (m, 1 H), 8.07–7.93 (m, 2 H), 7.91–7.80 (m, 1 H), 7.66–7.54 (m, 3 H), 7.52–7.38 (m, 3 H), 3.99 (s, 3 H), 3.90 (s, 6 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 192.6, 158.8, 153.2, 150.1, 144.2, 143.3, 141.7, 137.7, 133.0, 131.4, 130.2, 129.1, 126.9, 125.3, 124.2, 123.4, 122.8, 116.3, 109.0, 94.1, 61.0, 56.3.

ESI-MS: $m/z$ = 470 $[M + H]^+$.

HRMS (ESI): $m/z$ $[M + H]^+$ calcd for $C_{26}H_{20}N_3O_4S$: 470.1150; found: 470.1169.

**1-{2-(2-Aminophenyl)imidazo[1,2-*a*]pyridin-3-yl}-2-phenylethane-1,2-dione (3aa)**

Yield: 200 mg (62%); pale yellow solid; mp 240–242 °C.

IR (KBr): 3445, 2922, 1663, 1591, 1496, 1341, 1270, 1109, 803, 730 $cm^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 13.81 (s, 2 H), 8.91–8.80 (d, $J$ = 7.5 Hz, 1 H), 8.35–8.33 (m, 2 H), 8.20–8.14 (m, 1 H), 7.92–7.90 (m, 1 H), 7.75–7.69 (m, 2 H), 7.66–7.61 (m, 1 H), 7.50–7.48 (m, 2 H), 7.44–7.38 (m, 1 H), 7.23–7.17 (m, 1 H), 6.89–6.81 (m, 1 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 188.6, 183.4, 160.6, 144.7, 144.4, 136.2, 133.9, 131.0, 128.8, 128.3, 127.3, 125.3, 125.1, 124.2, 121.4, 121.2, 117.6, 113.1, 109.1.

ESI-MS: $m/z$ = 342 $[M + H]^+$.

HRMS (ESI): $m/z$ $[M + H]^+$ calcd for $C_{21}H_{16}N_3O_2$: 342.1237; found: 342.1243.

**6-Phenylpyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolines 6a–f; General Procedure**

To a two-necked round-bottomed flask equipped with a reflux condenser and a stopper was added benzaldehyde (**5**; 200 mg, 1.8 mmol, 1 equiv), molecular iodine (239 mg, 0.9 mmol, 0.5 equiv), and DMSO (5 mL) and the reaction mixture was stirred at r.t. for ca. 5 min. To this, 2-(imidazo[1,2-*a*]pyridin-2-yl)aniline (**1a**; 394 mg, 1.8 mmol, 1 equiv) was added and the reaction mixture was heated to 80 °C for 3 h. The course of the reaction was monitored by TLC. The reaction mixture was allowed to cool to r.t., then the iodine was quenched with 1 N aq $Na_2S_2O_3$ solution (10 mL) by stirring the reaction mixture at r.t. for ca. 10 min. The reaction mixture was then washed with water and extracted into EtOAc. The organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was passed through a column of silica gel (EtOAc–hexane, 40:60) to give pure **6**.

**6-Phenylpyrido[2′,1′:2,3]imidazo[4,5-*c*]quinoline (6a)**

Yield: 440 mg (80%); colorless solid; mp 210–212 °C.

IR (KBr): 2923, 1565, 1481, 1361, 1241, 1233, 1026, 950, 837, 758 $cm^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 8.98–8.92 (d, $J$ = 9.0 Hz, 1 H), 8.53–8.47 (m, 1 H), 8.21–8.08 (d, $J$ = 6.5 Hz, 1 H), 7.93–7.91 (d, $J$ = 9.1 Hz, 1 H), 7.82–7.79 (m, 1 H), 7.74–7.71 (m, 3 H), 7.68–7.63 (m, 3 H), 7.56–7.51 (m, 1 H), 6.94–6.84 (t, $J$ = 6.8 Hz, 1 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 149.9, 147.5, 144.1, 147.8, 137.1, 132, 130.4, 129.9, 129.3, 129.2, 128.7, 126.8, 127.1, 121.2, 118, 120, 112.3, 112.6.

ESI-MS: $m/z$ = 296 $[M + H]^+$.

HRMS (ESI): $m/z$ $[M + H]^+$ calcd for $C_{20}H_{14}N_3$: 296.1162; found: 296.1182.

**6-(*p*-Tolyl)Pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinoline (6b)**

Yield: 242 mg (83%); colorless solid; mp 220–222 °C.

IR (KBr): 2922, 1595, 1489, 1362, 1129, 1062, 952, 826, 754 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 8.89–8.97 (m, 2 H), 8.26–8.21 (d, $J$ = 6.8 Hz, 1 H), 8.18–8.10 (d, $J$ = 9.0 Hz, 1 H), 7.95–7.58 (m, 2 H), 7.76–7.31 (m, 3 H), 7.54–7.43 (m, 2 H), 7.09–6.99 (d, $J$ = 7.7 Hz, 1 H), 2.48 (s, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 152.2, 149.4, 146.4, 142.2, 133.1, 132.1, 131.9, 131.1, 130.4, 129.1, 128.1, 127.6, 125.1, 123.1, 120.4, 119.6, 118.4, 113.8, 21.6.

ESI-MS: $m/z$ = 310 $[M + H]^+$.

HRMS (ESI): $m/z$ $[M + H]^+$ calcd for $C_{21}H_{16}N_3$: 310.1319; found: 310.1338.

**6-(4-Fluorophenyl)pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinoline (6c)**

Yield: 237 mg (79%); colorless solid; mp 214–216 °C.

IR (KBr): 2924, 1501, 1428, 1362, 1222, 1160, 952, 844, 732 $cm^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 9.01–8.98 (d, $J$ = 7.7 Hz, 1 H), 8.97–8.93 (d, $J$ = 8.3 Hz, 1 H), 8.38–8.28 (m, 4 H), 8.14–8.11 (m, 1 H), 7.91–7.86 (m, 2 H), 7.74–7.71 (m, 1 H), 7.33–7.30 (m, 1 H), 7.26–7.19 (t, $J$ = 7.3 Hz, 1 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 163.4 (d, $^2J$ = 249.4 Hz), 149.6, 147.4, 147.0, 144.9, 134.3, 130.7 (d, $^1J$ = 8.8 Hz), 130.0, 129.4, 129.0, 126.9, 126.6, 122.6, 121.3, 120.3, 118.1, 116.2, 112.1.

ESI-MS: $m/z$ = 314 $[M + H]^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{13}FN_3$: 314.1074; found: 314.1088.

**6-(4-Chlorophenyl)pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinoline (6d)**

Yield: 241 mg (78%); colorless solid; mp 287–289 °C.

IR (KBr): 2923, 1581, 1401, 1394, 1221, 1034, 957, 821, 764 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.23 (s, 1 H), 8.11–8.06 (m, 4 H), 8.07–8.02 (m, 1 H), 7.98–7.93 (m, 2 H), 7.85–7.81 (m, 3 H), 7.12–7.10 (t, *J* = 7.2 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 146.8, 146.6, 138.3, 136.6, 131.8, 131.4, 131.2, 130.6, 130.3, 130.0, 129.7, 128.7, 127.1, 122.7, 120.3, 118.3, 113.1, 92.8.

ESI-MS: *m*/*z* = 330 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{13}ClN_3$: 330.0788; found: 330.0792.

**6-(4-Bromophenyl)pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinoline (6e)**

Yield: 265 mg (76%); colorless solid; mp 231–233 °C.

IR (KBr): 2921, 15.3, 1422, 1322, 1025, 956, 854, 745 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 8.86–8.81 (d, *J* = 9.0 Hz, 1 H), 8.23 (s, 1 H), 8.19–8.08 (d, *J* = 6.9 Hz, 1 H), 8.04–7.81 (d, *J* = 9.1 Hz, 1 H), 7.90–7.75 (m, 4 H), 7.73–7.60 (m, 3 H), 6.98–6.81 (t, *J* = 6.8 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 154.7, 147.2, 138.5, 133.7, 131.7, 130.4, 130.1, 129.8, 129.5, 129.2, 128.8, 128.7, 128.2, 127.6, 119.9, 117.3, 114.6.

ESI-MS: *m*/*z* = 374 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{13}BrN_{3:}$ 374.0278; found: 374.0287.

**4-(Pyrido[2′,1′:2,3]imidazo[4,5-*c*]quinolin-6-yl)benzonitrile (6f)**

Yield: 222 mg (74%); colorless solid; mp 254–256 °C.

IR (KBr): 2923, 1515, 1405, 1309, 1218, 1106, 1073, 972, 827, 792 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.14 (s, 1 H), 9.07–8.96 (m, 5 H), 8.94–8.89 (m, 4 H), 7.64–7.57 (m, 1 H), 6.94–6.91 (t, *J* = 6.8 Hz, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$+DMSO-$d_6$): δ = 149.2, 145.7, 145.6, 145.4, 142.8, 141.4, 136.9, 132.5, 130.8, 130.3, 130.2, 129.0, 126.1, 122.3, 117.45, 117.4, 112.8, 112.3, 91.8.

ESI-MS: *m*/*z* = 321 [M + H]$^+$.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{13}N_4$: 321.1127; found: 321.1134.

## Acknowledgment

We are grateful to SERB-DST, New Delhi, for financial support (grant no. SB/EMEQ-075/2013). Ashok is thankful to UGC for the award of a JRF.

## Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588366.

## References

(1) (a) Palmer, A. M.; Grobbel, B.; Jecke, C.; Brehm, C.; Zimmermann, P. J.; Buhr, W.; Feth, M. P.; Simon, W. A.; Kromer, W. *J. Med. Chem.* **2007**, *50*, 6240. (b) Miller, C. M.; McCarthy, F. O. *RSC Adv.* **2012**, *2*, 8883. (c) Izuhra, D.; Swager, T. M. *J. Am. Chem. Soc.* **2009**, *131*, 17724. (d) Zajac, M.; Hrobárik, P.; Magdolen, P.; Foltínová, P.; Zahradník, P. *Tetrahedron* **2008**, *64*, 10605.
(2) (a) Brase, S.; Gil, C.; Knepper, K. *Bioorg. Med. Chem. Lett.* **2002**, *10*, 2415. (b) Balaban, A. T.; Oniciu, D. C.; Katritzky, A. R. *Chem. Rev.* **2004**, *104*, 2777.
(3) (a) Anderson, E. A. *Org. Biomol. Chem.* **2011**, *9*, 3997. (b) Shao, Z.; Peng, F. Z. *Curr. Org. Chem.* **2011**, *15*, 4144.
(4) (a) Kianmehr, E.; Ghanbari, M.; Niri, M. N.; Faramarzi, R. *J. Comb. Chem.* **2010**, *12*, 41. (b) Jain, A. N. *J. Med. Chem.* **2004**, *47*, 947. (c) Harrison, T. S.; Keating, G. M. *CNS Drugs* **2005**, *19*, 65. (d) Hanson, S. M.; Morlock, E. V.; Satyshur, K. A.; Czajkowski, C. *J. Med. Chem.* **2008**, *51*, 7243. (e) Almirante, L.; Polo, L.; Mugnaini, A.; Provinciali, E.; Rugarli, P.; Biancotti, A.; Gamba, A.; Murmann, W. *J. Med. Chem.* **1965**, *8*, 305. (f) Linton, A.; Kang, P.; Ornelas, M.; Kephart, S.; Hu, Q.; Pairish, M.; Jiang, Y.; Guo, C. *J. Med. Chem.* **2011**, *54*, 7705.
(5) Upadhayaya, R. S.; Vandavasi, J. K.; Kardile, R. A.; Lahore, S. V.; Dixit, S. S.; Deokar, H. S.; Shinde, P. D.; Sarmah, M. P.; Chattopadhyaya, J. *Eur. J. Med. Chem.* **2010**, *45*, 1854.
(6) Eswaran, S.; Adhikari, A. V.; Kumar, R. A. *Eur. J. Med. Chem.* **2010**, *45*, 957.
(7) Eswaran, S.; Adhikari, A. V.; Pal, N. K.; Chowdhury, I. H. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 1040.
(8) Eswaran, S.; Adhikari, A. V.; Shetty, N. S. *Eur. J. Med. Chem.* **2009**, *44*, 4637.
(9) Yang, C. L.; Tseng, C. H.; Chen, Y. L.; Lu, C. M.; Kao, C. L.; Tseng, H. Y.; Wu, M. H.; Tzeng, C. C. *Eur. J. Med. Chem.* **2010**, *45*, 602.
(10) Tseng, C. H.; Tzeng, C. C.; Yang, C. L.; Lu, P. J.; Chen, H. L.; Li, H. Y.; Chuang, Y. C.; Yang, C. N.; Chen, Y. L. *J. Med. Chem.* **2010**, *53*, 6164.
(11) Chen, Y. W.; Chen, Y. L.; Tseng, C. H.; Liang, C. C.; Yang, C. N.; Yao, Y. C.; Lu, P. J.; Tzeng, C. C. *J. Med. Chem.* **2011**, *54*, 4446.
(12) Tseng, C. H.; Chen, Y. L.; Yang, C. L.; Cheng, C. M.; Han, C. H.; Tzeng, C. C. *Bioorg. Med. Chem.* **2012**, *20*, 4397.
(13) Chang, F. S.; Chen, W. C.; Wang, C. H.; Tzeng, C. C.; Chen, Y. L. *Bioorg. Med. Chem.* **2010**, *18*, 124.
(14) Tseng, C. H.; Chen, Y. L.; Chung, K. Y.; Wang, C. H.; Peng, S. I.; Cheng, C. M.; Tzeng, C. C. *Org. Biomol. Chem.* **2011**, *9*, 3205.
(15) Tseng, C. H.; Chen, Y. L.; Hsu, C. Y.; Chen, T. C.; Cheng, C. M.; Tso, H. C.; Lu, Y. J.; Tzeng, C. C. *Eur. J. Med. Chem.* **2013**, *59*, 274.
(16) Koh, E. J.; El-Gamal, M. I.; Oh, C. H.; Lee, S. H.; Sim, T.; Kim, G.; Choi, H. S.; Hong, J. H.; Lee, S.; Yoo, K. H. *Eur. J. Med. Chem.* **2013**, *70*, 10.
(17) Arafa, R. K.; Hegazy, G. H.; Piazza, G. A.; Abadi, A. H. *Eur. J. Med. Chem.* **2013**, *63*, 826.
(18) Ahmed, N.; Brahmbhatt, K. G.; Sabde, S.; Mitra, D.; Singh, I. P.; Bhutani, K. K. *Bioorg. Med. Chem.* **2010**, *18*, 2872.
(19) Peng, H. K.; Lin, C. K.; Yang, S. Y.; Tseng, C. K.; Tzeng, C. C.; Lee, J. C.; Yang, S. C. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 1107.
(20) Parkinson, T.; Pryde, D. C. *Fut. Med. Chem.* **2010**, *2*, 1181.
(21) Tseng, C. H.; Lin, C. K.; Chen, Y. L.; Hsu, C. Y.; Wu, H. N.; Tseng, C. K.; Lee, J. C. *Eur. J. Org. Chem.* **2014**, 66.
(22) Adhikary, P. K.; Das, S. K. *J. Med. Chem.* **1976**, *19*, 1352.
(23) Pandey, A. K.; Sharma, R.; Shivahare, R.; Arora, A.; Rastogi, N.; Gupta, S.; Chauhan, P. M. S. *J. Org. Chem.* **2013**, *78*, 1534.

(24) Sharma, S.; Saha, B.; Sawant, D.; Kundu, B. *J. Comb. Chem.* **2007**, *9*, 783.

(25) (a) Anand Kumar, P.; Sharma, R.; Singh, A.; Shukla, S.; Srivastava, K.; Puri, S. K.; Kumar, B.; Chauhan, P. M. S. *RSC Adv.* **2014**, *4*, 26757. (b) Kielesiński, Ł.; Tasior, M.; Gryko, D. T. *Org. Chem. Front.* **2015**, *2*, 21. (c) Avik Kumar, B.; Sougata, S.; Kamarul, M.; Alakananda, H. *Chem. Commun.* **2015**, *51*, 1555. (d) Kasiviswanadharaju, P.; Pinku, K.; Khima, P.; Anil, K. *Synthesis* **2015**, *47*, 887.

(26) Fan, X.-S.; Zhang, J.; Bin, L.; Zhang, X.-Y. *Chem. Asian J.* **2015**, *10*, 1281.

(27) (a) Narender Reddy, E.; Chiranjeevi, B.; Sudha Sravanti, K.; Ramesh, U.; Jagadeesh Babu, N.; Krishnaiah, A. *Bioorg. Med. Chem. Lett.* **2015**, *25*, 2918. (b) Ashok, K.; Madhu, Ch.; Chiranjeevi, B.; Jagadeesh Babu, N.; Krishnaiah, A. *Org. Biomol. Chem.* **2016**, *14*, 582.

(28) Madhu, Ch.; Narender Reddy, E.; Chiranjeevi, B.; Krishnaiah, A. *RSC Adv.* **2015**, *5*, 19418.