# An Efficient Method for Synthesis of Pyrano[3,2-*c*]pyridine Derivatives under Microwave Irradiation



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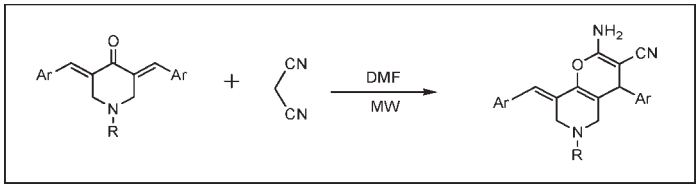


A series of pyrano[3,2-*c*]pyridine derivatives were synthesized *via* reactions of 3,5-dibenzylidenepiperidin-4-one and malononitrile in *N*,*N*-dimethylformamide under microwave irradiation. It is a simple, efficient, and promising synthetic method to construct pyrano[3,2-*c*]pyridine skeleton.

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## INTRODUCTION

Since the cytotoxic activity of (*E*)-3,5-bis (benzylidene)-4-piperidones **1** (Fig. 1) and their specificity toward leukemia cell lines with $IC_{50}$ values $<10$ $\mu M$ have been reported [1] in 1992, the design and synthesis of their derivatives have been an object of big interest because of their potential application. The practice of incorporating chalcones into heterocyclic nitrogenous ring has been noticed recently [2–6]. The studies show that compound **2** is potential broad-spectrum antitumor agents [4].

Microwave irradiation (MWI) of organic reactions has rapidly gained popularity because it accelerates a variety of synthetic transformations [7] and have the prominent advantages of short reaction time and high yield [8].

It is well known that the 2-amino-3-cyanopyrans was obtained by the reaction of chalcones with malononitrile, and several articles on this topic can be found in the literature [9]. However, there are few reports for the synthesis of **2**. These methods generally required long reaction time [4,5] or used EtONa [6] as catalyst. To provide vast new compounds for biomedical screening, a simple and efficient method for the synthesis of these molecules is urgently required.

In continuation of our recent interest in the construction of heterocyclic scaffolds [10], we herein describe a practical, inexpensive, rapid microwave-assisted method for the preparation of pyrano[3,2-*c*] pyridine derivatives *via* reactions of 3,5-dibenzylidenepiperidin-4-one and malononitrile in *N*,*N*-dimethylformamide (DMF) (Scheme 1).

## RESULTS AND DISCUSSION

To explore conditions of the reaction of 3,5-dibenzylidenepiperidin-4-one **3** and malononitrile **4** in DMF (Scheme 1) under MWI, various reaction conditions were investigated, including solvent and temperature. To search for the optimal reaction solvent, the reaction of 3,5-bis(4-chlorobenzylidene)-1-methylpiperidin-4-one (**3c**) and malononitrile **4**, was examined in ethylene glycol, DMF, glacial acetic acid, and ethanol, respectively (Table 1, entries 1–4) under MWI at the maximum power of 200 W. As shown in Table 1, the reaction in DMF resulted in higher yields and shorter reaction time than others. So DMF was chosen as the appropriate solvent. To further optimize the reaction condition, the same reaction was carried out in DMF at temperatures ranging from 90 to 140°C (Table 1, entries 5–9), with an increment of 10°C each time. As shown in Table 1, the yields of product was increased and the reaction time was shortened when the temperature was increased from 90 to 120°C, however, further increase of the temperature from 130 to 140°C failed to improve the yield (Table 1, entries 9 and 10). Therefore, 120°C was chosen as the most suitable temperature for all further microwave-assisted reactions.

Based on these optimized conditions [DMF, 120°C, 200 W (maximum power)], reactions of different 3,5-dibenzylidenepiperidin-4-ones and malononitrile were performed, a series of pyrano[3,2-*c*]pyridine derivatives were synthesized with good yields. The results (Table 2, entries 1–12) indicated that for 3,5-dibenzylidenepiperidin-4-one bearing different functional groups such as

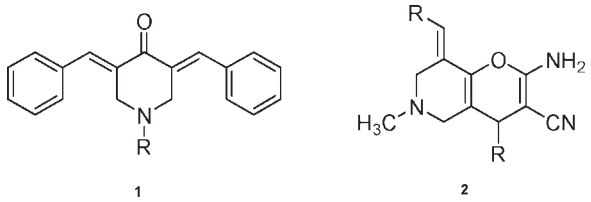


**Figure 1.** 3,5-Dibenzylidenepiperidin-4-one and its derivatives.

chloro, bromo, fluoro, nitro, or methyl the reaction proceeded smoothly in all cases. We have also observed the electronic effects: that is, 3,5-dibenzylidenepiperidin-4-one with electron-withdrawing groups (Table 2, entries 3–6) reacted rapidly, whereas electron-rich groups (Table 2, entry 2) decreased the reactivity, requiring longer reaction time.

A possible mechanism for the formation of the product **5** is outlined in Scheme 2. We proposed that the formation of **5** proceeds *via* an initial Michael addition reaction of chalcones and malononitrile to afford intermediate **6**, which then cyclized to give compound **5**.

The structures of all the synthesized compounds were established on the basis of their spectroscopic data. The IR spectrum of compound **5b** showed strong absorptions at 3389 $cm^{-1}$ and 3295 $cm^{-1}$ due to the $NH_2$ group, 2178 $cm^{-1}$ due to the CN group. The $^1H$ NMR spectrum of **5b** showed a broad singlet at δ 6.76 due to the $-NH_2$ proton and a singlet at δ 6.87 due to the =CH proton. In the IR spectrum of compound **5h**, the appearance of bands at 3329 $cm^{-1}$, 3279 $cm^{-1}$, and 2192 $^{-1}$ due to the $NH_2$ and CN triple bound. The appearance of a broad singlet at δ 6.90 due to the $NH_2$ protons and a singlet at δ 6.92 due to =CH in the $^1H$ NMR spectrum further confirmed the structure of product.

In conclusion, we have developed a simple and efficient method for the synthesis of pyrano[3,2-*c*]pyridine derivatives. The protocol includes particularly valuable features of excellent yield, shorten reaction time, reduced environmental impact, and straightforward procedure.

## EXPERIMENTAL

All reactions were performed in a monomodal Emrys™ Creator from Personal Chemistry, Uppsala, Sweden. Melting points were determined in open capillaries and are uncorrected.

**Scheme 1**

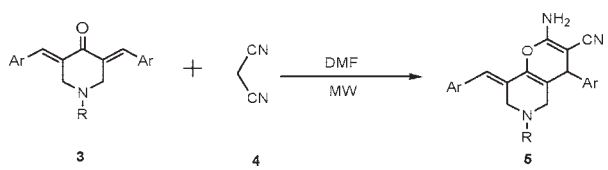


**Table 1**

Optimization for the synthesis of **5c**.

| Entry | Solvent | *T* (°C) | Time (min) | Yield (%) |
|---|---|---|---|---|
| 1 | HOAc | 100 | 8 | 45 |
| 2 | Glycol | 100 | 8 | 86 |
| 3 | DMF | 100 | 8 | 91 |
| 4 | EtOH | 100 | 8 | 83 |
| 5 | DMF | 90 | 8 | 90 |
| 6 | DMF | 110 | 7 | 92 |
| 7 | DMF | 120 | 6 | 94 |
| 8 | DMF | 130 | 6 | 92 |
| 9 | DMF | 140 | 6 | 90 |

IR spectra were recorded on an FTIR-tensor 27 spectrometer. $^1H$ NMR spectra were measured on a DPX 400 MHz spectrometer using TMS as an internal standard and DMSO-$d_6$ as solvent. Elemental analysis was determined by using a PerkinElmer 240c elemental analysis instrument.

**General procedure for the synthesis of compound 3N.** In a 50 mL reaction vial, a mixture of 4-piperidone (10 mmol), the appropriate aldehyde (20 mmol), 1 mL 10% NaOH and 30 mL 95% EtOH was stirred at room temperature for 0.5–2 h. The separated solid was then filtered.

**General procedure for the synthesis of compound 5 under MWI.** In a 10 mL reaction vial, the 3,5-dibenzylidenepiperidin-4-one 3 (1 mmol), malononitrile (1.1 mmol), and DMF (2 mL) were mixed and then capped. The mixture was irradiated at 200 W (initial power 150 W, maximum power 200 W) at 120°C for a given time. On completion (the reaction was monitored by TLC), the reaction mixture was cooled to room temperature and poured into water (70 mL), filtered to give the crude product, which was further purified by recrystallization from 95% EtOH to give pure product.

***2-Amino-8-benzylidene-5,6,7,8-tetrahydro-6-methyl-4-phenyl-4H-pyrano[3,2-c]pyridine-3-carbonitrile (5a).*** IR (KBr) 3338, 3284, 2189, 1683, 1640, 1619, 1594, 1489, 1453, 1415, 1399, 1326, 1272, 1218, 1171, 1110, 1050, 917, 904, 878, 766, 756, 699 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): δ 7.43–7.35 (m, 4H, ArH), 7.31–7.22 (m, 6H, ArH), 6.93 (s, 1H, =CH), 6.84 (brs, 2H, $NH_2$), 4.06 (s, 1H, CH), 3.48 (d, 1H, $J$ = 14.4 Hz, $CH_2$), 3.28 (d, 1H, $J$ = 14.4 Hz, $CH_2$), 3.00 (d, 1H, $J$ = 16.0 Hz, $CH_2$), 2.57 (d, 1H, $J$ = 16.0 Hz, $CH_2$), 2.15 (s, 3H, $CH_3$). $^{13}C$ NMR (DMSO-$d_6$): δ = 159.79, 143.49, 139.15, 135.93, 128.96, 128.69, 128.49, 127.60, 127.46, 127.14, 121.43, 120.44, 113.23, 112.71, 55.86, 54.56, 54.08, 44.50, 41.07. Anal. Calcd for $C_{23}H_{21}N_3O$: C, 77.72; H, 5.96; N, 11.82; found C, 77.83; H, 5.94; N, 11.79.

***8-(4-Methylbenzylidene)-2-amino-4-(4-methylphenyl)-5,6,7,8-tetrahydro-6-methyl-4H-pyrano[3,2-c]pyridine-3-carbonitrile (5b).*** IR (KBr) 3389, 3295, 2178, 1682, 1644, 1604, 1511, 1461, 1448, 1416, 1395, 1323, 1269, 1205, 1171, 1101, 1055, 911, 812 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): δ 7.22 (d, 2H, $J$ = 8.0 Hz ArH), 7.17–7.13 (m, 4H, ArH), 7.09 (d, 2H, $J$ = 8.0 Hz, ArH), 6.87 (s, 1H, =CH), 6.76 (brs, 2H, $NH_2$), 3.99 (s, 1H, CH), 3.46 (d, 1H, $J$ = 14.8 Hz, $CH_2$), 3.28 (d, 1H, $J$ = 17.2 Hz, $CH_2$), 2.96 (d, 1H, $J$ = 16.4 Hz, $CH_2$), 2.53 (d, 1H, $J$ = 17.6 Hz, $CH_2$), 2.31 (s, 3H, $CH_3$), 2.29 (s, 3H, $CH_3$), 2.14 (s, 3H, $CH_3$). $^{13}C$ NMR (DMSO-$d_6$): δ = 159.72, 140.55, 139.08, 136.53, 136.21, 133.09, 129.23, 129.09, 128.92, 127.50,

**Table 2**

Synthesis of compounds **5** under microwave irradiation.

| Entry | Product | R | Ar | Time/min | Yield (%) | Mp/°C |
|---|---|---|---|---|---|---|
| 1 | **5a** | Methyl | $C_6H_5$ | 6 | 93 | 200–202 |
| 2 | **5b** | Methyl | 4-$CH_3C_6H_4$ | 9 | 92 | 215–217 (214–215)[a] |
| 3 | **5c** | Methyl | 4-$ClC_6H_4$ | 6 | 94 | 238–240 |
| 4 | **5d** | Methyl | 3-$NO_2C_6H_4$ | 7 | 91 | 225–227 |
| 5 | **5e** | Methyl | 4-$NO_2C_6H_4$ | 7 | 92 | 238–240 |
| 6 | **5f** | Methyl | 4-$BrC_6H_4$ | 7 | 93 | 245–246 |
| 7 | **5g** | Benzyl | $C_6H_5$ | 6 | 94 | 226–228 |
| 8 | **5h** | Benzyl | 4-$ClC_6H_4$ | 7 | 94 | 243–245 |
| 9 | **5i** | Benzyl | 4-$FC_6H_4$ | 7 | 93 | 235–237 |
| 10 | **5j** | Benzyl | 3-$NO_2C_6H_4$ | 7 | 90 | 225–227 |
| 11 | **5k** | Benzyl | 4-$NO_2C_6H_4$ | 7 | 89 | 233–236 |
| 12 | **5l** | Benzyl | 4-$BrC_6H_4$ | 7 | 92 | 242–244 |

[a] Literature melting point.

126.80, 121.28, 120.48, 112.93, 55.99, 54.56, 54.17, 44.52, 40.70, 20.79, 20.65. Anal. Calcd for $C_{25}H_{25}N_3O$: C, 78.30, H, 6.57; N, 10.96; found C, 78.39; H, 6.56; N, 10.92.

***8-(4-Chlorobenzylidene)-2-amino-4-(4-chlorophenyl)-5,6,7,8-tetrahydro-6-methyl-4H-pyrano[3,2-c]pyridine-3-carbonitrile (5c).*** IR (KBr) 3365, 3289, 2180, 1681, 1645, 1605, 1489, 1461, 1449, 1413, 1393, 1321, 1267, 1207, 1169, 1092, 1056, 1014, 986, 911, 817, 737, 697 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): δ 7.48–7.43 (m, 4H, ArH), 7.26 (m, 4H, ArH), 6.92 (brs, 2H, $NH_2$), 6.89 (s, 1H, =CH), 4.12 (s, 1H, CH), 3.46 (d, 1H, $J$ = 13.6 Hz, $CH_2$), 3.28 (d, 1H, $J$ = 14.8 Hz, $CH_2$), 3.00 (d, 1H, $J$ = 16.0 Hz, $CH_2$), 2.55 (d, 1H, $J$ = 16.0 Hz, $CH_2$), 2.16 (s, 3H, $CH_3$). $^{13}C$ NMR (DMSO-$d_6$): δ = 159.79, 142.43, 139.23, 134.78, 131.76, 131.72, 130.71, 129.47, 128.70, 128.51, 128.13, 120.36, 120.19, 113.25, 55.54, 54.39, 53.92, 44.40, 40.39. Anal. Calcd for $C_{23}H_{19}Cl_2N_3O$: C, 65.10, H, 4.51; N, 9.90; found C, 65.01; H, 4.53; N, 9.94.

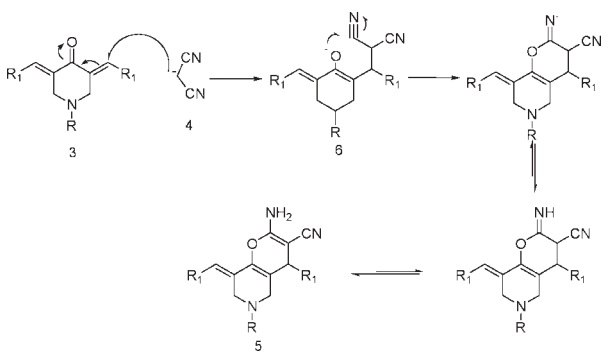
***8-(3-Nitrobenzylidene)-2-amino-5,6,7,8-tetrahydro-6-methyl-4-(3-nitrophenyl)-4H-pyrano[3,2-c]pyridine-3-carbonitrile (5d).*** IR (KBr) 3359, 3267, 2190, 1676, 1639, 1596, 1522, 1456, 1416, 1348, 1266, 1174, 1116, 1052, 984, 899, 818, 738, 714, 682 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): δ 8.19–8.14 (m, 2H, ArH), 8.09 (s, 1H, ArH) 8.06 (s, 1H, ArH), 7.75–7.69 (m, 4H, ArH), 7.05 (brs, 3H, $NH_2$, and =CH), 4.41 (s, 1H, CH), 3.53 (d, 1H, $J$ = 14.0 Hz, $CH_2$), 3.28 (d, 1H, $J$ = 14.8 Hz, $CH_2$), 3.09 (d, 1H, $J$ = 16.4 Hz, $CH_2$), 2.59 (d, 1H, $J$ = 16.0 Hz, $CH_2$), 2.17 (s, 3H, $CH_3$). $^{13}C$ NMR (DMSO-$d_6$): δ = 159.98, 148.06, 147.94, 145.66, 139.42, 137.45, 135.14, 134.46, 130.48, 130.09, 129.62, 123.37, 122.41, 122.04, 121.84, 119.98, 119.84, 113.67, 55.07, 54.14, 53.60, 44.25, 40.48. Anal. Calcd for $C_{23}H_{19}N_5O_5$: C, 62.02, H, 4.30; N, 15.72; found C, 62.17; H, 4.28; N, 15.66.

***8-(4-Nitrobenzylidene)-2-amino-5,6,7,8-tetrahydro-6-methyl-4-(4-nitrophenyl)-4H-pyrano[3,2-c]pyridine-3-carbonitrile (5e).*** IR (KBr) 3365, 3293, 2182, 1688, 1642, 1593, 1521, 1458, 1418, 1392, 1340, 1273, 1172, 1097, 1055, 907, 868, 809, 716 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): δ 8.26 (d, 4H, $J$ = 8.0 Hz, ArH), 7.54 (d, 4H, $J$ = 8.8 Hz, ArH) 7.06 (brs, 2H, $NH_2$), 7.03 (s, 1H, =CH), 4.36 (s, 1H, CH), 3.53 (d, 1H, $J$ = 14.4 Hz, $CH_2$), 3.48–3.43 (m, 1H, $CH_2$), 3.08 (d, 1H, $J$ = 16.4 Hz, $CH_2$), 2.56 (d, 1H, $J$ = 16.4 Hz, $CH_2$), 2.17 (s, 3H, $CH_3$). $^{13}C$ NMR (DMSO-$d_6$): δ = 159.91, 150.84, 146.75, 145.93, 142.74, 139.46, 130.70, 130.09, 128.98, 124.10, 123.70, 120.07, 119.95, 114.32, 56.01, 54.75, 54.25, 53.81, 44.30, 40.69. Anal. Calcd for $C_{23}H_{19}N_5O_5$: C, 62.02, H, 4.30; N, 15.72; found C, 61.92; H, 4.32; N, 15.77.

***8-(4-Bromobenzylidene)-2-amino-4-(4-bromophenyl)-5,6,7,8-tetrahydro-6-methyl-4H-pyrano[3,2-c]pyridine-3-carbonitrile (5f).*** IR (KBr) 3364, 3283, 2181, 1681, 1644, 1590, 1486, 1459, 1409, 1391, 1321, 1267, 1169, 1104, 1074, 1010, 910, 895, 828, 814, 734 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): δ 7.61–7.56 (m, 4H, ArH), 7.23–7.18 (m, 4H, ArH), 6.89 (brs, 2H, $NH_2$), 6.87 (s, 1H, =CH), 4.11 (s, 1H, CH), 3.46 (d, 1H, $J$ = 14.0 Hz, $CH_2$), 3.26 (d, 1H, $J$ = 14.0 Hz, $CH_2$), 3.00 (d, 1H, $J$ = 16.4 Hz, $CH_2$), 2.53 (d, 1H, $J$ = 16.4 Hz, $CH_2$), 2.16 (s, 3H, $CH_3$). $^{13}C$ NMR (DMSO-$d_6$): δ = 159.72, 142.77, 139.18, 135.05, 131.55, 131.36, 130.93, 129.78, 128.11, 120.35, 120.30, 120.18, 120.11, 113.16, 55.39, 54.32, 53.85, 44.33, 40.40. Anal. Calcd for $C_{23}H_{19}Br_2N_3O$: C, 53.83, H, 3.73; N, 8.19; found C, 53.96; H, 3.70; N, 8.15.

***2-Amino-6-benzyl-8-benzylidene-5,6,7,8-tetrahydro-4-phenyl-4H-pyrano[3,2-c]pyridine-3-carbonitrile (5g).*** IR (KBr) 3299, 3259, 2189, 1684, 1639, 1618, 1592, 1491, 1453, 1400, 1374, 1349, 1269, 1218, 1169, 1100, 1075, 1042, 919, 878, 746, 696 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): δ 7.37–7.32 (m, 4H, ArH), 7.29–7.25 (m, 2H, ArH), 7.23–7.19 (m, 4H, ArH), 7.18–7.16 (m, 3H, ArH), 7.09–7.07 (m, 2H, ArH), 6.95 (s, 1H, =CH), 6.86 (brs, 2H, $NH_2$), 4.01 (s, 1H, CH), 3.63 (d, 1H, $J$ = 14.4 Hz,

**Scheme 2**



$CH_2$), 3.45 (m, 3H, $CH_2$), 3.07 (d, 1H, $J$ = 16.0 Hz, $CH_2$), 2.69 (d, 1H, $J$ = 16.0 Hz, $CH_2$). $^{13}$C NMR (DMSO-$d_6$): δ = 159.79, 143.48, 139.47, 137.74, 135.89, 128.87, 128.64, 128.38, 128.00, 127.56, 127.10, 126.91, 121.83, 120.39, 112.87, 59.89, 56.05, 52.26, 51.69, 41.07. Anal. Calcd for $C_{29}H_{25}N_3O$: C, 80.72, H, 5.84; N, 9.74; found C, 80.86; H, 5.83; N, 9.70.

***8-(4-Chlorobenzylidene)-2-amino-6-benzyl-4-(4-chlorophenyl)-5,6,7,8-tetrahydro-4H-pyrano[3,2-c]pyridine-3-carbonitrile (5h).*** IR (KBr) 3329, 3279, 2192, 1683, 1649, 1598, 1489, 1411, 1395, 1375, 1325, 1265, 1214, 1169, 1091, 1049, 1013, 917, 884, 826, 753, 700 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$): δ 7.43–7.39 (m, 4H, ArH), 7.23–7.17 (m, 7H, ArH), 7.07–7.06 (m, 2H, ArH), 6.92 (s, 1H, =CH), 6.90 (brs, 2H, $NH_2$), 4.07 (s, 1H, CH), 3.61 (d, 1H, $J$ = 14.8 Hz, $CH_2$), 3.46–3.42 (m, 3H, $CH_2$), 3.06 (d, 1H, $J$ = 16.8 Hz, $CH_2$), 2.66 (d, 1H, $J$ = 16.0 Hz, $CH_2$). $^{13}$C NMR (DMSO-$d_6$): δ = 159.78, 142.45, 139.46, 137.69,134.73, 131.70, 130.62, 129.45 128.66, 128.60, 128.42, 127.99, 127.74, 126.94, 120.79, 120.19, 112.86, 112.72, 59.65, 55.60, 51.81, 51.61, 40.30. Anal. Calcd for $C_{29}H_{23}Cl_2N_3O$: C, 69.60, H, 4.63; N, 8.40; found C, 69.75; H, 4.62; N, 8.37.

***8-(4-Fluorobenzylidene)-2-amino-6-benzyl-4-(4-fluorophenyl)-5,6,7,8-tetrahydro-4H-pyrano[3,2-c]pyridine-3-carbonitrile (5i).*** IR (KBr) 3334, 3298, 2197, 1684, 1650, 1602, 1507, 1417, 1398, 1375, 1267, 1225, 1157, 1091, 916, 831, 780, 756, 697 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$): δ 7.25–7.20 (m, 4H, ArH), 7.19–7.14 (m, 7H, ArH), 7.08–7.06 (m, 2H, ArH), 6.92 (s, 1H, =CH), 6.83 (brs, 2H, $NH_2$), 4.05 (s, 1H, CH), 3.59 (d, 1H, $J$ = 14.0 Hz, $CH_2$), 3.45 (s, 2H, $CH_2$), 3.40 (d, 1H, $J$ = 14.4 Hz, $CH_2$), 3.05 (d, 1H, $J$ = 16.0 Hz, $CH_2$), 2.65 (d, 1H, $J$ = 16.0Hz, $CH_2$). $^{13}$C NMR (DMSO-$d_6$): δ = 162.28, 159.72, 139.63, 139.37, 137.69, 132.28, 130.93, 130.85, 129.49, 129.40, 128.62, 127.99, 126.94, 120.86, 120.32, 115.51, 115.43, 115.30, 115.21, 112.66, 59.75, 55.84, 51.98, 51.57. Anal. Calcd for $C_{29}H_{23}F_2N_3O$: C, 74.50; H, 4.96; N, 8.99; found C, 74.66; H, 4.93; N, 8.95.

***8-(3-Nitrobenzylidene)-2-amino-6-benzyl-5,6,7,8-tetrahydro-4-(3-nitrophenyl)-4H-pyrano[3,2-c]pyridine-3-carbonitrile (5j).*** IR (KBr) 3337, 3293, 2184, 1679, 1647, 1596, 1522, 1465, 1399, 1351, 1263, 1218, 1159, 1085, 914, 815, 739, 695, 685 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$): δ 8.16–8.17 (m, 1H, ArH), 8.12–8.10 (m, 1H, ArH), 8.03 (brs, 2H, $NH_2$), 7.70–7.65 (m, 4H, ArH), 7.12–7.11 (m, 3H, ArH), 7.07 (s, 1H, =CH), 7.06–7.04 (m, 4H, ArH), 4.35 (s, 1H, CH), 3.66 (d, 1H, $J$ = 14.4 Hz, $CH_2$), 3.54 (d, 1H, $J$ = 15.2 Hz, $CH_2$), 3.49–3.34 (m, 2H, $CH_2$), 3.13 (d, 1H, $J$ = 16.4 Hz, $CH_2$), 2.69 (d, 1H, $J$ = 16.0 Hz, $CH_2$). $^{13}$C NMR (DMSO-$d_6$): δ = 159.78, 142.45, 139.46, 137.69, 134.73, 131.70, 130.62, 129.45, 128.66, 128.60, 128.42, 127.99, 127.74, 126.93, 120.79, 112.87, 59.65, 56.01, 55.60, 51.89, 51.81, 51.62, 40.29. Anal. Calcd for $C_{29}H_{23}N_5O_5$: C, 66.79; H, 4.45; N, 13.43; found C, 66.96; H, 4.42; N, 13.39.

***8-(4-Nitrobenzylidene)-2-amino-6-benzyl-5,6,7,8-tetrahydro-4-(4-nitrophenyl)-4H-pyrano[3,2-c]pyridine-3-carbonitrile (5k).*** IR (KBr) 3329, 3301, 2200, 1681, 1650, 1591, 1517, 1421, 1398, 1340, 1269, 1218, 1168, 1108, 920, 895, 859, 811, 748, 700 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$): δ 8.24–8.19 (m, 4H, ArH), 7.51–7.48 (m, 4H, ArH), 7.15 (s, 1H, =CH), 7.14–7.13 (m, 2H, ArH), 7.08–7.06 (m, 3H, ArH), 7.05 (brs 2H, $NH_2$), 4.31 (s, 1H, CH), 3.69 (d, 1H, $J$ = 14.8 Hz, $CH_2$), 3.53 (d, 1H, $J$ = 14.8 Hz, $CH_2$), 3.48 (s, 2H, $CH_2$), 3.13 (d, 1H, $J$ = 16.4 Hz, $CH_2$), 2.66 (d, 1H, $J$ = 15.6 Hz, $CH_2$). $^{13}$C NMR (DMSO-$d_6$): δ = 159.90, 150.89, 146.73, 145.92, 142.73, 139.70, 137.52, 130.34, 130.01, 128.97, 128.57, 127.98, 126.95, 124.03, 123.60, 113.88, 59.42, 54.85, 51.58, 40.59. Anal. Calcd for $C_{29}H_{23}N_5O_5$: C, 66.79; H, 4.45; N, 13.43; found C, 66.64; H, 4.47; N, 13.48.

***8-(4-Bromobenzylidene)-2-amino-6-benzyl-4-(4-bromophenyl)-5,6,7,8-tetrahydro-4H-pyrano[3,2-c]pyridine-3-carbonitrile (5l).*** IR (KBr) 3326, 3293, 2196, 1681, 1644, 1594, 1485, 1407, 1392, 1373, 1322, 1267, 1170, 1098, 1071, 1010, 917, 887, 815, 749, 696 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$): δ 751–7.48 (m, 4H, ArH), 7.14–7.12 (m, 5H, ArH), 7.10 (m, 2H, ArH) 7.02–7.00 (m, 2H, ArH), 6.86 (brs, 2H, $NH_2$), 6.84 (s, 1H, =CH), 3.99 (s, 1H, CH), 3.56 (d, 1H, $J$ = 14.4 Hz, $CH_2$), 3.40–3.36 (m, 3H ,$CH_2$), 3.00 (d, 1H, $J$ = 16.0 Hz, $CH_2$), 2.60 (d, 1H, $J$ = 16.0 Hz, $CH_2$). $^{13}$C NMR (DMSO-$d_6$): δ = 159.77, 142.87, 139.46, 137.69, 135.06, 131.59, 131.34, 130.92, 129.83, 128.60, 128.01, 120.32, 120.23, 112.84, 59.62, 55.48, 51.75, 51.67, 40.36. Anal. Calcd for $C_{29}H_{23}Br_2N_3O$: C, 59.10, H, 3.94; N, 7.13; found C, 58.95; H, 3.95; N, 7.16.

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