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CONVENIENT SYNTHESIS OF 6-AMINO-3,4-DIHYDRO-2*H*-PYRIMIDO[2,1-*a*]ISOQUINOLINE-7-CARBONITRILES AND 5-AMINO-2,3-DIHYDROIMIDAZO[2,1-*a*]ISOQUINOLINE-6-CARBONITRILES

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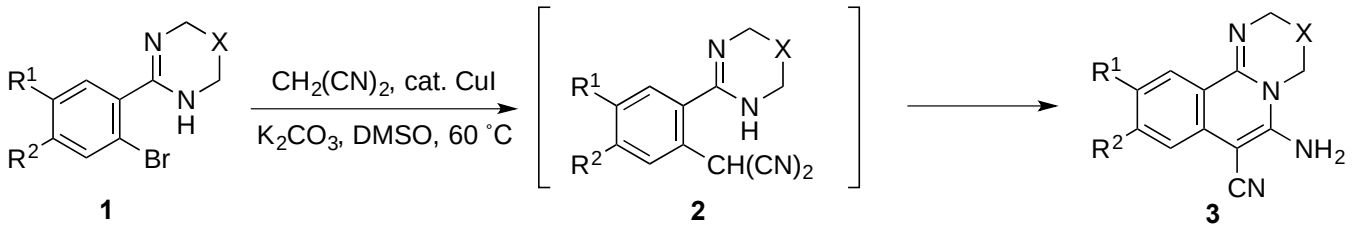
Abstract – An efficient method for the preparation of 6-amino-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitriles and 5-amino-2,3-dihydroimidazo[2,1-*a*]isoquinoline-6-carbonitriles by the copper(I) iodide catalyzed reaction of 2-(2-bromophenyl)-1,4,5,6-tetrahydropyrimidines and 2-(2-bromophenyl)-4,5-dihydro-3*H*-imidazoles, respectively, with 1,3-propanedinitrile (malononitrile) in DMSO in the presence of excess potassium carbonate has been developed.

Recently, the successful use of 2-(2-bromophenyl)-1,4,5,6-tetrahydropyrimidines and 2-(2-bromophenyl)-4,5-dihydro-3*H*-imidazole as the precursors in the preparation of pyrimido[1,2-*c*][1,3]benzothiazin-6-imines and related tricyclic heterocycles has been reported by Fujii, Ohno, and co-workers.[1] We were interested in investigating the reaction of these precursors with 1,3-propanedinitrile (malononitrile). We envisioned that this reaction would be expected to afford 6-amino-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitriles and 5-amino-2,3-dihydroimidazo-[2,1-*a*]isoquinoline-6-carbonitriles, and found that the uses of copper(I) iodide as a catalyst and potassium carbonate as a base effected the formation of these expected products. The biological activities of compounds with 2*H*-pyrimido[2,1-*a*]isoquinoline[2] or imidazo[2,1-*a*]isoquinoline[3] structure have stimulated the development of methods for the preparation of these derivatives.[4,5] However, there have been, so far, no reports on synthetic approaches to these derivatives carrying an enamino nitrile moiety. We now wish to describe the results of our study, which provide the first method for the general preparation of such heterocyclic derivatives.

A range of 2-(2-bromophenyl)-1,4,5,6-tetrahydropyrimidines and 2-(2-bromophenyl)-4,5-dihydro-1*H*-imidazoles (**1**) were synthesized in good yields from commercially available 2-bromobenzaldehydes on treatment with 1,3-propanediamines and 1,2-ethanediamine, respectively, utilizing the procedure reported previously.[1] The one-pot preparation of 6-amino-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitriles and 5-amino-2,3-dihydroimidazo[2,1-*a*]isoquinoline-6-carbonitriles (**3**) from these starting materials was carried out according to the procedure illustrated in Scheme 1. Thus, compounds (**1**) were allowed to react with 1,3-propanedinitrile in dimethyl sulfoxide at 60 ˚C in the presence of a catalytic (10 mol%) amount of copper(I) iodide and excess potassium carbonate. The reaction sequence *via* the intermediates (**2**) proceeded smoothly and completed within 15 min to furnish, after addition of water and subsequent recrystallization of the resulting precipitate, the desired products (**3**). The results obtained by using nine starting materials are summarized in Table 1. The yields of the products are generally good, while those of the imidazo derivatives (**3g-h**) (Entries 7–9) are somewhat lower than those of the pyrimido derivatives (**3a-f**) (Entries 1-6). We reasoned that the intramolecular cyclization of the imidazoyl intermediates (**2**: X = nil) would be slightly more difficult than that of the pyrimidinyl intermediates (**2**: X = CH_2, CMe_2).



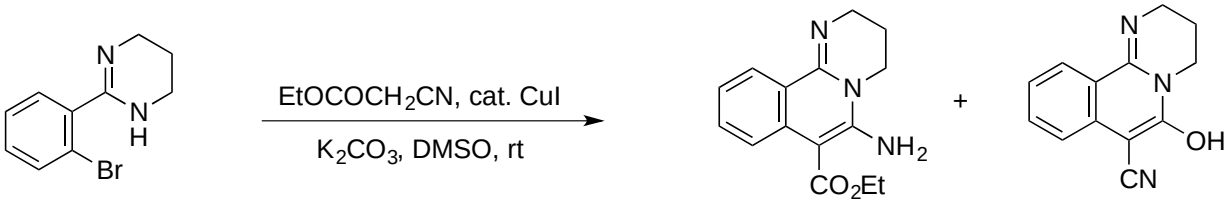
Scheme 1

Table 1. Preparation of 6-amino-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitriles and 5-amino-2,3-dihydroimidazo[2,1-*a*]isoquinoline-6-carbonitriles **(3)**

Entry	**1**	**3**	Yield/%[a]
1	**1a** ($R^1 = R^2 = H$, X = CH_2)	**3a**	81
2	**1b** ($R^1 = R^2 = H$, X = CMe_2)	**3b**	79
3	**1c** (R^1 = Cl, R^2 = H, X = CH_2)	**3c**	81
4	**1d** (R^1 = Cl, R^2 = H, X = CMe_2)	**3d**	80
5	**1e** ($R^1 = R^2$ = OMe, X = CH_2)	**3e**	78
6	**1f** ($R^1 = R^2$ = OMe, X = CMe_2)	**3f**	84
7	**1g** ($R^1 = R^2 = H$, X = nil)	**3g**	68
8	**1h** (R^1 = Cl, R^2 = H, X = nil)	**3h**	76
9	**1i** ($R^1 = R^2$ = OMe, X = nil)	**3i**	67

[a] Yields of isolated products.

Subsequently, we were interested in applying the present method to the synthesis of 6-amino-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carboxylates. So, the reaction of 2-(2-bromophenyl)-1,4,5,6-tetrahydropyrimidine (**1a**) with ethyl 2-cyanoacetate under the above-mentioned conditions was carried out. Unfortunately, however, it allowed us to obtain the desired product, ethyl 6-amino-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carboxylate (**4**), as a minor product. The major product of this reaction was 6-hydroxy-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitrile (**5**). These results are shown in Scheme 2.



Scheme 2

In conclusion, the results reported in this paper present a procedure that provides an efficient and rapid route for the preparation of 6-amino-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitriles and 5-amino-2,3-dihydroimidazo[2,1-*a*]isoquinoline-6-carbonitriles. This is the first example for the preparation of 2*H*-pyrimido[2,1-*a*]isoquinoline and imidazo[2,1-*a*]isoquinoline derivatives having an enamino nitrile moiety, which could be further elaborated to more complex polycyclic heterocycles. The present method may be of use in organic synthesis because of the simplicity of the operations and the ready availability of the starting materials.

EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded with a Perkin–Elmer Spectrum 65 FTIR spectrophotometer. ^{1}H NMR spectra were recorded using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz. ^{13}C NMR spectra were recorded using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 125 MHz. Low-resolution MS spectra (EI, 70 eV) were measured by a JEOL JMS-AX505 HA spectrometer. High-resolution MS spectra (DART, positive) were measured by a Thermo Scientific Exactive spectrometer. TLC was carried out on 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.

Starting Materials. All chemicals used in this study were commercially available.

2-(2-Bromophenyl)-1,4,5,6-tetrahydropyrimidines and 2-(2-Bromophenyl)-4,5-dihydro-1*H*-imidazoles (1). These compounds were prepared by the reaction of 2-bromobenzaldehydes with propane-1,3-diamines and ethane-1,2-diamine under the reported conditions.[1] Physical, spectral, and analytical data for new compounds follow.

2-(2-Bromophenyl)-5,5-dimethyl-1,4,5,6-tetrahydropyrimidine (1b): yield: 84%; a white solid; mp 187–189 °C (hexane–CH_2Cl_2); IR (KBr) 3387, 1627 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, 6H), 3.14 (s, 4H), 4.87 (br, 1H), 7.20 (td, *J* = 7.6, 1.5 Hz, 1H), 7.31 (td, *J* = 7.6, 1.5 Hz, 1H), 7.45 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.54 (dd, *J* = 7.6, 1.5 Hz, 1H). Anal. Calcd for $C_{12}H_{15}BrN_2$: C, 53.95; H, 5.66; N, 10.49. Found: C, 53.86; H, 5.74; N, 10.37.

2-(2-Bromo-5-chlorophenyl)-1,4,5,6-tetrahydropyrimidine (1c): yield: 63%; a pale-yellow solid; mp 137–139 °C (CH_2Cl_2); IR (KBr) 3375, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.85–1.89 (m, 2H), 3.45 (t, *J* = 6.1 Hz, 4H), 4.82 (br, 1H), 7.21 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.40 (d, *J* = 2.3 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H). Anal. Calcd for $C_{10}H_{10}BrClN_2$: C, 43.91; H, 3.68; N, 10.24. Found: C, 43.84; H, 3.89; N, 10.37.

2-(2-Bromo-5-chlorophenyl)-5,5-dimethyl-1,4,5,6-tetrahydropyrimidine (1d): yield: 76%; a white solid; mp 163–164 °C (CH_2Cl_2); IR (KBr) 3396, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, 6H), 3.13 (br s, 4H), 4.85 (br, 1H), 7.18 (dd, *J* = 8.4, 3.1 Hz, 1H), 7.45 (d, *J* = 3.1 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H). Anal. Calcd for $C_{12}H_{14}BrClN_2$: C, 47.79; H, 4.68; N, 11.75. Found: C, 48.04; H, 4.44; N, 11.61.

2-(2-Bromo-4,5-dimethoxyphenyl)-1,4,5,6-tetrahydropyrimidine (1e): yield: 84%; a pale-yellow solid; mp 78–80 °C (hexane–CH_2Cl_2); IR (KBr) 3369, 1622 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.86–1.90 (m, 2H), 3.48 (t, *J* = 6.1 Hz, 4H), 3.87 (s, 3H), 3.89 (s, 3H), 5.27 (br, 1H), 6.97 (s, 1H), 7.00 (s, 1H). Anal. Calcd for $C_{12}H_{15}BrClN_2O_2$: C, 48.18; H, 5.05; N, 9.36. Found: C, 48.15; H, 5.24; N, 9.45.

2-(2-Bromo-4,5-dimethoxyphenyl)-5,5-dimethyl-1,4,5,6-tetrahydropyrimidine (1f): yield: 89%; a white solid; mp 128–130 °C (hexane–CH_2Cl_2); IR (KBr) 3396, 1630, 1604 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, 6H), 3.13 (br s, 4H), 3.87 (s, 3H), 3.89 (s, 3H), 5.26 (br, 1H), 6.97 (s, 1H), 7.00 (s, 1H). Anal. Calcd for $C_{14}H_{19}BrN_2O_2$: C, 51.39; H, 5.85; N, 8.56. Found: C, 51.30; H, 5.94; N, 8.50.

2-(2-Bromo-5-chlorophenyl)-4,5-dihydro-1*H*-imidazole (1h): yield: 85%; a pale-yellow solid; mp 75–78 °C (hexane–CH_2Cl_2); IR (KBr) 3340, 1614 1612 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.61 (br s, 2H), 3.97 (br s, 2H), 5.05 (br, 1H), 7.24 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 2.3 Hz, 1H). Anal. Calcd for $C_9H_8BrClN_2$: C, 41.65; H, 3.11; N, 10.79. Found: C, 41.38; H, 3.12; N, 10.52.

2-(2-Bromo-4,5-dimethoxyphenyl)-4,5-dihydro-1*H*-imidazole (1i): yield: 80%; a pale-yellow solid; mp 140–142 °C (CH_2Cl_2); IR (KBr) 3329, 1612 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.79 (br s, 4H), 3.89 (s, 3H), 3.90 (s, 3H), 5.27 (br, 1H), 7.00 (s, 1H), 7.30 (s, 1H). Anal. Calcd for $C_{11}H_{13}BrN_2O_2$: C, 46.33; H, 4.60; N, 9.82. Found: C, 46.29; H, 4.63; N, 9.70.

Typical Procedure for the Preparation of Compounds (3). 6-Amino-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitrile (3a). A mixture of **1a** (0.20 g, 0.87 mmol) and $CH_2(CN)_2$ (0.12 g, 1.7 mmol) in DMSO (4 mL) containing CuI (17 mg, 0.087 mmol) and K_2CO_3 (0.48 g, 3.5 mmol) was heated at 60 °C under stirring for 15 min. After cooling to rt, water (20 mL) was added. The precipitate was collected by filtration under reduced pressure and recrystallized from hexane–THF to give **3a** (0.16 g, 81%): a yellow solid; mp 199–201 °C; IR (KBr) 3391, 3244, 2180, 1615 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.83 (br s, 2H), 3.48 (br s, 2H), 3.73 (br s, 2H), 6.96–6.98 (m, 3H), 7.10 (d, J = 7.3 Hz, 1H), 7.38 (t, J = 7.3 Hz, 1H), 7.99 (d, J = 7.3 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 19.82, 43.23, 43.51, 60.90, 118.98, 119.76, 121.29, 122.20, 125.49, 130.97, 132.89, 145.00, 153.97; MS *m/z* 224 (M^+, 100). Anal. Calcd for $C_{13}H_{12}N_4$: C, 69.62; H, 5.39; N, 24.98. Found: C, 69.48; H, 5.57; N, 24.93.

6-Amino-3,3-dimethyl-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitrile (3b): a pale-yellow solid; mp 211–213 °C (THF); IR (KBr) 3382, 3241, 2195, 1619, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, 6H), 3.38 (s, 2H), 3.41 (s, 2H), 4.79 (br s, 2H), 7.15 (td, J = 7.6, 1.5 Hz, 1H), 7.36 (dd, J = 7.6, 1.5 Hz, 1H), 7.45 (td, J = 7.6, 1.5 Hz, 1H), 8.16 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 24.73, 27.00, 54.09, 55.84, 65.56, 118.85, 121.30, 121.84, 124.09, 125.92, 131.40, 131.61, 144.91, 152.83; MS *m/z* 252 (M^+, 100). Anal. Calcd for $C_{15}H_{16}N_4$: C, 71.40; H, 6.39; N, 22.21. Found: C, 71.11; H, 6.51; N, 22.10.

6-Amino-10-chloro-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitrile (3c): a yellow solid; mp 250–251 °C ($CHCl_3$); IR (KBr) 3370, 3177, 2190, 1622, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.03–2.06 (m, 2H), 3.67 (t, J = 5.4 Hz, 2H), 3.82 (t, J = 6.1 Hz, 2H), 4.82 (br s, 2H), 7.27 (d, J = 8.4 Hz, 1H), 7.38 (d, J = 8.4, 2.3 Hz, 1H), 8.12 (d, J = 2.3 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 19.68, 43.28, 43.58, 60.36, 118.69, 121.86, 122.52, 124.62, 126.33, 130.93, 131.97, 143.95, 154.10; MS *m/z* 258 (M^+, 100). Anal. Calcd for $C_{13}H_{11}ClN_4$: C, 60.35; H, 4.29; N, 21.66: Found: C, 60.29; H, 4.47; N, 21.61.

6-Amino-10-chloro-3,3-dimethyl-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitrile (3d): a beige solid; mp 273–275 °C (Et_2O–THF); IR (KBr) 3334, 3179, 2196, 1619, 1602 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, 6H), 3.38 (s, 2H), 3.40 (s, 2H), 4.79 (br s, 2H), 7.29 (d, J = 8.4 Hz, 1H), 7.39 (dd, J = 8.4, 1.5 Hz, 1H), 8.17 (d, J = 1.5 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 24.12, 26.57, 53.38, 55.35, 60.76, 118.60, 121.93, 122.07, 124.72, 126.44, 131.02, 131.96, 142.89, 154.14; MS *m/z* 286 (M^+, 100). Anal. Calcd for $C_{15}H_{15}ClN_4$: C, 62.83; H, 5.27; N, 19.54. Found: C, 62.57; H, 5.56; N, 19.27.

6-Amino-9,10-dimethoxy-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitrile (3e): a yellow solid; mp 230–233 °C (hexane–CH_2Cl_2); IR (KBr) 3408, 3320, 2192, 1623, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.01–2.05 (m, 2H), 3.66 (t, J = 6.1 Hz, 2H), 3.83 (t, J = 6.1 Hz, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 4.73 (br s, 2H), 6.76 (s, 1H), 7.60 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.16, 43.60, 43.63, 56.01, 56.06, 65.10, 102.89, 107.02, 115.02, 119.02, 125.91, 145.86, 147.10, 151.89, 152.66; MS *m/z* 284 (M^+, 100). Anal. Calcd for $C_{15}H_{16}N_4O_2$: C, 63.37; H, 5.67; N, 19.71. Found: C, 63.30; H, 5.78; N, 19.69.

6-Amino-9,10-dimethoxy-3,3-dimethyl-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitrile (3f): a yellow solid; mp 252–253 °C (hexane–CH_2Cl_2); IR (KBr) 3355, 3225, 2185, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, 6H), 3.36 (s, 2H), 3.45 (s, 2H), 3.95 (s, 3H), 3.96 (s, 3H), 4.82 (br, 2H), 6.76 (s, 1H), 7.67 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 24.76, 27.02, 54.19, 55.77, 56.03, 56.12, 65.92, 102.85, 107.31, 114.75, 119.04, 126.00, 144.66, 147.07, 151.99, 152.70. HR-MS. Calcd for $C_{17}H_{21}N_4O_2$ (M+H): 313.1664. Found: *m/z* 313.1658. Anal. Calcd for $C_{17}H_{20}N_4O_2$: C, 65.37; H, 6.45; N, 17.94. Found: C, 65.36; H, 6.61; N, 17.87.

5-Amino-2,3-dihydroimidazo[2,1-*a*]isoquinoline-6-carbonitrile (3g): a pale-yellow solid; mp 274–276 °C (THF); IR (KBr) 3401, 3242, 2182, 1638, 1609 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.00 (t, J = 9.2 Hz, 2H), 4.24 (t, J = 9.2 Hz, 2H), 4.78 (br s, 2H), 7.15 (t, J = 7.6 Hz, 1H), 7.40 (d, J = 7.6 Hz, 1H), 7.48 (dd, J = 8.4, 7.6 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 46.01, 52.83, 59.95, 115.61, 118.88, 120.40, 122.22, 125.94, 132.24, 136.02, 152.39, 153.57. HR-MS. Calcd for $C_{12}H_{11}N_4$ (M+H): 211.0983. Found: *m/z* 211.0978. Anal. Calcd for $C_{12}H_{10}N_4$: C, 68.56; H, 4.79; N, 26.65. Found: C, 68.41; H, 5.02; N, 26.54.

5-Amino-9-chloro-2,3-dihydroimidazo[2,1-*a*]isoquinoline-6-carbonitrile (3h): a pale-yellow solid; mp 288–290 °C (Et_2O–$CHCl_3$); IR (KBr) 3395, 3230, 2182, 1631, 1612 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.93–3.98 (m, 4H), 7.14 (d, J = 8.4 Hz, 1H), 7.26 (br 2H), 7.46 (dd, J = 8.4, 2.3 Hz, 1H), 7.71 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 46.24, 52.97, 59.79, 116.78, 118.55, 122.52, 124.85, 126.08, 132.22, 135.07, 151.60, 152.50. HR-MS. Calcd for $C_{12}H_{10}ClN_4$ (M+H): 245.0594. Found: *m/z* 245.0591. Anal. Calcd for $C_{12}H_9ClN_4$: C, 58.90; H, 3.71; N, 22.90. Found: C, 58.68; H, 3.80; N, 22.60.

5-Amino-8,9-dimethoxy-2,3-dihydroimidazo[2,1-*a*]isoquinoline-6-carbonitrile (3i): a pale-yellow solid; mp 285–287 °C (Et_2O–$CHCl_3$); IR (KBr) 3396, 3265, 2174, 1623 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.91 (s, 3H), 3.97 (s, 3H), 4.01 (t, J = 9.2 Hz, 2H), 4.23 (t, J = 9.2 Hz, 2H), 4.71 (br s, 2H), 6.80 (s, 1H), 7.38 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 46.22, 55.36 (2C), 55.51, 61.26, 102.13, 107.31, 110.90, 118.86, 126.06, 145.55, 151.61, 153.19, 153.31. HR-MS. Calcd for $C_{14}H_{15}N_4O_2$ (M+H): 271.1195. Found: *m/z* 271.1177. Anal. Calcd for $C_{14}H_{14}N_4O_2$: C, 62.21; H, 5.22; N, 20.73. Found: C, 62.10; H, 5.19; N, 20.67.

Ethyl 6-Amino-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carboxylate (4) and 6-Hydroxy-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline-7-carbonitrile (5). A mixture of **1a** (0.20 g, 0.87 mmol) and ethyl 2-cyanoacetate (0.20 g, 1.7 mmol) in DMSO (4 mL) containing CuI (17 mg, 0.087 mmol) and K_2CO_3 (0.48 g, 3.5 mmol) was stirred for 15 min at rt. Water (10 mL) was added and the precipitate was filtered off. The filtrate was extracted with AcOEt (3 × 10 mL) and combined extracts were washed with water (3 × 10 mL) and brine (10 mL). After drying over anhydrous Na_2SO_4, evaporation of the solvent gave a residual solid, which was recrystallized from hexane–CH_2Cl_2 to give **4** (75 mg, 32%); yellow needles; mp 145–147 °C; IR (KBr) 3295, 3152, 1653, 1620, 1601 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (t, J =

7.3 Hz, 3H), 2.00–2.05 (m, 2H), 3.64 (t, J = 5.3 Hz, 2H), 3.76 (t, J = 6.2 Hz, 2H), 4.37 (q, J = 7.3 Hz, 2H), 7.09 (dd, J = 7.8, 7.3 Hz, 1H), 7.23 (br s, 2H), 7.38 (ddd, J = 8.2, 7.3, 0.9 Hz, 1H), 8.18 (d, J = 7.8 Hz, 1H), 8.19 (d, J = 8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.54, 20.50, 43.18, 43.80, 59.94, 81.62, 122.97, 123.22, 124.46, 125.60, 130.37, 133.11, 147.18, 154.25, 169.81; MS *m/z* 271 (M^+, 100). Anal. Calcd for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.20; H, 6.47; N, 15.48. The above precipitate was recrystallized from THF to give **5** (92 mg, 47%); a yellow solid; mp 299–302 °C (decomp) (THF); IR (KBr) 3277, 2193, 1638, 1624 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.02 (br s, 2H), 3.50 (br s, 2H), 3.99 (br s, 2H), 7.01 (t, J = 7.3 Hz, 1H), 7.27 (d, J = 7.3 Hz, 1H), 7.53 (t, J = 7.3 Hz, 1H), 7.99 (d, J = 7.3 Hz, 1H), 9.54 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 18.00, 47.26, 48.57, 69.21, 108.05, 119.89, 120.15, 120.58, 124.38, 133.72, 139.63, 153.04, 158.55; MS *m/z* 225 (M^+, 100). Anal. Calcd for $C_{13}H_{11}N_3O$: C, 69.32; H, 4.92; N, 18.66. Found: C, 69.16; H, 4.88; N, 18.64.

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