Synthesis of 2-Aminoindole-3-carboxylic Acid Derivatives by the Copper(I) Iodide Catalyzed Reaction of *N*-(2-Iodophenyl)formamides with Malononitrile or Cyanoacetates

Kazuhiro Kobayashi,* Toshihide Komatsu, Yuki Yokoi, Hisatoshi Konishi

Division of Applied Chemistry, Department of Chemistry and Biotechnology, Graduate School of Engineering, Tottori University, 4-101 Koyama-minami, Tottori 680-8552, Japan
Fax +81(857)315263; E-mail: kkoba@chem.tottori-u.ac.jp

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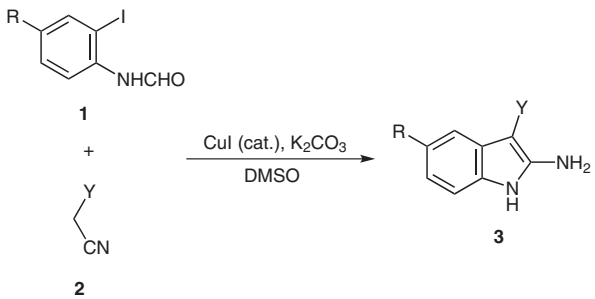
Abstract: An efficient method for the synthesis of 2-aminoindole-3-carbonitriles and 2-aminoindole-3-carboxylates by the reaction of *N*-(2-iodophenyl)formamides with malononitrile and cyanoacetates, respectively, in the presence of a catalytic amount of copper(I) iodide using potassium carbonate as a base is reported.

Key words: 2-aminoindole-3-carboxylates, 2-aminoindole-3-carbonitriles, *N*-(2-iodophenyl)formamides, copper(I) iodide, coupling

Elaborations of 2-aminoindole-3-carbonitrile[1a] and 3-aminoindole-3-carboxylates[1b,c] to the corresponding highly fused and biologically important heterocyclic compounds have been reported in the literature. These indole derivatives were prepared by the treatment of 1-chloro(or bromo)-2-nitrobenzenes with malononitrile or ethyl cyanoacetate in the presence of an appropriate base followed by reduction of the nitro group of the resulting substitution products.[1–3] We became interested in pursuing a new and general procedure for the preparation of 3-aminoindole-3-carboxylic acid derivatives. On the other hand, Miura et al. have already reported that the copper(I) iodide catalyzed reaction of iodobenzenes with malononitrile and cyanoacetates in the presence of a base gives arylmalononitriles and arylcyanoacetates, respectively.[4] We therefore envisaged that a similar copper(I) iodide catalyzed reaction of 2-iodoanilines with malononitrile and cyanoacetates would yield 2-aminoindole-3-carbonitriles and 2-aminoindole-3-carboxylates, respectively. In the course of our investigations, it was found that the reaction of *N*-(2-iodophenyl)formamides with malononitrile and cyanoacetates could be catalyzed by copper(I) iodide in the presence of potassium carbonate to give 2-aminoindole-3-carbonitriles and 2-aminoindole-3-carboxylates, respectively. Herein, we report the results of our study, which provides a new and efficient method for the synthesis of these 2-aminoindole-3-carboxylic acid derivatives.

In order to synthesize 2-aminoindole-3-carbonitrile (**3a**), 2-iodoaniline was first subjected to the reaction with malononitrile (**2a**) (2 equiv) in DMSO containing a catalytic amount (10 mol%) of copper(I) iodide and potassium carbonate (4 equiv) at 120 °C. These conditions are those used for the coupling reaction of iodobenzenes with **2a** by Miura et al.[4] However, the reaction resulted in the formation of an intractable mixture of products. This result may be ascribed to the reaction of the amino group with malononitrile before its substitution with the iodo moiety.

Next, the use of *N*-(2-iodophenyl)formamide (**1a**), easily prepared by N-formylation of 2-iodoaniline, as a substrate in order to avoid the above mentioned undesired reactions was examined. It was found that the synthesis of **3a** and ethyl 2-aminoindole-3-carboxylate (**3b**) by the reaction of **1a** with **2a** and ethyl cyanoacetate (**2b**), respectively, could be achieved as depicted in Scheme 1. Thus, *N*-(2-iodophenyl)formamide (**1a**) was allowed to react with malononitrile (**2a**) under the above-mentioned conditions for one hour. Aqueous workup and purification of the crude product using column chromatography on silica gel[5] afforded the desired product **3a** in a satisfactory yield (Table 1, entry 1). The reaction of **1a** with **2b** under the same conditions also proceeded relative cleanly to afford the desired product **3b** in a comparable yield (entry 2). The use of 20 mol% of the catalyst did not improve the yields of **3a**. Copper(I) bromide also proved to work well in this reaction, but the yield of **3a** was somewhat lower (46%) than that with copper(I) iodide.



Scheme 1 Preparation of 2-aminoindole-3-carboxylic acid derivatives

In order to investigate the scope of the present synthetic method, the reactions using *N*-(2-iodophenyl)formamides **1b–f** carrying a substituent at the 4-position, which could be easily prepared from commercially available or known[6,7] 2-iodoanilines upon treatment with formic acid, as substrates under the similar conditions as mentioned for the synthesis of **2a** and **2b**, were carried out. They proceeded successfully to afford the desired products **3c–l** in

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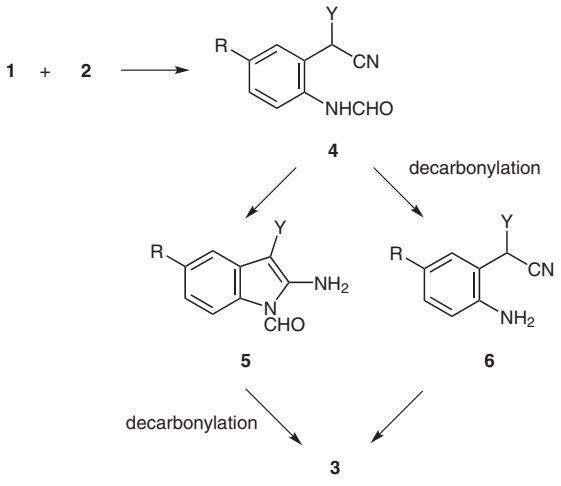
Table 1 Preparation of 2-Aminoindole-3-carboxylic Acid Derivatives **3**

Entry	1	2	Temp (°C)	Time	3 (Yield, %)[a]
1	**1a** (R = H)	**2a** (Y = CN)	120	1 h	**3a** (64)
2	**1a**	**2b** (Y = CO_2Et)	120	10 min	**3b** (59)
3	**1a**	**2c** [Y = $CO_2(CH_2)_2OEt$]	110	1 h	**3c** (60)
4	**1b** (R = Me)	**2a**	120	45 min	**3d** (56)
5	**1b**	**2c**	80	3 h	**3e** (54)
6	**1c** (R = *i*-Pr)	**2a**	120	1 h	**3f** (60)
7	**1c**	**2b**	80	1 h	**3g** (58)
8	**1d** (R = Cl)	**2a**	100	45 min	**3h** (60)
9	**1d**	**2b**	80	1.5 h	**3i** (58)
10	**1d**	**2c**	80	45 min	**3j** (52)
11	**1e** (R = OMe)	**2a**	90	20 min	**3k** (38)
12	**1f** (R = CO_2Et)	**2b**	80	20 min	**3l** (53)
13	**1f**	**2c**	80	10 min	**3m** (55)

[a] Isolated yields.

the yields summarized in Table 1, entries 3–12. Each of these reactions was conducted as follows. First, the reaction mixture was heated at 60 °C, and the temperature was raised at a 10 °C interval until TLC analyses had revealed that the reaction proceeded at a reasonable rate. After confirmation of complete consumption of the starting **2** by TLC analyses, the reaction was quenched by adding 10% hydrochloric acid after cooling. Preparation of 2-ethoxyethyl 2-aminoindole-3-carboxylates (**3c**, **3e**, **3j**, and **3m**) was successfully performed using 2-ethoxyethyl cyanoacetate (**2c**) (entries 3, 5, 10, and 13). An electron-donating methoxy group proved to decrease the yield of the corresponding product **3k** (entry 11), while methyl, isopropyl, and electron-withdrawing chloro and ethoxycarbonyl groups did not affect the yields of the products (entries 4–10, 12 and 13). We speculate that the poor yield of **3k** may be attributed to its somewhat lower stability during the reaction. Attempts to improve the yield of **3k** by conducting reactions at lower temperatures were all in vain; the reactions did not proceed to any satisfactory extent after rather extended reaction times. It is worth mentioning here that neither cyano-*N*,*N*-dimethylacetamide nor benzoylacetonitrile performed well in the present reaction to give no more than trace amounts of the expected 2-aminoindole derivatives; in each case complicated reaction mixture was obtained.

The reaction sequence leading to the formation of **3** from 2-iodophenylformamides **1** and malononitrile or cyanoacetates is thought to proceed as depicted in Scheme 2. Thus, coupling of **1** with one of the active methylene compounds generates the intermediate **4**. Intramolecular cyclization of this intermediate provides 1-formylindole intermediate **5**, which on decarbonylation gives **3**. Alternatively, decarbonylation from **4** may first occur to furnish the amino nitrile intermediate **6**, which cyclizes intramolecularly to give **3**. Unfortunately, however, we have no evidence to clarify which is the correct route to **3**. IR and ^{1}H NMR analyses of the reaction mixtures interrupted before completion of the reaction of **1a** with ethyl cyanoacetate (with and without aqueous workup) provided no informative results. After coupling of **1** with malononitrile or cyanoacetates, the cyclization/decarbonylation or decarbonylation/cyclization sequence appears to proceed very quickly.



Scheme 2 Proposed pathways to the products

In conclusion, we have developed a concise method for the synthesis of 2-aminoindole-3-carboxylic acid derivatives based on the reaction of *N*-(2-iodopheny)form-

amides with malononitrile or cyanoacetates catalyzed by copper(I) iodide. The easiness of experimental operations and the ready availability of the starting materials make the present indole synthesis attractive.

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were determined with a Shimadzu FTIR-8300 spectrophotometer as KBr disks. The ^{1}H NMR spectra were determined using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz. The ^{13}C NMR spectra were determined using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 125 MHz. Low-resolution mass spectra (EI, 70 eV) were measured by a JEOL JMS AX505 HA spectrometer. TLC was carried out on a Merck Kieselgel 60 PF_{254}. Column chromatography was performed using Wako Gel C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use. 2-Iodo-4-methylaniline and 2-iodo-4-(1-methylethyl)aniline were prepared by the iodination of the respective anilines under the conditions reported previously.[6] 2-Iodo-4-methoxyaniline was prepared from 4-methoxyaniline according to the procedure reported by Murphy et al.[7] Ethyl 4-formylamino-3-iodobenzoate (**1f**) was prepared by the method previously reported by us.[8] All other chemicals used in this study were commercially available.

***N*-(2-Iodophenyl)formamides 1**
These compounds were prepared by N-formylation of the respective 2-iodoanilines with formic acid in toluene under azeotropic conditions.[8]

***N*-(2-Iodophenyl)formamide (1a)[9,10]**
Yield: 96%; beige solid; mp 112–113 °C (toluene) (Lit.[9] mp 113–113.5 °C).

IR: 3323, 1660 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 6.94 and 7.00 (2 dd, *J* = 7.8, 7.3 Hz each, combined 1 H), 7.31–7.42 (m, 1 H), 7.76 (dd, *J* = 7.8, 1.4 Hz, 1 H), 7.87 and 7.89 (2 d, *J* = 7.8 Hz, 1 H), 8.32 (s, 1 H), 9.54 (br s, 1 H).

***N*-(2-Iodo-4-methylphenyl)formamide (1b)**
Yield: 79%; beige solid; mp 100–102 °C (hexane–CH_2Cl_2).

IR: 3268, 1667 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.29 and 2.31 (2 s, combined 3 H), 7.08–8.59 (m, 5 H).

Anal. Calcd for C_8H_8INO: C, 36.81; H, 3.09; N, 5.37. Found: C, 36.77; H, 3.18; N, 5.24.

***N*-[2-Iodo-4-(1-methylethyl)phenyl]formamide (1c)**
Yield: 75%; pale-yellow solid; mp 80–82 °C (hexane–CH_2Cl_2).

IR: 3188, 1661 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.22 and 1.44 (2 d, *J* = 6.9 Hz each, combined 6 H), 2.80–2.90 (m, 1 H), 7.12–8.60 (m, 5 H).

Anal. Calcd for $C_{10}H_{12}INO$: C, 41.54; H, 4.18; N, 4.84. Found: C, 41.49; H, 4.37; N, 4.70.

***N*-(4-Chloro-2-iodophenyl)formamide (1d)**
Yield: 97%; beige solid; mp 139–140 °C (hexane–CH_2Cl_2).

IR: 3273, 1669 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.13–8.62 (m, 5 H).

Anal. Calcd for $C_7H_{12}ClINO$: C, 29.87; H, 1.79; N, 4.98. Found: C, 29.75; H, 1.73; N, 4.90.

***N*-(2-Iodo-4-methoxyphenyl)formamide (1e)**
Yield: 76%; beige solid; mp 129–132 °C (hexane–CH_2Cl_2).

IR: 3187, 1658 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.79 and 3.80 (2 s, combined 3 H), 6.90–8.45 (m, 5 H).

Anal. Calcd for $C_8H_8INO_2$: C, 34.68; H, 2.91; N, 5.06. Found: C, 34.63; H, 2.92; N, 4.88.

2-Aminoindole-3-carbonitrile (3a);[11] Typical Procedure
A mixture of **1a** (0.25 g, 1.0 mmol) and malononitrile (0.13 g, 2.0 mmol) in DMSO (2.5 mL) containing CuI (19 mg, 0.10 mmol) and K_2CO_3 (0.55 g, 4.0 mmol) was heated at 120 °C for 1 h under stirring. To the cooled (0 °C) resulting mixture was added 10% aq HCl until evolution of CO_2 gas had ceased. H_2O (10 mL) was added and the mixture was extracted with EtOAc (3 × 10 mL). The combined extracts were washed with H_2O (3 × 10 mL) and then brine (10 mL), and dried (Na_2SO_4). After evaporation of the solvent, the residue was filtered through a 2 cm pad of neutral alumina (Merck Alumina 60 Neutral F_{254}) using EtOAc–hexane (1:1) as solvent. The filtrate was concentrated and subjected to column chromatography on silica gel (EtOAc–hexane, 1:1) to give **3a** as a beige solid; yield: 0.10 g (64%); mp 186–187 °C (hexane–THF) (Lit.[1a] mp 187–188 °C) (Table 1).

IR: 3397, 3269, 3239, 2189, 1643, 1624 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.69 (br s, 2 H), 7.08 (dd, *J* = 7.8, 1.4 Hz, 1 H), 7.14–7.17 (m, 2 H), 7.43 (dd, *J* = 7.8, 1.4 Hz, 1 H), 7.98 (br s, 1 H).

Ethyl 2-Aminoindole-3-carboxylate (3b)[12,13]
Beige solid; mp 179–181 °C (hexane–THF) (Lit.[12] mp 178–180 °C).

IR: 3460, 3352, 3258, 1648, 1614, 1602 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.44 (t, *J* = 7.3 Hz, 3 H), 4.37 (q, *J* = 7.3 Hz, 2 H), 5.69 (br s, 2 H), 7.04 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.10 (d, *J* = 7.8 Hz, 1 H), 7.14 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.81 (br s, 2 H).

^{13}C NMR (DMSO-d_6): δ = 14.74, 57.99, 83.59, 109.66, 117.99, 119.28, 120.35, 126.34, 132.62, 153.54, 165.84.

2-Ethoxyethyl 2-Aminoindole-3-carboxylate (3c)
Beige solid; mp 90–92 °C (hexane–CH_2Cl_2).

IR: 3456, 3345, 1651, 1625, 1616 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.24 (t, *J* = 6.9 Hz, 3 H), 3.62 (q, *J* = 6.9 Hz, 2 H), 3.81 (t, *J* = 5.0 Hz, 2 H), 4.47 (t, *J* = 5.0 Hz, 2 H), 5.66 (br s, 2 H), 6.99–7.04 (m, 2 H), 7.12 (td, *J* = 7.6, 1.5 Hz, 1 H), 7.81 (d, *J* = 7.6 Hz, 1 H), 8.09 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 15.14, 62.21, 66.69, 68.89, 85.69, 109.56, 119.11, 120.50, 121.61, 126.58, 132.07, 152.62, 166.77.

MS: *m*/*z* = 248 (100%, [M$^+$]).

Anal. Calcd for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.83; H, 6.78; N, 11.08.

2-Amino-5-methylindole-3-carbonitrile (3d)
Pale-yellow solid; mp 185–187 °C (hexane–THF).

IR: 3381, 3293, 3221, 2187, 1641, 1630 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.49 (s, 3 H), 6.62 (br s, 2 H), 6.69 (d, *J* = 8.2 Hz, 1 H), 6.91 (s, 1 H), 6.98 (d, *J* = 8.2 Hz, 1 H), 10.52 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 21.06, 61.39, 109.86, 115.37, 117.93, 120.61, 128.49, 129.19, 130.18, 153.78.

MS: *m*/*z* = 171 (100%, [M$^+$]).

Anal. Calcd for $C_{10}H_9N_3$: C, 70.16; H, 5.30; N, 24.54. Found: C, 69.92; H, 5.35; N, 24.44.

2-Ethoxyethyl 2-Amino-5-methylindole-3-carboxylate (3e)
Beige solid; mp 125–127 °C (hexane–THF).

IR: 3458, 3354, 3271, 1661, 1643, 1620, 1603 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 1.26 (t, *J* = 7.3 Hz, 3 H), 2.41 (s, 3 H), 3.63 (q, *J* = 7.3 Hz, 2 H), 3.81 (t, *J* = 5.0 Hz, 2 H), 4.47 (t, *J* = 5.0 Hz, 2 H), 5.62 (br s, 2 H), 6.84 (d, *J* = 8.2 Hz, 1 H), 6.94 (d, *J* = 8.2 Hz, 1 H), 7.64 (br s, 1 H), 7.80 (br s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 15.15, 21.56, 62.16, 66.69, 68.91, 85.38, 109.22, 119.39, 121.50, 125.50, 130.24, 130.95, 154.83, 170.58.

MS: *m*/*z* = 262 (100%, $[M^+]$).

Anal. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.10; H, 6.92; N, 10.68. Found: C, 64.02; H, 6.95; N, 10.54.

2-Amino-5-(1-methylethyl)indole-3-carbonitrile (3f)
Pale-yellow solid; mp 168–170 °C (hexane–THF).

IR (KBr): 3431, 3345, 3304, 2185, 1636, 1622 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 1.19 (d, *J* = 6.9 Hz, 6 H), 2.83–2.91 (sept, *J* = 6.9 Hz, 1 H), 6.62 (br s, 2 H), 6.77 (dd, *J* = 8.2, 1.4 Hz, 1 H), 6.95 (d, *J* = 1.4 Hz, 1 H), 7.01 (d, *J* = 8.2 Hz, 1 H), 10.53 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 24.53, 33.49, 61.61, 109.93, 112.56, 118.05, 118.19, 128.34, 130.46, 140.81, 153.88.

MS: *m*/*z* = 199 (100%, $[M^+]$).

Anal. Calcd for $C_{12}H_{13}N_3$: C, 72.33; H, 6.58; N, 21.09. Found: C, 72.03; H, 6.55; N, 20.94.

Ethyl 2-Amino-5-(1-methylethyl)indole-3-carboxylate (3g)
Beige solid; mp 122–124 °C (hexane–CH_2Cl_2).

IR: 3474, 3372, 3219, 1653, 1622, 1603 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 1.29 (d, *J* = 6.9 Hz, 6 H), 1.45 (t, *J* = 7.3 Hz, 3 H), 2.98 (sept, *J* = 6.9 Hz, 1 H), 4.38 (q, *J* = 7.3 Hz, 2 H), 5.62 (br s, 2 H), 6.92 (dd, *J* = 8.2, 1.8 Hz, 1 H), 6.98 (d, *J* = 8.2 Hz, 1 H), 7.68 (br s, 1 H), 7.79 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 14.79, 24.70, 34.42, 59.43, 85.79, 109.51, 116.85, 119.18, 126.68, 130.53, 142.69, 152.81, 167.67.

MS: *m*/*z* = 246 (100%, $[M^+]$).

Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.26; H, 7.50; N, 11.08.

2-Amino-5-chloroindole-3-carbonitrile (3h)
Beige solid; mp 209–212 °C (hexane–THF).

IR: 3468, 3366, 2197, 1638, 1630 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 6.82 (br s, 2 H), 6.89 (dd, *J* = 8.2, 2.3 Hz, 1 H), 7.06 (d, *J* = 2.3 Hz, 1 H), 7.08 (d, *J* = 8.2 Hz, 1 H), 10.88 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 61.67, 111.42, 114.21, 117.04, 119.20, 128.49, 129.89, 130.82, 154.62.

MS: *m*/*z* = 191 (100%, $[M^+]$).

Anal. Calcd for $C_9H_6ClN_3$: C, 56.41; H, 3.16; N, 21.93. Found: C, 56.35; H, 3.15; N, 22.05.

2-Ethyl 2-Amino-5-chloroindole-3-carboxylate (3i)
Beige solid; mp 191–193 °C (hexane–THF).

IR: 3457, 3350, 1655, 1641, 1605 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 1.30 (t, *J* = 6.9 Hz, 3 H), 4.22 (q, *J* = 6.9 Hz, 2 H), 6.80 (br s, 2 H), 6.86 (d, *J* = 8.4 Hz, 1 H), 7.09 (d, *J* = 8.4 Hz, 1 H), 7.46 (s, 1 H), 10.77 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 14.76, 58.28, 83.48, 110.97, 117.03, 118.82, 124.95, 128.31, 131.36, 154.24, 165.44.

MS: *m*/*z* = 238 (100%, $[M^+]$).

Anal. Calcd for $C_{11}H_{11}ClN_2O_2$: C, 55.36; H, 4.65; N, 11.74. Found: C, 55.17; H, 5.33; N, 9.87.

2-Ethoxyethyl 2-Amino-5-chloroindole-3-carboxylate (3j)
Beige solid; mp 142–144 °C (hexane–THF).

IR: 3474, 3347, 1632, 1613 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 1.28 (t, *J* = 7.3 Hz, 3 H), 3.65 (q, *J* = 7.3 Hz, 2 H), 3.83 (t, *J* = 5.0 Hz, 2 H), 4.47 (t, *J* = 5.0 Hz, 2 H), 5.70 (br s, 2 H), 6.92–6.96 (m, 2 H), 7.74 (br s, 1 H), 8.04 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 15.11, 61.48, 65.56, 68.23, 83.38, 110.89, 117.20, 118.80, 124.95, 128.16, 131.32, 154.21, 170.19.

MS: *m*/*z* = 282 (100%, $[M^+]$).

Anal. Calcd for $C_{13}H_{15}ClN_2O_3$: C, 55.23; H, 5.35; N, 9.91. Found: C, 55.09; H, 4.78; N, 11.54.

2-Amino-5-methoxyindole-3-carbonitrile (3k)
Beige solid; mp 170–172 °C (hexane–THF).

IR: 3399, 3285, 2187, 1645, 1628 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 3.71 (s, 3 H), 6.48 (dd, *J* = 8.7, 2.3 Hz, 1 H), 6.638 (br s, 2 H), 6.641 (d, *J* = 2.3 Hz, 1 H), 6.99 (d, *J* = 8.7 Hz, 1 H), 10.47 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 55.33, 62.15, 99.36, 107.40, 110.76, 117.94, 126.57, 129.21, 154.14, 154.66.

MS: *m*/*z* = 187 (100%, $[M^+]$).

Anal. Calcd for $C_{10}H_9N_3O$: C, 64.16; H, 4.85; N, 22.45. Found: C, 63.96; H, 4.88; N, 22.56.

Diethyl 2-Aminoindole-3,5-dicarboxylate (3l)
Beige solid; mp 198–201 °C (hexane–THF).

IR: 3449, 3315, 1675, 1632 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 1.38 and 1.40 (2 t, *J* = 7.3 Hz each, combined 6 H), 4.31 and 4.33 (2 q, *J* = 7.3 Hz each, combined 4 H), 6.94 (br s, 2 H), 7.25 (d, *J* = 8.3 Hz, 1 H), 7.62 (d, *J* = 8.3 Hz, 1 H), 8.29 (s, 1 H), 11.09 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 14.34, 14.71, 58.32, 60.67, 83.70, 109.45, 119.48, 121.22, 122.03, 126.63, 136.05, 154.35, 165.49, 166.86.

MS: *m*/*z* = 276 (100%, $[M^+]$).

Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.83; H, 5.94; N, 10.16.

2-Ethoxyethyl 2-Amino-5-(ethoxycarbonyl)indole-3-carboxylate (3m)
Beige solid; mp 161–163 °C (hexane–THF).

IR: 3470, 3363, 1690, 1668, 1618 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 1.14 (t, *J* = 7.3 Hz, 3 H), 1.30 (t, *J* = 7.3 Hz, 3 H), 3.54 (q, *J* = 7.3 Hz, 2 H), 3.70 (t, *J* = 5.0 Hz, 2 H), 4.24–4.30 (m, 4 H), 6.85 (br s, 2 H), 7.18 (d, *J* = 8.2 Hz, 1 H), 7.56 (dd, *J* = 8.2, 1.8 Hz, 1 H), 8.24 (d, *J* = 1.8 Hz, 1 H), 11.01 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 14.30, 15.10, 59.93, 61.78, 65.69, 68.26, 83.59, 109.38, 119.47, 121.27, 122.08, 124.90, 128.02, 151.46, 166.77 (2 C).

MS: *m*/*z* = 320 (100%, $[M^+]$).

Anal. Calcd for $C_{16}H_{20}N_2O_5$: C, 59.99; H, 6.29; N, 8.74. Found: C, 59.89; H, 6.38; N, 8.77.

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