Convenient Synthesis of 2-Amino-1,8-naphthyridines, Building Blocks for Host–Guest and Self-Assembling Systems

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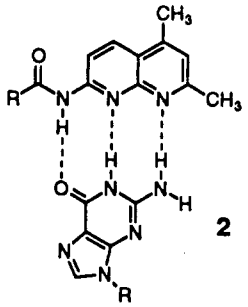
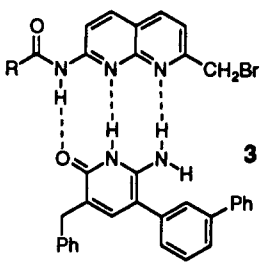
Application of the Reimer–Tiemann reaction to 2,6-diaminopyridine afforded a 26% yield of 2,6-diaminopyridine-3-carboxaldehyde (4) and a small amount (4%) of 2,6-diaminopyridine-3,5-dicarboxaldehyde. Alternatively, conversion of 2,6-diaminopyridine to 2,6-bis(pivaloylamino)pyridine (6), directed lithiation with *n*-butyllithium, treatment with *N*-formylmorpholine, and hydrolysis produced 4 in 67% overall yield. The Friedländer condensation of 4 with a variety of activated and unactivated ketones afforded 2-amino-1,8-naphthyridines and bis(2-amino-1,8-naphthyridines) in moderate to good yields, providing a convenient synthesis of useful building blocks for new host–guest and self-assembling systems.

The donor–acceptor–acceptor (DAA) arrangement of hydrogen bonding sites in 2-carboxamidonaphthyridines (e.g. 1) allows it to pair with guanine (2) in much the same way that cytosine does. Indeed, an HPLC bonded phase generated by covalently linking 1a to silica gel (R = $(CH_2)_{10}$-$SiMe_2O$–silica) showed excellent retention of tri-*O*-acetylguanosine.[1] We recently quantified the strength of this interaction and found that carboxamidonaphthyridine 1a (R = Me) tightly complexes guanosine 2 (R = tri-*O*-



1a



1b

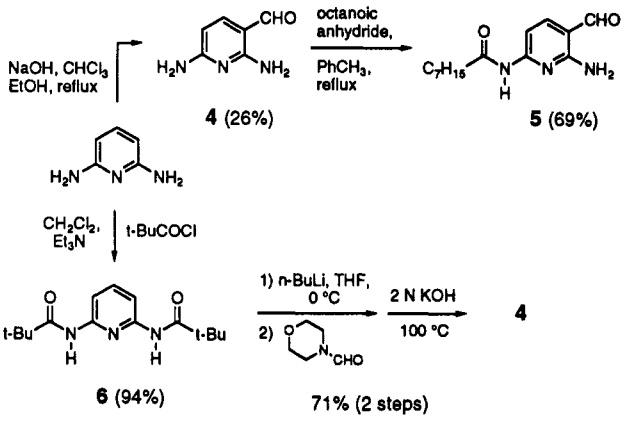
2

3

pentanoylribose) in chloroform-*d* with $K_{assoc} \geq 10^4\ M^{-1}$.[2] In an earlier report, Kelly showed that carboxamidonaphthyridine 1b (R = Me) bound to 6-amino-2-pyridone 3 with a similar binding affinity ($K_{assoc} = 1.7 \times 10^4\ M^{-1}$), and this served as a subunit in a "bisubstrate reaction template".[3]

Not only do the carboxamidonaphthyridine moiety and its complement (2 or 3) bind each other tightly,[2-4] but the lower symmetry of the AAD·DDA hydrogen bonding arrangement affords a level of geometrical control that is absent in the other two possible triple hydrogen bonding arrangements, AAA·DDD and ADA·DAD, both of which can combine in a head-to-head and head-to-tail fashion.

Scheme I



For these reasons, the AAD·DDA hydrogen bonding arrangement is particularly appealing in the context of hydrogen bond-mediated cyclic self-assembly.[5,6] While 2-amino-5,7-dimethyl-1,8-naphthyridine 1a (free amine) can be conveniently prepared by Knorr cyclization of 2,6-diaminopyridine and acetylacetone, more elaborate 1,8-naphthyridines cannot easily be made in this way.[7] Herein we report a convenient and versatile synthesis of 2-amino- and 2-carboxamido-1,8-naphthyridines that uses the Friedländer condensation.[8]

The Friedländer approach to 2-aminonaphthyridines required 2,6-diaminopyridine-3-carboxaldehyde (4). Two routes to 4 are outlined in Scheme I. The Reimer–Tiemann reaction is a well-precedented method of formylating phenols and the reaction has been successfully extended to a few heterocyclic compounds lacking hydroxyl groups.[9] Reaction of commercially available 2,6-diaminopyridine

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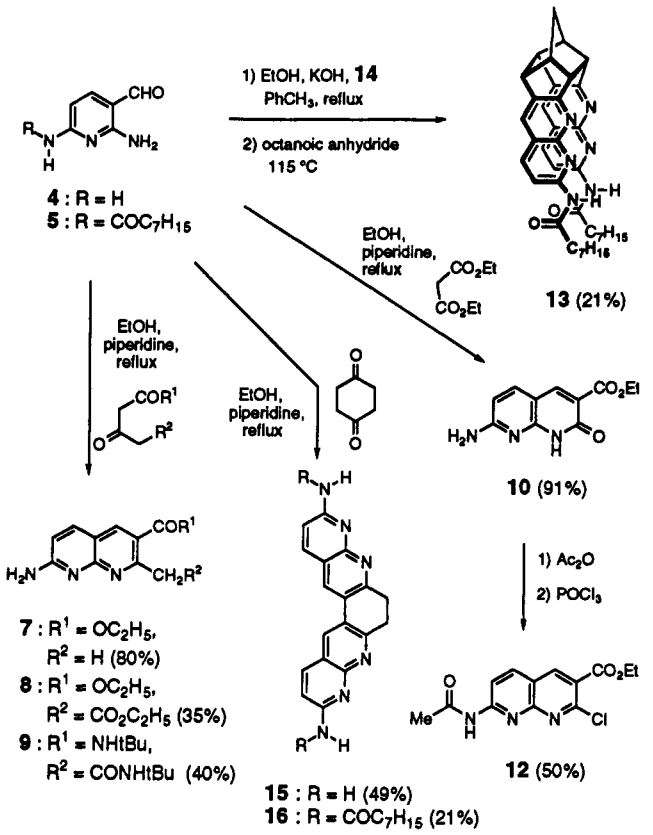
Scheme II



under Reimer–Tiemann conditions afforded **4** in a single step in 26% yield, with a small amount (4%) of 2,6-diamino-3,5-pyridinedicarboxaldehyde. The remaining mass was polar material that was removed by continuous extraction followed by chromatography. An alternative three-step procedure involved ortho-lithiation of 2,6-bis(pivaloylamino)pyridine (**6**) and treatment with *N*-formylmorpholine.[10] Hydrolysis with 2 N KOH afforded **4** in 67% yield for the three steps.

o-Aminoaldehyde **4** smoothly participated in Friedländer condensations with a variety of activated and unactivated ketones (Scheme II). For example, treatment of **4** with ethyl acetoacetate and piperidine in refluxing ethanol produced aminonaphthyridine **7** in 80% yield. Likewise, reaction of **4** with diethyl 3-oxoglutarate and *N,N'*-di-*tert*-butyl-3-oxoglutaramide[11] under the same reaction conditions afforded naphthyridines **8** and **9** in yields of 35 and 40%, respectively. Condensation with diethyl malonate afforded naphthyridinone **10** in 91% yield.[12] The acetylamino derivative **11** was produced in 88% yield by acetylation of **10** with acetic anhydride, which in turn was converted into chloronaphthyridine **12** in 57% yield by treatment with phosphorus oxychloride. The functionality in **12** is particularly well-suited for elaboration into more sophisticated hosts for guests containing the DDA hydrogen bonding array.

Bis-naphthyridines were prepared by Friedländer condensation of **4** with diketones. By analogy to the work of Marchand and Thummel[13] using simpler *o*-aminoaryl aldehydes, bis(carboxamidonaphthyridine) **13** was synthesized in 21% yield by reaction of tetracyclo-[6.3.0.0^{4,11}.0^{5,9}]undecane-2,7-dione[14] (**14**) with 2 equiv of **4** followed by treatment with octanoic anhydride. The long-chain amide groups markedly increased the solubility of **13** in organic solvents and allowed it to be more easily purified and characterized. The Friedländer reaction of **4** and 1,4-cyclohexanedione afforded bis(aminonaphthyridine) **15** in 49% crude yield.[15] This compound also proved to have low solubility in organic solvents. It was found that the 6-amino group in **4** could be selectively acylated with octanoic anhydride to form **5**, which also participated in the Friedländer condensation. Thus, the more soluble bis(carboxamidonaphthyridine) **16** was produced directly from **5** in 21% yield. For naphthyridines needing improved solubility, **5** is the preferred precursor.

The structure of **13** and **16** appear well suited to bind two aminopyridone moieties (e.g. guanosine). While the two binding sites in **16** diverge, those in **13** are in close proximity, so that they might act to complex, or template the synthesis of, GpG derivatives. Additionally, both compounds have the potential to serve as building blocks for new supramolecular aggregates. There are a myriad of other mono- and polynaphthyridines that can be readily prepared using the chemistry outlined in Schemes I and II, and these might also act as useful building blocks in new host–guest and self-assembling systems. Such applications are currently under investigation and will be described in due course.

Experimental Section

General. The following solvents were freshly distilled prior to use: tetrahydrofuran (THF) from sodium and benzophenone, methanol (CH_3OH) from magnesium turnings, methylene chloride (CH_2Cl_2) and triethylamine from calcium hydride. All other solvents and reagents were of reagent grade quality and used without further purification. All reactions were run under a nitrogen atmosphere unless otherwise noted.

^1H and ^{13}C NMR spectra were recorded on a General Electric QE-300. Spectra were obtained in chloroform-*d* unless otherwise noted. Chemical shifts are reported in parts per million (ppm) with residual protio solvent or tetramethylsilane as an internal reference, and coupling constants are reported in hertz (Hz). Infrared (IR) spectra were recorded on an IBM IR-32 FTIR spectrometer; absorptions are reported in cm^{-1}. Mass spectra (MS) were obtained on a Finnigan-AT CH-5 or Finnigan-MAT-731 spectrometer. Melting points are uncorrected. Elemental analyses were performed at the University of Illinois School of Chemical Sciences.

2,6-Diaminopyridine-3-carboxaldehyde (4). Method A. To a mechanically stirred solution of 81.0 g (0.74 mol) of 2,6-diaminopyridine in 580 mL of ethanol was added a hot aqueous solution of 750 g of sodium hydroxide in 1 L of water, under a normal atmosphere. The resulting dark-brown heterogeneous solution was heated to 80–85 °C and 1.5 L of chloroform was added dropwise(*caution: exothermic*) over 24 h. After heating for an additional 20 h, the reaction mixture was cooled to room temperature and the thick black mixture was filtered, washing the solid with about 200 mL of ethanol. A small amount of product was extracted from the solid by suspending it in acetone, filtering, and concentrating the filtrate. The aqueous ethanol filtrate was continuously extracted with ether for 24 h. The

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combined ether extracts were dried over sodium sulfate and filtered, and the solvent was removed under reduced pressure to afford a black solid. The solid was loaded onto silica (10 g of crude product dissolved in acetone combined with 50 g silica and solvent removed under reduced pressure) and flash chromatographed (1:1 ethyl acetate–petroleum ether) to afford 5.87 g (4%) of 2,6-diaminopyridine-3,5-dicarboxaldehyde as a yellow powder: mp 294 °C dec (lit.[16] 295 °C dec). Further elution with ethyl acetate afforded 27.0 g (26%) of **4** as a bright yellow powder: mp 158.5–159.5 °C; ^{1}H NMR (DMSO-d_6) δ 9.30 (s, 1H, CHO), 7.91 (br s, 1 H, NH), 7.44 (d, $J_{4,5}$ = 8.5, 1 H, H-4), 6.90 (br s, 1 H, NH), 6.78 (br s, 2 H, NH_2), 5.81 (d, $J_{4,5}$ = 8.5, 1 H, H-5); ^{13}C NMR (DMSO-d_6) δ 187.8, 162.4, 160.1, 144.2, 104.5, 98.5; IR (Nujol) 3451, 3353, 1611; MS (EI, 70 eV) m/z 137 (M^+, 100). An analytical sample was prepared by crystallization from ethyl acetate–petroleum ether (yellow needles). Anal. Calcd for $C_6H_7N_3O$: C, 52.55; H, 5.14; N, 30.64. Found: C, 52.55; H, 5.13; N, 30.61.

2,6-Bis(pivaloylamino)pyridine (6). To an ice-cooled solution of 30 g (0.28 mol) of 2,6-diaminopyridine and 68 g (0.66 mol) of triethylamine in 300 mL of CH_2Cl_2 was added dropwise a solution of 73 g (0.60 mol) of pivaloyl chloride in 100 mL of CH_2Cl_2. The reaction was stirred for 6 h at 0 °C and quenched with 50 mL of water. The organic layer was separated, washed with 20 mL of a 5% aqueous solution of sodium bicarbonate, dried over magnesium sulfate, and evaporated under reduced pressure. The crude solid was recrystallized from ethyl acetate–hexane or cyclohexane to afford 73 g (94%) of **6** as a white solid: mp 110 °C; ^{1}H NMR δ 7.92 (d, J = 8.1, 2H, H-3, H-5), 7.73 (br s, 2H, NH), 7.69 (t, J = 8.1, 1H, H-4), 1.37 (s, 18H, CH_3); ^{13}C NMR δ 176.7, 149.5, 140.7, 109.2, 39.7, 27.4; IR (Nujol) 3424, 3303, 1682, 1661; MS (EI, 70 eV) m/z 277 (M^+, 100). Anal. Calcd for $C_{15}H_{23}N_3O_2$: C, 64.96; H, 8.36; N, 15.15. Found: C, 64.95; H, 8.40; N, 15.13.

2,6-Diaminopyridine-3-carboxaldehyde (4). Method B. To a solution of 2 g (7.2 mmol) of **6** in 25 mL of THF cooled to 0 °C (−78 °C on larger scale) was added dropwise 15.8 mL (25 mmol) of a 1.6 M solution of *n*-butyllithium in hexane, maintaining the temperature below 10 °C. The resulting yellow solution was left overnight at 0–5 °C (white precipitate formed) and quenched with a solution of 1.7 g (14.4 mmol) of *N*-formylmorpholine in 10 mL of THF. The mixture was warmed to room temperature, poured into water, and extracted three times with ether. The combined ether layers were washed with a saturated aqueous solution of sodium chloride, dried over magnesium sulfate, and evaporated under reduced pressure to afford 2,6-bis(dipivaloylamino)pyridine-3-carboxaldehyde with 90–95% purity: ^{1}H NMR δ 11.44 (br s, 1H, NH), 9.77 (s, 1H, CHO), 9.42 (br s, 1H, NH), 8.13 (d, $J_{4,5}$ = 8.5, 1H, H-4), 7.95 (d, $J_{4,5}$ = 8.5, 1H, H-5), 1.33 (s, 9H, CH_3), 1.30 (s, 9H, CH_3); MS (EI, 70 eV) m/z 305 (M^+, 100). The crude material was dissolved in 30 mL of a 2 N aqueous solution of potassium hydroxide and heated under nitrogen to 100 °C for 5 h. The reaction was cooled in an ice bath and extracted with CH_2Cl_2 (4 × 50 mL). The combined organic layers were dried over magnesium sulfate and evaporated to dryness, and the residue was recrystallized from ethyl acetate–hexane to afford 0.71 g (71%) of **4** as a light-yellow solid. The physical properties of this material were identical to those obtained from method A.

2-Amino-6-(octanoylamino)pyridine-3-carboxaldehyde (5). A mixture of 4.0 g (29 mmol) of **4**, 8.0 g (29 mmol) of octanoic anhydride, and 100 mL of toluene was heated to reflux for 26 h. The reaction mixture was cooled to room temperature and toluene was removed under reduced pressure. The residue was flash chromatographed (17% ethyl acetate–petroleum ether) to afford 5.32 g (69%) of **5** as a bright yellow powder: mp 122–125 °C; ^{1}H NMR δ 9.70 (s, 1H, CHO), 8.31 (br s, 1H, NH), 7.78 (d, $J_{4,5}$ = 8.4, 1H, H-4), 7.64 (d, $J_{4,5}$ = 8.4, 1H, H-5), 6.6 (v br s, 2H, NH_2), 2.36 (t, J = 7.5, 2H, $COCH_2$), 1.67 (m, 2H, $COCH_2CH_2$), 1.28 (m, 8H, CH_2), 0.85 (m, 3H, CH_3); ^{13}C NMR δ 190.7, 172.3, 157.8, 156.7, 146.8, 111.0, 102.9, 37.8, 31.6, 29.1, 28.9, 25.1, 22.5, 14.0; IR ($CHCl_3$) 3497, 3413, 3355, 1705, 1665; MS (EI, 70 eV) m/z 263 (M^+, 11), 137 (100). Anal. Calcd for $C_{14}H_{21}N_3O_2$: C, 63.85; H, 8.04; N, 15.96. Found: C, 63.95; H, 8.04; N, 15.91.

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Ethyl 7-Amino-2-methyl-1,8-naphthyridine-3-carboxylate (7). A mixture of 3.0 g (22 mmol) of **4**, 5.6 mL (44 mmol) of ethyl acetoacetate, 44 mL of absolute ethanol, and 0.6 mL (6.1 mmol) of piperidine was heated to reflux. After 61 h, 1.4 mL (14 mmol) of piperidine was added to the homogenous mixture. After an additional 47 h, 2.8 mL (22 mmol) of ethyl acetoacetate and 1 mL piperidine were added. After a total reaction time of 7 days, the reaction mixture was cooled to room temperature and placed in the freezer (−25 °C) overnight. The yellow precipitate and brown crystals were collected by filtration, washed with cold ethanol, and vacuum-dried to afford 4.05 g (80%) of **7**: mp 240–243 °C; ^{1}H NMR δ 8.54 (s, 1 H, H-4), 7.89 (d, $J_{6,7}$ = 8.7, 1H, H-6), 6.74 (d, $J_{6,7}$ = 8.7, 1H, H-7), 5.19 (br s, 2H, NH_2), 4.40 (q, J = 7.1, 2H, CO_2CH_2), 2.96 (s, 3H, 2-CH_3), 1.43 (t, J = 7.1, 3H, $CO_2CH_2CH_3$); ^{13}C NMR (DMSO-d_6) δ 166.1, 162.6, 160.7, 157.9, 139.8, 138.4, 118.5, 114.3, 113.7, 60.8, 25.9, 14.5; IR ($CHCl_3$) 3413, 1715; MS (EI, 70 eV) m/z 231 (M^+, 100). Anal. Calcd for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.45; H, 5.76; N, 18.00.

Ethyl 7-Amino-3-carbethoxy-1,8-naphthyridine-2-acetate (8). A mixture of 100 mg (0.73 mmol) of **4**, 230 μL (1.14 mmol) of diethyl acetone-1,3-dicarboxylate, 3.0 mL of absolute ethanol, and 7 drops of piperidine was heated at reflux for 80 h. An additional 120 μL (0.59 mmol) of diethyl acetone-1,3-dicarboxylate was added, the reaction mixture refluxed for an additional 63 h, and cooled in the freezer (−25 °C) for 20 h. The yellow precipitate was collected and washed with cold ethanol to afford 58 mg of **8**. A second crop provided 20 mg of **8** (combined yield, 35%): mp 180–183 °C; ^{1}H NMR (DMSO-d_6) δ 8.60 (s, 1H, H-4), 8.05 (d, $J_{5,6}$ = 8.3, 1H, H-5), 7.22 (br s, 2H, NH_2), 6.83 (d, $J_{5,6}$ = 8.8, 1H, H-6), 4.26 (q, J = 7.1, 2H, $ArCO_2CH_2$), 4.16 (s, 2H, $ArCH_2$), 4.05 (q, J = 7.1, 2H, $CH_2CO_2CH_2$), 1.30 (t, J = 7.9, 3H, $ArCO_2CH_2CH_3$), 1.15 (t, J = 7.0, 3H, $CH_2CO_2CH_2CH_3$); ^{13}C (DMSO-d_6) δ 170.3, 165.5, 162.5, 157.7, 156.7, 139.8, 138.1, 118.3, 114.8, 114.1, 60.8, 60.2, 44.3, 14.6, 14.1; IR ($CHCl_3$) 3413, 1723; MS (EI, 70 eV) m/z 303 (M^+, 35), 159 (100). Anal. Calcd for $C_{15}H_{17}N_3O_4$: C, 59.40; H, 5.65; N, 13.85. Found: C, 59.37; H, 5.67; N, 13.83.

***N*-*tert*-Butyl-7-amino-3-(*tert*-butylcarbamoyl-1,8-naphthyridine-2-acetamide (9).** A mixture of 260 mg (1.86 mmol) of **4**, 710 mg (2.76 mmol) of *N,N'*-di-*tert*-butyl-3-oxoglutaramide, and 5 mL of absolute ethanol was heated to reflux and 6 drops of piperidine was added. After refluxing 24 h, an additional 1 equiv 470 mg (1.83 mmol) of glutaramide was added. After an additional 22 h the reaction was cooled to room temperature and the solvent was removed under reduced pressure. The residue was flash chromatographed (5% CH_3OH–CH_2Cl_2) to afford 260 mg (40%; 50% based on recovered **4**) of **9** as an off-white solid: mp 270-272 °C; ^{1}H NMR (DMSO-d_6) δ 8.68 (s, 1H, NH), 8.10 (s, 1H, NH), 8.10 (s, 1H, H-4), 7.94 (d, $J_{5,6}$ = 8.8, 1H, H-5), 6.90 (br s, 2H, NH_2), 6.79 (d, $J_{5,6}$ = 8.8, 1H, H-6), 3.84 (s, 2H, CH_2), 1.36 (s, 9H, *tert*-Bu), 1.25 (s, 9H, *tert*-Bu); ^{13}C NMR (DMSO-d_6) δ 169.7, 167.1, 161.4, 156.2, 155.1, 137.5, 136.9, 127.9, 114.6, 113.5, 50.8, 50.4, 44.0, 28.6, 28.5; IR ($CHCl_3$) 3414, 3320, 3258, 1647; MS (FD) m/z 357. Anal. Calcd for $C_{19}H_{27}N_5O_2$: C, 63.84; H, 7.61; N, 19.59. Found: C, 63.87; H 7.61; N, 19.42.

7-Amino-3-carbethoxy-1,8-naphthyridin-2(1*H*)-one (10). A mixture of 1.0 g (7.3 mmol) of **4**, 11 mL (73 mmol) of diethyl malonate, 3 mL (30 mmol) of piperidine, and 25 mL of absolute ethanol was heated to reflux. After 24 h the mixture was filtered and the solid washed with ethanol to afford 1.43 g of product. The filtrate was refluxed for an additional 31 h and an additional 110 mg of product was collected to give a total of 1.54 g (91%) of **10** as a yellow powder: mp > 350 °C; ^{1}H NMR (DMSO-d_6) δ 11.66 (br s, 1H, NH), 8.29 (s, 1H, H-4), 7.74 (d, $J_{5,6}$ = 8.6, 1H, H-5), 7.15 (br s, 2H, NH_2), 6.64 (d, $J_{5,6}$ = 8.6, 1H, H-6), 4.18 (q, J = 7.0, 2H, CH_2), 1.25 (t, J = 7.0, 3H, CH_3); MS (EI, 70 eV) 233 (M^+, 22); MS (EI, 70 eV) m/z 233 (M^+, 22), 161 (100); Anal. Calcd for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.75; N, 18.02. Found: C, 56.57; H, 4.76; N, 17.89.

7-(Acetylamino)-3-carbethoxy-1,8-naphthyridin-(1*H*)2-one (11). To a suspension of 3.0 g (12.9 mmol) of **10** in 20 mL of acetic anhydride was added 5 mL of triethylamine. The suspension was heated at reflux for 14 h, cooled to room temperature, filtered, and washed with diethyl ether to afford 3.1 g (88%) of **11** as a yellow solid: mp > 350 °C; ^{1}H NMR (DMSO-d_6) δ 12.18 (br s, 1H, NH), 10.70 (br s, 1H, NH), 8.42 (s,

1H, H-4), 8.17 (d, $J_{5,6}$ = 8.6, 1H, H-5), 7.93 (d, $J_{5,6}$ = 8.6, 1H, H-6), 4.25 (q, J = 7.1, 2H, CH_2), 1.26 (t, J = 7.1, 3H, CH_3); MS (EI, 70eV) m/z 275 (M^+, 18). Anal. Calcd for $C_{13}H_{13}N_3O_4$: C, 56.73; H, 4.76; N, 15.27. Found: C, 56.92; H, 4.70; N, 14.89.

Ethyl 7-(Acetylamino)-2-chloro-1,8-naphthyridine-3-carboxylate (12). A mixture of 10 mL of phosphorus oxychloride and 1.85 g (6.7 mmol) of 11 was heated at reflux for 13 h. The excess phosphorus oxychloride was removed under reduced pressure and ice-water was carefully added to the mixture. The black precipitate was collected, dried, and flash chromatographed (2% CH_3OH–CH_2Cl_2) to afford 1.1 g (57%) of 12 as yellow solid: mp > 300 °C; ^1H NMR δ 8.85 (br s, 1H, NH), 8.65 (s, 1H, H-4), 8.61 (d, $J_{5,6}$ = 8.9, 1H, H-5), 8.27 (d, $J_{5,6}$ = 8.9, 1H, H-6), 4.47 (q, J = 7.2, 2H, CH_2), 1.45 (t, J = 7.2, 3H, CH_3); MS (EI, 70 eV) m/z 293 (M^+, 22). Anal. Calcd for $C_{13}H_{12}N_3O_3Cl$: C, 53.16; H, 4.12; N, 14.31; Cl, 12.07. Found: C, 52.82; H, 4.07; N, 14.68; Cl, 12.06.

2,3:7,6-Bis(6′,7′-(2′-(octanoylamino)[1,8]naphthyridino))-tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undecane (13). A mixture of 1.10 g (6.24 mmol) of tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undecane-2,7-dione (14), 1.85 g (13.5 mmol) of 4, 60 mL of toluene, 4 mL of absolute ethanol, and 3.4 mL of a 20% methanolic solution of potassium hydroxide was refluxed for 24 h with azeotropic removal of water (Dean–Stark with 4-Å molecular sieves). The mixture was cooled to room temperature and filtered to afford 1.07 g of a reddish-brown solid. The solid was heated with 5 mL of octanoic anhydride to 115 °C (external temperature) for 12 h. The volatiles were removed by Kugelrohr distillation, and the resulting brown solid was flash chromatographed (2% CH_3OH–chloroform) to afford 267 mg (21%) of 13 as an off-white solid: mp 264–266 °C; ^1H NMR δ 8.34 (d, $J_{3',4'}$ = 8.6, 2 H, H-4′), 7.86 (br d, 2 H, H-3′), 7.43 (br s, 2 H, H-5′), 3.63 (br d, 4 H, H-1, H-4, H-5, H-8), 2.05–2.28 (m, 6 H, H-9, H-11, H-2″), 1.30–1.45 (br d, 2 H, H-10), 0.75–1.28 (br m, 26 H, H-3″, H-4″, H-5″, H-6″, H-7″, H-8″); ^{13}C NMR δ 173.1, 138.7, 138.5, 129.2, 118.2, 115.6, 59.4, 53.3, 49.0, 36.9, 35.7, 31.6, 29.1, 28.6, 25.0, 22.5, 14.0; IR (Nujol) 3190, 1700; MS (EI, 70 eV) m/z 630 (15, M^+), 378 (57), 196 (100); HRMS calcd for $C_{39}H_{46}N_6O_2$ 630.3682, found 630.3686.

3,10-Bis(octanoylamino)-6,7-dihydrodipyrido[3,2-*b*:2′,3′-*j*]-[4,7]phenanthroline (16). A mixture of 500 mg (1.9 mmol) of 6, 142 mg (1.3 mmol) of 1,4-cyclohexanedione, 15 mL of absolute ethanol, and 1.0 mL (10 mmol) of piperidine was heated to reflux for 11 h. The reaction was cooled to room temperature and placed in a freezer (−25 °C) for 12 h. The yellow precipitate was collected, washed with cold ethanol, and air-dried to afford 227 mg (21%) of 14 as a yellow powder: mp 292–295 °C; ^1H NMR δ 8.58 (br s, 2H, NH_2), 8.57 (d, $J_{1,2}$ = 9.0, 2H, H-1, H-12), 8.49 (s, 2H, H-13, H-14), 8.25 (d, $J_{1,2}$ = 9.0, 2H, H-2, H-11), 3.49 (s, 4H, H-6, H-7), 2.49 (t, J = 7.5, 4H, $COCH_2$), 1.78 (m, 4H, $COCH_2CH_2$), 1.28 (m, 16H, CH_2), 0.87 (t, J = 6.7, 6H, CH_3); ^{13}C NMR δ 172.5, 162.4, 154.3, 153.8, 139.2, 130.9, 125.9, 119.8, 115.1, 38.0, 32.5, 31.6, 29.1, 29.0, 25.3, 22.6, 14.1; MS (FD) m/z 566. Anal. Calcd for $C_{34}H_{42}N_6O_2$: C, 72.06; H, 7.47, N, 14.83. Found: C, 72.04; H, 7.53; N, 14.72.

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Supplementary Material Available: Copy of ^1H NMR for 13 (1 page). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.