Supporting Information

Rapid Access to 3-(Aminomethyl)isoquinoline-Fused Polycyclic Compounds by Copper-Catalyzed Domino Four-Component Coupling, Cascade Cyclization and Oxidation

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Experimental Section

General Methods. Exact mass (HRMS) spectra were recorded on JMS-HX/HX 110A mass spectrometer. ^1H NMR spectra were recorded using a JEOL AL-400 spectrometer at 400 MHz frequency. Chemical shifts are reported in δ (ppm) relative to Me_4Si (in CDCl_3) as internal standard. ^{13}C NMR spectra were recorded using a JEOL AL-400 and referenced to the residual CHCl_3 signal. Infrared (IR) spectra were obtained on a JASCO FT/IR-4100 FT-IR spectrometer with JASCO ATR PRO410-S. Melting points were measured by a hot stage melting points apparatus (uncorrected). Microwave reaction was conducted in a sealed glass vessel (capacity 10 mL) using CEM Discover microwave reactor with a run time of no more than 10 min. For column chromatography, Wakosil C-300, Aluminium oxide 90 (Merck), or Chromatorex[®] (FUJI SILYSIA CHEMICAL LTD.) was employed.

2-Ethynylbenzaldehyde (1a). To a stirred suspension of 2-bromobenzaldehyde (2.00 g, 10.8 mmol), $\text{PdCl}_2(\text{PPh}_3)_2$ (152 mg, 0.22 mmol), CuI (41.2 mg, 0.22 mmol) was added trimethylsilylacetylene (1.77 mL, 12.97 mmol) at room temperature under argon. The reaction mixture was stirred for 30 min at 80 °C followed by filtration through a pad of celite. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography over silica gel with hexane/AcOEt (50:1) as the eluent to give a solid mass. This solid was treated with K_2CO_3 (0.50 g, 3.64 mmol) in MeOH (20 mL) for 15 min at room temperature, and the solvent was removed under the reduced pressure. The residue was extracted with CH_2Cl_2 and the extract was washed with saturated aqueous Na_2CO_3 , and dried over MgSO_4 . The filtrate was concentrated under reduced pressure to give a solid mass which was purified by column chromatography over silica gel with hexane/AcOEt (50:1) to give the title compound **1a** (0.9 g, 62% yield from 2-bromobenzaldehyde). Recrystallization from *n*-hexane gave pure **1a** as colorless crystals: mp 65 °C; IR (neat): 2097 ($\text{C}\equiv\text{C}$), 1686 ($\text{C}=\text{O}$); ^1H NMR (400 MHz, CDCl_3) δ 3.47 (s, 1H, $\text{C}\equiv\text{CH}$), 7.47-7.52 (m, 1H, Ar), 7.55-7.63 (m, 2H, Ar), 7.92-7.95 (m, 1H, Ar), 10.54 (d, J = 0.7 Hz, 1H, CHO); ^{13}C NMR (100 MHz, CDCl_3) δ 79.2, 84.2, 125.5, 127.2, 139.2, 133.7, 133.9, 136.6, 191.4. *Anal.* calcd for $\text{C}_9\text{H}_6\text{O}$: C, 83.06; H, 4.65. Found: C, 82.99; H, 4.61.

2-Ethynyl-4-fluorobenzaldehyde (1b). By a procedure identical to that described for the preparation of **1a**, 2-bromo-4-fluorobenzaldehyde (1.00 g, 4.93 mmol) was converted to **1b** (434 mg, 62%) as a solid mass, which was recrystallized from *n*-hexane: colorless crystals; mp 103 °C; IR (neat): 2103 ($\text{C}\equiv\text{C}$), 1689 ($\text{C}=\text{O}$); ^1H NMR (400 MHz, CDCl_3) δ 3.52 (s, 1H, $\text{C}\equiv\text{CH}$), 7.16-7.21 (m, 1H, Ar), 7.29 (dd, J = 8.8, 2.4 Hz, 1H, Ar), 7.97 (dd, J = 8.8, 5.9 Hz, 1H, Ar), 10.46 (s, 1H, CHO); ^{13}C NMR (100 MHz, CDCl_3) δ 78.0, 85.4, 117.2 (d, J = 21.6 Hz), 120.5 (d, J = 24.0 Hz), 127.9 (d, J = 10.8 Hz), 130.1 (d, J = 9.6 Hz), 133.3 (d, J = 3.6 Hz), 165.5 (d, J = 256.3 Hz), 189.7. *Anal.* calcd for $\text{C}_9\text{H}_5\text{FO}$: C, 72.97; H, 3.40. Found: C, 73.09; H, 3.14.

2-Ethynyl-5-fluorobenzaldehyde (1c). By a procedure identical to that described for the preparation of **1a**, 2-bromo-5-fluorobenzaldehyde (1.00 g, 4.93 mmol) was converted to **1c** (542 mg, 77%) as a solid mass which was recrystallized from *n*-hexane: colorless crystals; mp 109 °C; IR (neat): 2101 (C≡C), 1693 (C=O); ¹H NMR (400 MHz, CDCl₃) δ 3.46 (s, 1H, C≡CH), 7.25-7.30 (m, 1H, Ar), 7.59-7.64 (m, 2H, Ar), 10.49 (d, *J* = 3.2 Hz, 1H, CHO); ¹³C NMR (100 MHz, CDCl₃) δ 78.2, 84.0, 113.8 (d, *J* = 22.8 Hz), 121.2 (d, *J* = 22.8 Hz), 121.5 (d, *J* = 3.6 Hz), 135.9 (d, *J* = 7.2 Hz), 138.6 (d, *J* = 7.2 Hz), 162.7 (d, *J* = 254.3 Hz), 190.1. *Anal.* calcd for C₉H₅FO: C, 72.97; H, 3.40. Found: C, 73.26; H, 3.31.

2-Ethynyl-4-methylbenzaldehyde (1d). By a procedure identical with that described for the preparation of **1a**, 2-bromo-4-methylbenzaldehyde (1.00 g, 5.02 mmol) was converted to **1d** (555 mg, 76%) as a solid mass which was recrystallized from *n*-hexane: colorless crystals; mp 81 °C; IR (neat): 2101 (C≡C), 1685 (C=O); ¹H NMR (400 MHz, CDCl₃) δ 2.41 (s, 3H, CH₃), 3.42 (s, 1H, C≡CH), 7.29 (d, *J* = 8.0 Hz, 1H, Ar), 7.43 (s, 1H, Ar), 7.83 (d, *J* = 8.0 Hz, 1H, Ar), 10.47 (s, 1H, CHO); ¹³C NMR (100 MHz, CDCl₃) δ 21.5, 79.4, 83.7, 125.5, 127.3, 130.2, 134.3, 134.4, 144.8, 191.1. *Anal.* calcd for C₁₀H₈O: C, 83.31; H, 5.59. Found: C, 83.29; H, 5.74.

2-Ethynyl-5-methoxybenzaldehyde (1e). By a procedure identical with that described for the preparation of **1a**, 2-bromo-5-methoxybenzaldehyde (1.00 g, 4.65 mmol) was converted to **1e** (593 mg, 80%) as a solid mass which was recrystallized from *n*-hexane: colorless crystals; mp 98 °C; IR (neat): 2098 (C≡C), 1677 (C=O); ¹H NMR (400 MHz, CDCl₃) δ 3.37 (s, 1H, C≡CH), 3.87 (s, 3H, OMe), 7.11 (dd, *J* = 8.5, 2.7 Hz, 1H, Ar), 7.41 (d, *J* = 2.7 Hz, 1H, Ar), 7.53 (d, *J* = 8.5 Hz, 1H, Ar), 10.50 (s, 1H, CHO); ¹³C NMR (100 MHz, CDCl₃) δ 55.6, 79.2, 82.7, 109.9, 118.1, 121.4, 135.2, 138.0, 160.1, 191.3. *Anal.* calcd for C₁₀H₈O₂: C, 74.99; H, 5.03. Found: C, 75.15; H, 4.81.

6-[(*N,N*-Diisopropylamino)methyl]-9-fluoro-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline (12b). By a procedure identical to that described for the preparation of **12a** from **1a**, **1b** (28.5 mg, 0.19 mmol) was converted into **12b** (33.3 mg, 55%) as a pale yellow solid: mp 123–125 °C; ¹H NMR (400 MHz, CDCl₃) δ 1.04 (d, *J* = 6.6 Hz, 12H, 4 × CH₃), 1.90-1.96 (m, 2H, 3-CH₂), 3.05-3.15 (m, 2H, 2 × CH(CH₃)₂), 3.47 (s, 2H, NCH₂), 3.62 (t, *J* = 5.6 Hz, 2H, NCH₂), 4.11 (t, *J* = 5.9 Hz, 2H, NCH₂), 5.99 (s, 1H, 7-H), 6.82 (dd, *J* = 9.4, 2.6 Hz, 1H, Ar), 6.90-6.95 (m, 1H, Ar), 8.24 (dd, *J* = 8.9, 6.0 Hz, 1H, Ar); ¹³C NMR (100 MHz, CDCl₃) δ 20.3 (4C), 21.0, 43.5, 44.4, 47.4 (2C), 47.9, 104.1, 109.8 (d, *J* = 21.5 Hz), 113.8 (d, *J* = 22.3 Hz), 123.8, 128.4, (d, *J* = 9.1 Hz), 136.1 (d, *J* = 9.9 Hz), 142.4, 149.1, 164.2 (d, *J* = 248.3 Hz); MS (FAB) *m/z* (%): 316 (MH⁺, 100); HRMS (FAB) calcd for C₁₉H₂₇FN₃ (MH⁺): 316.2189; found: 316.2188.

6-[(*N,N*-Diisopropylamino)methyl]-10-fluoro-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline (12c). By a procedure identical to that described for the preparation of **12a** from **1a**, **1c** (28.5 mg, 0.19 mmol) was converted into **12c** (44.6 mg, 74%) as a pale yellow solid: mp 139–141 °C; ¹H NMR (400 MHz, CDCl₃) δ 1.03 (d, *J* = 6.6 Hz, 12H, 4 × CH₃), 1.90-1.95 (m, 2H, 3-CH₂), 3.05-3.15

(m, 2H, 2 × CH(CH₃)₂), 3.47 (s, 2H, NCH₂), 3.63 (t, *J* = 5.5 Hz, 2H, NCH₂), 4.12 (t, *J* = 5.7 Hz, 2H, NCH₂), 6.01 (s, 1H, 7-H), 7.07-7.18 (m, 2H, Ar), 8.24 (dd, *J* = 10.6, 2.6 Hz, 1H, Ar); ¹³C NMR (100 MHz, CDCl₃) δ 20.2 (4C), 20.9, 43.3, 44.5, 47.2 (2C), 47.8, 103.9, 111.1 (d, *J* = 23.2 Hz), 118.1 (d, *J* = 23.2 Hz), 126.7 (d, *J* = 7.4 Hz), 129.2, (d, *J* = 8.3 Hz), 130.4 (d, *J* = 2.5 Hz), 140.0 (d, *J* = 2.5 Hz), 148.9 (d, *J* = 3.3 Hz), 161.3 (d, *J* = 244.1 Hz); MS (FAB) *m/z* (%): 316 (MH⁺, 100); HRMS (FAB) calcd for C₁₉H₂₇FN₃ (MH⁺): 316.2189; found: 316.2180.

6-[(*N,N*-Diisopropylamino)methyl]-9-methyl-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline

(12d). By a procedure identical to that described for the preparation of **12a** from **1a**, **1d** (27.7 mg, 0.19 mmol) was converted into **12d** (42.2 mg, 71%) as a pale yellow solid: mp 132–135 °C; ¹H NMR (400 MHz, CDCl₃) δ 1.03 (d, *J* = 6.6 Hz, 12H, 4 × CH₃), 1.90-1.95 (m, 2H, 3-CH₂), 2.36 (s, 3H, ArCH₃), 3.05-3.15 (m, 2H, 2 × CH(CH₃)₂), 3.46 (s, 2H, NCH₂), 3.63 (t, *J* = 5.6 Hz, 2H, NCH₂), 4.11 (t, *J* = 5.9 Hz, 2H, NCH₂), 5.99 (s, 1H, 7-H), 6.98-7.00 (m, 1H, Ar), 7.08 (dd, *J* = 8.3, 1.5 Hz, 1H, Ar), 8.15 (d, *J* = 8.3 Hz, 1H, Ar); ¹³C NMR (100 MHz, CDCl₃) δ 20.2 (4C), 20.9, 21.4, 43.4, 44.2, 47.1 (2C), 47.9, 105.4, 124.6, 124.9, 125.6, 127.6, 134.0, 140.4, 140.6, 150.0; MS (FAB) *m/z* (%): 312 (MH⁺, 100); HRMS (FAB) calcd for C₂₀H₃₀N₃ (MH⁺): 312.2440; found: 312.2443.

6-[(*N,N*-Diisopropylamino)methyl]-10-methoxy-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline

(12e). By a procedure identical to that described for the preparation of **12a** from **1a**, **1e** (30.8 mg, 0.19 mmol) was converted into **12e** (34.8 mg, 55%) as a pale yellow solid: mp 174–176 °C; ¹H NMR (400 MHz, CDCl₃) δ 1.03 (d, *J* = 6.6 Hz, 12H, 4 × CH₃), 1.92-1.97 (m, 2H, 3-CH₂), 3.05-3.15 (m, 2H, 2 × CH(CH₃)₂), 3.49 (s, 2H, NCH₂), 3.67 (t, *J* = 5.5 Hz, 2H, NCH₂), 3.90 (s, 3H, OMe), 4.16 (t, *J* = 5.7 Hz, 2H, NCH₂), 6.02 (s, 1H, 7-H), 7.02 (dd, *J* = 8.5, 2.7 Hz, 1H, Ar), 7.14 (d, *J* = 8.5 Hz, 1H, Ar), 7.75-7.77 (m, 1H, Ar); ¹³C NMR (100 MHz, CDCl₃) δ 20.2 (4C), 21.0, 43.5, 45.6, 47.0 (2C), 47.9, 55.6, 105.0, 106.2, 120.3, 126.6, 127.8, 128.4, 138.2, 149.8, 158.4; MS (FAB) *m/z* (%): 328 (MH⁺, 100); HRMS (FAB) calcd for C₂₀H₃₀ON₃ (MH⁺): 328.2389; found: 328.2383.

6-(Piperidin-1-ylmethyl)-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline (12f). A mixture of paraformaldehyde **2** (17.3 mg, 0.58 mmol), piperidine **3b** (57.0 μL, 0.58 mmol) and CuCl (1.9 mg, 0.019 mmol) in DMF (1.5 mL) was stirred under O₂ at rt for 1 h. Then 2-ethynylbenzaldehyde **1a** (25.0 mg, 0.19 mmol) was added at rt, and the mixture was additionally stirred at this temperature for 1.5 h. After the Mannich-type reaction was completed monitored by TLC, propanediamine **8a** (48.1 mL, 0.58 mmol) and MS 4Å (37.5 mg) were added and the mixture was stirred at 120 °C for 1 h. The mixture was concentrated in vacuo and purified by column chromatography over alumina with CHCl₃/CH₃OH (20:1) as the eluent to give **12f** (41.3 mg 72%) as a brown oil: ¹H NMR (400 MHz, CDCl₃) δ 1.40-1.47 (m, 2H, CH₂), 1.52-1.57 (m, 4H, 2 × CH₂), 1.92-1.98 (m, 2H, 3-CH₂), 2.35-2.43 (m, 4H, 2 × CH₂), 3.19 (s, 2H, NCH₂), 3.65 (t, *J* = 5.6 Hz, 2H, NCH₂), 4.09 (t, *J* = 5.9 Hz, 2H, NCH₂), 5.87 (s, 1H, 7-H), 7.17 (d, *J* = 7.6 Hz, 1H, Ar) 7.23-7.27 (m, 1H, Ar), 7.35-7.39 (m, 1H, Ar), 8.25 (d, *J* = 8.0 Hz, 1H, Ar); ¹³C NMR (100 MHz, CDCl₃) δ 21.1, 24.3, 26.1 (2C), 43.7, 44.6,

54.1 (2C), 61.5, 105.2, 124.9, 125.5, 126.1, 127.7, 130.1, 133.7, 138.7, 149.7; MS (FAB) m/z (%): 282 (MH^+ , 100); HRMS (FAB) calcd for $C_{18}H_{24}N_3$ (MH^+): 282.1970; found: 282.1974.

6-[(*N,N*-Diallylamino)methyl]-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline (12g). By a procedure similar to that described for the preparation of **12a** from **1a**, **1a** (25.0 mg, 0.19 mmol) was converted into **12g** (17.0 mg, 30%) using diallylamine **3c** (71.1 μ L, 0.58 mmol): brown oil; 1H NMR (400 MHz, $CDCl_3$) δ 1.92-1.98 (m, 2H, 3- CH_2), 3.10-3.12 (m, 4H, 2 $\times$ NCH_2), 3.34 (s, 2H, NCH_2), 3.65 (t, J = 5.5 Hz, 2H, NCH_2), 4.07 (t, J = 5.9 Hz, 2H, NCH_2), 5.16-5.21 (m, 4H, 2 $\times$ $C=CH_2$), 5.79-5.89 (m, 2H, 2 $\times$ $C=CH$), 5.94 (s, 1H, 7-H), 7.18 (d, J = 7.6 Hz, 1H, Ar) 7.25-7.29 (m, 1H, Ar), 7.36-7.41 (m, 1H, Ar), 8.26 (d, J = 8.0 Hz, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 44.0, 44.3, 56.0, 56.2 (2C), 106.2, 118.2 (2C), 125.0, 125.7, 126.5, 127.3, 130.4, 133.7, 134.9 (2C), 138.9, 149.8; MS (FAB) m/z (%): 294 (MH^+ , 100); HRMS (FAB) calcd for $C_{19}H_{24}N_3$ (MH^+): 294.1970; found: 294.1969.

6-[[*N,N*-Bis((*R*)-1-phenylethyl)amino]methyl]-3,4-dihydro-2*H*-pyrimido[2,1-*a*]isoquinoline (12h). By a procedure similar to that described for the preparation of **12a** from **1a**, **1a** (25 mg, 0.19 mmol) was converted into **12h** (30.9 mg, 38%) using bis[(*R*)-1-phenylethyl]amine **3d** (87.9 μ L, 0.38 mmol): colorless solid; mp 174–176 $^{\circ}C$; 1H NMR (400 MHz, $CDCl_3$) δ 1.42-1.68 (m, 8H, 3- CH_2 and 2 $\times$ CH_3), 2.77-2.83 (m, 1H, NCH), 3.43-3.58 (m, 5H, NCH and 2 $\times$ NCH_2), 4.17 (q, J = 6.9 Hz, 2H, 2 $\times$ CH_3CH), 6.05 (s, 1H, 7-H), 7.11-7.38 (m, 13H, Ar), 8.19 (d, J = 8.0 Hz, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5 (2C), 20.8, 42.6, 44.3, 47.8, 55.1 (2C), 106.0, 124.8, 125.5, 126.1, 126.8 (2C), 127.6, 127.8 (4C), 128.1 (4C), 130.1, 133.6, 139.9, 143.5 (2C), 149.5; MS (FAB) m/z (%): 422 (MH^+ , 100); HRMS (FAB) calcd for $C_{29}H_{32}N_3$ (MH^+): 422.2596; found: 422.2602.

5-[(*N,N*-Diisopropylamino)methyl]-2,3-dihydroimidazo[2,1-*a*]isoquinoline (13). By a procedure similar to that described for the preparation of **12a** from **1a**, **1a** (25.0 mg, 0.19 mmol) was converted into **13** (30.5 mg, 56%) using ethylenediamine **8b** (38.7 μ L, 0.58 mmol): brown oil; 1H NMR (400 MHz, $CDCl_3$) δ 1.04 (d, J = 6.6 Hz, 12H, 4 $\times$ CH_3), 3.06-3.16 (m, 2H, 2 $\times$ $CHCH_3$), 3.43 (s, 2H, NCH_2), 4.03-4.09 (m, 2H, NCH_2), 4.20-4.26 (m, 2H, NCH_2), 5.97 (s, 1H, 7-H), 7.24-7.27 (m, 2H, Ar), 7.41-7.45 (m, 1H, Ar), 8.10 (d, J = 8.3 Hz, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3 (4C), 47.2, 47.50, 47.54 (2C), 53.1, 102.8, 121.7, 125.2, 125.6, 126.0, 131.2, 136.5, 140.9, 158.6; MS (FAB) m/z (%): 284 (MH^+ , 100); HRMS (FAB) calcd for $C_{18}H_{26}N_3$ (MH^+): 284.2127; found: 284.2134.

7-[(*N,N*-Diisopropylamino)methyl]-2,3,4,5-tetrahydro[1,3]diazepino[2,1-*a*]isoquinoline (14). By a procedure similar to that described for the preparation of **12a** from **1a**, **1a** (25.0 mg, 0.19 mmol) was converted into **14** (29.8 mg, 63%) using butanediamine **8c** (57.9 μ L, 0.38 mmol) under argon: brown oil; 1H NMR (400 MHz, $CDCl_3$) δ 1.05 (d, J = 6.8 Hz, 12H, 4 $\times$ CH_3), 1.93-1.99 (m, 2H, CH_2), 2.03-2.09 (m, 2H, CH_2), 3.09-3.19 (m, 2H, 2 $\times$ $CHCH_3$), 3.50 (s, 2H, NCH_2), 3.89-3.92 (m, 2H, NCH_2), 4.03-4.06 (m, 2H, NCH_2), 6.12 (s, 1H, 8-H), 7.16 (d, J = 7.6 Hz, 1H, Ar), 7.22-7.26 (m,

1H, Ar), 7.33-7.37 (m, 1H, Ar), 8.16 (d, $J = 7.8$ Hz, 1H, Ar); ^{13}C NMR (100 MHz, CDCl_3) δ 20.2 (4C), 25.4, 26.6, 47.2 (2C), 47.7, 47.8, 48.2, 105.9, 124.4, 125.6, 126.0, 128.5, 129.8, 134.1 142.6, 153.9; MS (FAB) m/z (%): 312 (MH^+ , 100); HRMS (FAB) calcd for $\text{C}_{20}\text{H}_{30}\text{N}_3$ (MH^+): 312.2440; found: 312.2433.

8-[(*N,N*-Diisopropylamino)methyl]-3,4,5,6-tetrahydro-2*H*-[1,3]diazocino[2,1-*a*]isoquinoline

(15). By a procedure similar to that described for the preparation of **12a** from **1a**, **1a** (25.0 mg, 0.19 mmol) was converted into **15** (7.2 mg, 12%) using pentanediamine **8d** (67.8 μL , 0.38 mmol): brown oil; ^1H NMR (400 MHz, CDCl_3) δ 1.03 (d, $J = 6.6$ Hz, 12H, $4 \times \text{CH}_3$), 1.63-1.69 (m, 2H, CH_2), 1.91-2.04 (m, 4H, $2 \times \text{CH}_2$), 3.08-3.18 (m, 2H, $2 \times \text{CHCH}_3$), 3.44 (s, 2H, NCH_2), 4.20 (t, $J = 6.2$ Hz, 2H, NCH_2), 4.43 (t, $J = 6.6$ Hz, 2H, NCH_2), 6.16 (s, 1H, 9-H), 7.17 (d, $J = 7.6$ Hz, 1H, Ar), 7.23-7.26 (m, 1H, Ar), 7.34-7.38 (m, 1H, Ar), 8.31 (d, $J = 8.0$ Hz, 1H, Ar); ^{13}C NMR (100 MHz, CDCl_3) δ 20.2 (4C), 20.6, 29.2, 30.7, 45.4, 46.6, 47.2 (2C), 47.6, 106.3, 124.5, 126.1, 126.9, 129.4, 129.8, 134.2, 141.7, 150.2; MS (FAB) m/z (%): 326 (MH^+ , 100); HRMS (FAB) calcd for $\text{C}_{21}\text{H}_{32}\text{N}_3$ (MH^+): 326.2596; found: 326.2597.

6-[(*N,N*-Diisopropylamino)methyl]benzimidazo[2,1-*a*]isoquinoline (16). By a procedure similar to that described for the preparation of **12a** from **1a**, **1a** (25.0 mg, 0.19 mmol) was converted into **16** (28.1 mg, 58%) using phenylendiamine **8e** (62.3 μL , 0.38 mmol) under argon: pale yellow solid; mp 152–154 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 1.16 (d, $J = 6.3$ Hz, 12H, $4 \times \text{CH}_3$), 3.22-3.32 (m, 2H, $2 \times \text{CHCH}_3$), 4.36 (d, $J = 1.2$ Hz, 2H, NCH_2), 7.36-7.40 (m, 1H, Ar), 7.49-7.53 (m, 2H, Ar and 5-H), 7.60-7.68 (m, 2H, Ar), 7.74 (d, $J = 7.3$ Hz, 1H, Ar), 8.06 (d, $J = 8.0$ Hz, 1H, Ar), 8.14 (d, $J = 8.3$ Hz, 1H, Ar), 8.84-8.86 (m, 1H, Ar); ^{13}C NMR (100 MHz, CDCl_3) δ 20.9 (4C), 47.6, 49.5 (2C), 109.0, 114.7, 119.9, 121.4, 122.2, 124.0, 125.0, 126.3, 127.0, 129.8, 130.9, 131.8, 140.9, 144.3, 148.6; MS (FAB) m/z (%): 332 (MH^+ , 100); HRMS (FAB) calcd for $\text{C}_{22}\text{H}_{26}\text{N}_3$ (MH^+): 332.2127; found: 332.2133.

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 EXMOD single_pulse_dec
 OBFRQ 125.77 MHz
 OBSET 7.87 KHz
 OBFIN 4.21 Hz
 POINT 26214
 FREQU 31446.06 Hz
 SCANS 512
 ACQTM 0.8336 sec
 PD 2.0000 sec
 PW1 3.83 usec
 IRNUC 1H
 CTEMP 25.1 c
 SLVNT CDCl₃
 EXREF 77.00 ppm
 BF 1.20 Hz
 RGAIN 60

K-186

C:\Documents and Settings\Yusukebe0108Vデスクトップ\NMR\K-186\NON_E26_FT.als

DFILE K-186NON_E26_FT.als
 COMNT K-186
 DATIM Thu Jul 19 23:44:38 2007
 OBNUC 1H
 EXMOD NON
 OBFRQ 399.65 MHz
 OBSET 124.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 7992.01 Hz
 SCANS 8
 ACQTM 4.1001 sec
 PD 2.9000 sec
 PW1 5.50 usec
 IRNUC 1H
 CTEMP 24.2 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 20

single pulse decoupled gated NOE

C:\Documents and Settings\Yyusukebe0108Yデスクトップ\NMRYKK-186-carbon-1.als

DFILE K-186-carbon-1.als
 COMNT single pulse decoupled gated NOE
 DATIM 12-10-2007 18:51:01
 OBNUC ¹³C
 EXMOD single_pulse_dec
 OBFRQ 125.77 MHz
 OBSET 7.87 KHz
 OBFIN 4.21 Hz
 POINT 26214
 FREQU 31446.06 Hz
 SCANS 512
 ACQTM 0.8336 sec
 PD 2.0000 sec
 PW1 3.83 usec
 IRNUC ¹H
 CTEMP 24.6 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 1.20 Hz
 RGAIN 58

C:\Documents and Settings\Yusukebe0108\Desktop\YNNMRVKYK-1821NON_E25_FT.xls

single pulse decoupled gated NOE

C:\Documents and Settings\Yusukebe0108\デスクトップ\YNMRYKKYK-182-carbon-1.als

DFILE K-182-carbon-1.als
 COMNT single pulse decoupled gated NOE
 DATIM 12-10-2007 12:39:34
 OBNUC ¹³C
 EXMOD single_pulse_dec
 OBFRQ 125.77 MHz
 OBSET 7.87 KHz
 OBFIN 4.21 Hz
 POINT 26214
 FREQU 31446.06 Hz
 SCANS 512
 ACQTM 0.8336 sec
 PD 2.0000 sec
 PW1 3.83 usec
 IRNUC ¹H
 CTEMP 25.0 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 1.20 Hz
 RGAIN 60

K-184

C:\Documents and Settings\Yusukebe0108Y\Desktop\YNMRYK-K-184\NON_E21_FT.als

DFILE K-184NON_E21_FT.als
 COMNT K-184
 DATIM Thu Jul 19 19:44:10 2007
 OBNUC 1H
 EXMOD NON
 OBFRQ 399.65 MHz
 OBSET 124.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 7992.01 Hz
 SCANS 8
 ACQTM 4.1001 sec
 PD 2.9000 sec
 PW1 5.50 usec
 IRNUC 1H
 CTEMP 23.2 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 20

single pulse decoupled gated NOE

C:\Documents and Settings\yusukebe0108\デスクトップ\NMKVYK-184-carbon-1.als

DFILE K-184-carbon-1.als
 COMNT single pulse decoupled gated NOE
 DATIM 12-10-2007 13:09:32
 OBNUC ¹³C
 EXMOD single_pulse_dec
 OBFRQ 125.77 MHz
 OBSET 7.87 KHz
 OBFIN 4.21 Hz
 POINT 26214
 FREQU 31446.06 Hz
 SCANS 512
 ACQTM 0.8336 sec
 PD 2.0000 sec
 PW1 3.83 usec
 IRNUC ¹H
 CTEMP 24.6 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 1.20 Hz
 RGAIN 60

C:\Documents and Settings\Yusukebe0108\Desktop\YNNMRVKYK-1881NON_E43_FT.xls

DFILE	K-1881NON_E43_FT.als
COMNT	K-188
DATIM	Fri Jul 20 23:23:20 2007
OBNUC	1H
EXMOD	NON
OBFRQ	399.65 MHz
OBSET	124.00 KHz
OBFIN	10500.00 Hz
POINT	32768
FREQU	7992.01 Hz
SCANS	8
ACQTM	4.1001 sec
PD	2.9000 sec
PW1	5.50 usec
IRNUC	1H
CTEMP	23.9 c
SLVNT	CDCL3
EXREF	0.00 ppm
Bf	0.12 Hz
RGAIN	18

single pulse decoupled gated NOE

C:\Documents and Settings\Yusukebe0108Yデスクトップ\NMR\K-188-carbon-1.als

DFILE K-188-carbon-1.als
 COMNT single pulse decoupled gated NOE
 DATIM 12-10-2007 19:22:13
 OBNUC 13C
 EXMOD single_pulse_dec
 OBFRQ 125.77 MHz
 OBSET 7.87 KHz
 OBFIN 4.21 Hz
 POINT 26214
 FREQU 31446.06 Hz
 SCANS 512
 ACQTM 0.8336 sec
 PD 2.0000 sec
 PW1 3.83 usec
 IRNUC 1H
 CTEMP 24.5 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 1.20 Hz
 RGAIN 58

G:\論文\Wisoquinoline-fused tricyclic compounds\1H NMR 久保田\ValiceY11a-1H.als

11a-1H.als
 Thu Jan 29 17:56:28 2009
 1H
 EXMOD NON
 OBFRQ 399.65 MHz
 OBSET 124.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 7992.01 Hz
 SCANS 8
 ACQTM 4.1001 sec
 PD 2.9000 sec
 PW1 5.50 usec
 1H
 CDCL3
 CTEMP 20.7 c
 SLVNT
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 14

G:\Y論文\Wisoquinoline-fused tricyclic compounds\SIYNMR 久保田\ValiceY11b-1H.als

11b-1H.als
 COMNT Fri Jan 09 08:53:20 2009
 DATIM 1H
 EXMOD NON
 OBFREQ 399.65 MHz
 OBSET 124.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 7992.01 Hz
 SCANS 8
 ACQTM 4.1001 sec
 PD 2.9000 sec
 PW1 5.50 usec
 IRNUC 1H
 CTEMP 19.8 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 13

G:\V_{論文}\Wisoquinoline-fused tricyclic compounds\SVINMR 久保田\ValiceY11c-1H.als

11c-1H.als
 Thu Jan 22 21:17:50 2009
 1H
 EXMOD NON
 OBFRQ 399.65 MHz
 OBSET 124.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 7992.01 Hz
 SCANS 8
 ACQTM 4.1001 sec
 PD 2.9000 sec
 5.50 usec
 1H
 18.9 c
 CDCL3
 0.00 ppm
 0.12 Hz
 10

G:\論文\tricyclic compounds\13C NMR 久保田\11c-13C.als

DFILE 11c-13C.als
 COMNT
 DATIM Fri Jan 23 22:15:03 2009
 OENUC 13C
 EXMOD BCM
 OBFRQ 100.40 MHz
 OBSET 125.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 27118.64 Hz
 SCANS 144
 ACQTM 1.2083 sec
 PD 1.7920 sec
 PW1 5.10 usec
 IRNUC 1H
 CTEMP 20.1 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 1.20 Hz
 RGAIN 25

G:\論文\Wisoquinoline-fused tricyclic compounds\1H NMR 久保田\ValiceY11d-1H.als

11d-1H.als
 Thu Jan 22 21:23:31 2009
 1H
 EXMOD NON
 OBFREQ 399.65 MHz
 OBSET 124.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 7992.01 Hz
 SCANS 8
 ACQTM 4.1001 sec
 PD 2.9000 sec
 PW1 5.50 usec
 1H
 CDCL3
 18.9 c
 0.00 ppm
 0.12 Hz
 10
 RGAIN

G:\論文\Wisoquinoline-fused tricyclic compounds\1H NMR 久保田\ValiceY11e-1H.als

11e-1H.als
 DFILE
 COMNT
 DATIM Wed Jan 14 21:52:12 2009
 OBNUC 1H
 EXMOD NON
 OBFREQ 399.65 MHz
 OBSET 124.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 7992.01 Hz
 SCANS 8
 ACQTM 4.1001 sec
 PD 2.9000 sec
 PW 5.50 usec
 IRNUC 1H
 CTEMP 18.9 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 14

G:\論文\Wisoquinoline-fused tricyclic compounds\1H NMR 久保田\11f-1H.als

11f-1H.als
 Tue Feb 10 23:09:06 2009
 1H
 EXMOD NON
 OBFRQ 399.65 MHz
 OBSET 124.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 7992.01 Hz
 SCANS 8
 ACQTM 4.1001 sec
 PD 2.9000 sec
 5.50 usec
 1H
 CDCL3
 19.6 c
 0.00 ppm
 0.12 Hz
 14
 RGAIN

G:\論文\Isoquinoline-fused tricyclic compounds\1H NMR 久保田\11g-1H.als

G:\論文\Isoquinoline-fused tricyclic compounds\13C NMR 久保田\11g-13C.als

DFILE 11g-13C.als
 COMNT
 DATIM Wed Feb 11 19:55:17 2009
 OBNUC 13C
 EXMOD BCM
 OBFRQ 100.40 MHz
 OBSET 125.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 27118.64 Hz
 SCANS 1024
 ACQTM 1.2083 sec
 PD 1.7920 sec
 PW1 5.10 usec
 IRNUC 1H
 CTEMP 20.4 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 0.12 Hz
 RGAIN 25

G:\論文\Isoquinoline-fused tricyclic compounds\1H NMR 久保田\11i-1H.als

DFILE 11i-1H.als
 COMNT
 DATIM Fri Jan 16 16:44:22 2009
 OBNUC 1H
 EXMOD NON
 OBFRQ 399.65 MHz
 OBSET 124.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 7992.01 Hz
 SCANS 8
 ACQTM 4.1001 sec
 PD 2.9000 sec
 PW1 5.50 usec
 IRNUC 1H
 CTEMP 18.0 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 14

G:\論文\Wisoquinoline-fused tricyclic compounds\1H NMR 久保田\11j-1H.als

11j-1H.als
 Thu Jan 22 21:34:11 2009
 1H
 EXMOD NON
 OBFRQ 399.65 MHz
 OBSET 124.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 7992.01 Hz
 SCANS 8
 ACQTM 4.1001 sec
 PD 2.9000 sec
 5.50 usec
 1H
 CDCL3
 18.9 c
 0.00 ppm
 0.12 Hz
 11
 RGAIN

G:\論文\Isoquinoline-fused tricyclic compounds\1H NMR 久保田\ValiceY11k-1H.als

11k-1H.als
 Sun Feb 15 11:20:26 2009
 1H
 NON
 399.65 MHz
 124.00 KHz
 10500.00 Hz
 32768
 7992.01 Hz
 8
 4.1001 sec
 2.9000 sec
 5.50 usec
 1H
 21.3 c
 CDCL3
 0.00 ppm
 0.12 Hz
 17

G:\論文\Isoquinoline-fused tricyclic compounds\13C NMR 久保田\11k-13C.als

11k-13C. als
 Mon Feb 16 09:00:22 2009
 13C
 EXMOD BCM
 OBFRQ 100.40 MHz
 OBSET 125.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 27118.64 Hz
 SCANS 19041
 ACQTM 1.2083 sec
 PD 1.7920 sec
 PW1 5.10 usec
 1H
 IRNUC 20.9 c
 CTEMP CDCL3
 SLVNT 77.00 ppm
 EXREF 0.12 Hz
 BF 25
 RGAIN

G:\論文\Wisoquinoline-fused tricyclic compounds\SVI\NMR 久保田\ValiceY111-1H.als

111-1H.als
 COMET
 DATIM Sat Jan 17 19:58:50 2009
 OBNUC 1H
 EXMOD NON
 OBFREQ 399.65 MHz
 OBSET 124.00 KHz
 OBFIN 10500.00 Hz
 POINT 32768
 FREQU 7992.01 Hz
 SCANS 8
 ACQTM 4.1001 sec
 PD 2.9000 sec
 PW1 5.50 usec
 IRNUC 1H
 CTEMP 18.4 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 13