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Synthesis of the G−C DNA Base Hybrid with a Functional Tail

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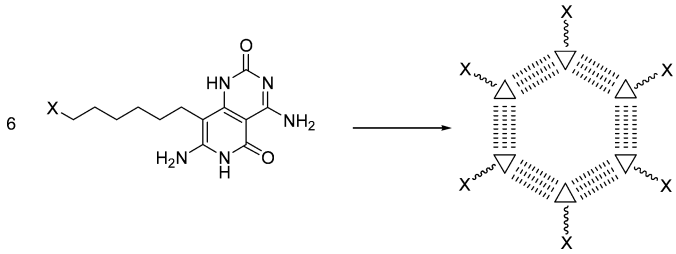
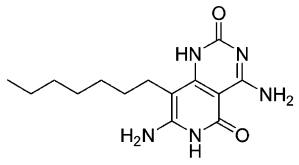


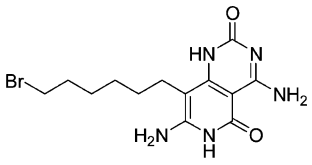
Molecules which possess the hydrogen bonding codes of both guanine and cytosine ("G−C DNA base hybrids") are known to organize in a hexagonal array both in solution and the solid state. Including an easily derivatizable functional group in the molecule allows the co-organization of virtually any species in the hexagonal periphery. Simple 5- and 6-step procedures are described for the synthesis of DNA base hybrids with tail groups which are terminated by electrophilic (primary bromide) and nucleophilic (primary alcohol) functions, respectively.

Introduction

The G−C DNA base hybrid **1** has been shown to be an efficient and unambiguous means of generating hexagonal order on the molecular scale.[1] This is accomplished by the pairing of reciprocal, asymmetric G−C hydrogen-bonding codes (i.e., DDA−AAD) which permit no ambiguity in the recognition process and confer an overall greater thermodynamic stability to the assembly than the popular C_n-symmetric *s*-triazine or pyrimidine-based H-bonding heterocycles.[2] As it stands, base hybrid **1** has a solubilizing hydrocarbon tail, which is of course a functional dead end. The validation of this work as a method of actually organizing something besides the bicycle itself in a hexameric array has awaited the means to connect species to it, most conveniently via the tail, which would then be co-organized in the hexagonal periphery. We now describe a simple approach to tail-functionalized G-C base hybrid modules **2** and **3**, which may be applied to the hexagonal self-assembly of virtually anything which can be chemically linked to their tail-functions.



1



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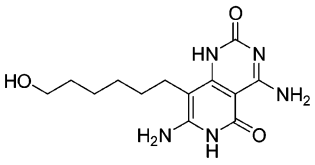

3

Why hexagonal self-assembly? Hexagonal order is an important functional principle in nature. Both peptides and nucleosides may be found in hexameric bundles, the former in transbilayer pores[3] and various enzymes,[4−6] the latter, for

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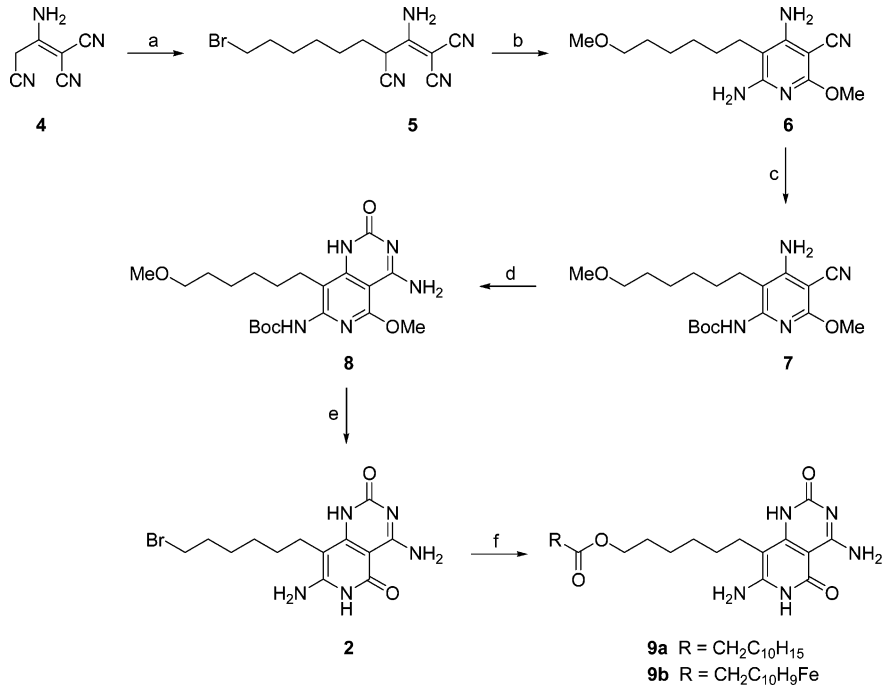
SCHEME 1 [a]



[a] Reagents and conditions: (a) $Br(CH_2)_6Br$, DIPEA, $Bu_4N^+I^-$, DME, 85 °C, 20 h (72%); (b) NaOMe, MeOH, 65 °C, 48 h (72%); (c) LHMDS, Boc_2O, THF, −78 °C → rt, 2 h (93%); (d) ClCONCO, CH_2Cl_2, 1 h then NaOMe, MeOH, 2 h (66%); (e) 33% HBr−AcOH, reflux, 4 h (69%); (f) RCO_2Na, DMF, 120 °C, 18 h.

example, in viral pRNA assembled via six tetrads of A−U, C−G, G−C, C−G interactions.[7] Novel synthetic materials which can function as multielectron redox systems have also been produced which incorporate electrochemically active porphine,[8] tetrathiafulvalene,[9] ferrocene,[10] and C_{60}[11] substituents in discrete hexameric arrays, although these systems typically employ covalent synthesis to achieve the desired order. Some applications of non-natural hexagonal self-assembly to specific purposes have been reported, perhaps the best known example being Zimmerman's isophthalic acid dendrimer.[12] Lehn has made use of rosette-forming barbituric acid−melamine subunit partners to organize porphyrins[13] and metallocrowns[14] noncovalently, but the resulting array is trigonal due to the A_3B_3 nature of the assembly. More recently, Fenniri has described G−C hybrid-type bicycles with extra-annular chiral substituents which cause the hexamers to stack with helical screw sense.[15] Although these molecules also represent tail-substituted base hybrid systems, their 14-step preparation from barbituric acid leaves substantial room for an improved synthetic approach. Other known DDA−AAD hybrid systems[16,17] introduce tail groups (for solubilizing purposes) early in the course of a multistep synthesis. This methodology, however, limits the nature of the appendage to those which can withstand the reaction conditions en route to the product and which are indifferent to inevitable material losses.

The aggregate $\mathbf{1}_6$ is a closed array, and although discrete organizational states are relevant to certain applications, current materials technologies make extensive use of open hexagonal phases and networks, such as can be achieved using subunits with trigonally disposed coordination sites.[18] Molecules such as **2** and **3** thus also represent a step toward the eventual merger of hexagonal supermacrocycles through their tails, thereby opening up additional dimensions for the propagation of such assemblies.

Results and Discussion

The starting material for the synthesis of base hybrid **2** is the commercially available malononitrile dimer **4** (Scheme 1). Alkylation with inexpensive 1,6-dibromohexane proceeds in a satisfactory manner in the presence of a ca. 2-fold excess of alkylating agent to give bromide **5**. Reaction of **5** with sodium methoxide not only effects cyclization to the persubstituted

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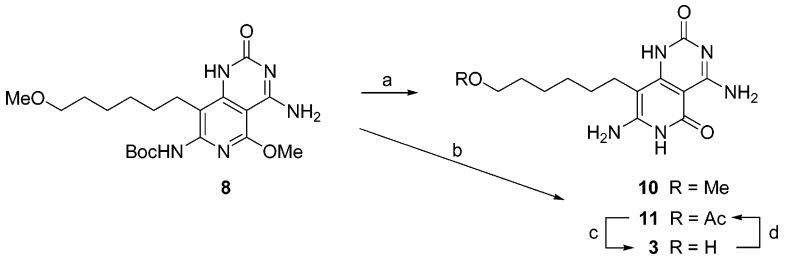
SCHEME 2 [a]



[a] Reagents and conditions: (a) Me_3SiCl, NaI, MeCN, 82 °C, 2 h (88%); (b) 33% HBr−AcOH, 4 h (92%); (c) 9 M NH_3−MeOH, 4 d (92%); (d) AcOH, DCC, DMAP, DMF, 12 h (73%).

pyridine but also results in nucleophilic substitution of the primary bromide to give **6**. Boc-protection of the more reactive 6-amino group provides **7**, the annulation of which with chlorocarbonyl isocyanate followed by basic workup gives bicycle **8**. Reaction of **8** with refluxing HBr in acetic acid simultaneously removes the Boc group, unmasks the pyridone carbonyl function, and reconverts the terminal methyl ether of the tail group into bromide to give tail-functionalized base hybrid **2** in good yield.

Compound **2** represents a versatile functional module for supermacrocycle synthesis, a platform for generating hexagonal order in both solution and the solid state. It is derivatized by the action of nucleophiles. To demonstrate this, we chose to prepare ester-terminated hybrids **9a** and **9b** by reaction of **2** with the sodium salts of adamantane acetic acid and ferrocene acetic acid, respectively (Scheme 1). The assembly of the latter bears some likeness to covalently[10,19−21] and noncovalently[22] synthesized cyclic polymetallocene aggregates.

Hybrid **3**, which can be derivatized by the action of electrophiles, could be prepared by modifying the reaction conditions in the deprotection of **8**. Interestingly, treatment with in situ generated TMS iodide, which was originally used in the synthesis of **1**, cleaved the Boc protecting group and the aromatic methyl ether but had no effect on the OMe group of the chain (Scheme 2). However, treatment of **8** with HBr in acetic acid under mild conditions (room temperature) led to acetate **11**, which could be cleaved with methanolic ammonia to **3**. That the acylation of **3** would be selective for the hydroxyl group in the presence of the amino functions of the bicyclic core was demonstrated by reaction with acetic acid in the presence of DCC, which gave back the precursor **11** in good yield.

Although the aggregation of hexameric subunits closely related to **1**−**3** (i.e., with DDA−AAD hydrogen bonding faces) has been extensively studied in solution,[15−17] the only DNA base hybrid to be characterized crystallographically is **1**.[1] In this case, the unusually large unit cell ($V > 10^5$ Å^3) necessitated the collection of data from a synchrotron radiation source. In this structure, the $\mathbf{1}_6$ hexamers overlapped each other to describe a highly porous solid with an interwoven network of channels. We had speculated that the inclusion of polar functions and/or large terminal substituents in the tail group of the base hybrid might alter the crystal packing. Dissolution of these molecules in hot DMSO followed by slow cooling to room temperature results in well-defined crystals of cubic habit which, like those of **1**, do not extinguish plane polarized light and do not diffract sufficiently using a molybdenum X-ray source. These results suggests either the new base hybrids are crystallographically isostructural to **1** or that the crystals suffer from substantial disorder.

Conclusion

Although other H-bonding subunits capable of producing hexagonal order on the molecular scale have been described,[15−17] none have been designed for simple derivatization to allow the co-organization of functional species in the hexagonal periphery. The updating of the design of the G−C base hybrid **1** to include functionality in the tail which can be derivatized in the final step of a concise, straightforward synthesis now provides a practical basis for the exploitation of this organizational principle. Applications will be found wherever hexagonal states of aggregation impart novel properties or function, whether in solution or the solid state. New derivatives of **2** and **3** are being prepared (work in progress) whose properties will be reported elsewhere.

Experimental Section

3-Amino-4-(6-bromohexyl)-2-cyanopent-2-enedinitrile (5). To a solution of **4** (5.00 g, 37.8 mmol) in DME (100 mL) was added diisopropylethylamine (13.8 mL, 10.2 g, 79.2 mmol). After the solution was stirred for 1 h, 1,6-dibromohexane (28.9 mL, 45.8 g, 188 mmol) and tetrabutylammonium iodide (0.500 g, 1.35 mmol) were added. The mixture was heated at reflux with light excluded for 20 h and then cooled to room temperature. Stirring was continued for 1 h, and the precipitated ammonium salts were removed by filtration and washed with ethyl acetate (×3). The organic fractions were combined and the solvents evaporated. The black residue was partitioned between aqueous hydrochloric acid (0.5 M, 500 mL) and methylene chloride (250 mL). The aqueous phase was extracted with additional methylene chloride (×3), the combined organic extracts were dried, and the solvent was evaporated to leave a dark brown oil. Chromatography (30% ethyl acetate/hexanes) gave **5** as a yellow solid (8.02 g, 72%): mp 35−36 °C (from MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40−1.62 (m, 6H), 1.88 (quintet, J = 7.0 Hz, 2H), 1.94−2.06 (m, 2H), 3.43 (t, J = 6.7 Hz, 2H), 3.98 (t, J = 6.3 Hz, 1H,), 6.92 (1H, bs), 7.07 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.4, 27.3, 27.4, 32.1, 32.2, 33.6, 35.4, 53.5, 112.9, 113.4, 115.9, 167.9; HRMS (EI) calcd for $C_{12}H_{15}N_4Br$ m/z 294.0480, found m/z 294.0489.

4,6-Diamino-3-cyano-2-methoxy-5-(6-methoxyhexyl)pyridine (6). Compound **5** (0.500 g, 1.69 mmol) was added to a solution

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of sodium methoxide prepared from sodium metal (0.242 g, 10.5 mmol) and methanol (15 mL). The resulting solution was heated at reflux for 48 h. The solvent was evaporated and the residue partitioned between pH 7 aq phosphate buffer (0.4 M, 20 mL) and methylene chloride (20 mL). The aqueous phase was extracted with additional methylene chloride (×4). The combined organic fractions were dried, and the solvent was evaporated to leave an orange oil. Chromatography (40% ethyl acetate/hexanes) gave **6** as a white solid (0.338 g, 72%): mp 113−114 °C (from MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (m, 4H), 1.48 (m, 2H), 1.57 (m, 2H), 2.25 (t, J = 7.8 Hz, 2H), 3.32 (s, 3H), 3.37 (t, J = 6.3 Hz, 2H), 3.86 (s, 3H), 4.60 (s, 2H), 4.66 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4, 25.9, 27.1, 29.37, 29.43, 53.5, 58.5, 71.5, 72.6, 94.4, 116.6, 155.1, 157.1, 163.8. Anal. Calcd for $C_{14}H_{22}N_4O_2$: C, 60.4; H, 8.0; N, 20.1. Found: C, 60.3; H, 7.8; N, 20.0.

4-Amino-6-(*tert*-butyloxycarbonylamino)-3-cyano-2-methoxy-5-(6-methoxyhexyl)pyridine (7). Di-*tert*-butyl dicarbonate (4.00 g, 18.3 mmol) was added to a solution of **6** (4.50 g, 16.2 mmol) in dry THF (170 mL) at −78 °C. After the solution was stirred for 15 min, a solution of lithium hexamethyldisilazide in THF (1.0 M, 40.0 mL, 40.0 mmol) was quickly added. The reaction mixture was allowed to come to room temperature over 1 h and then stirred for an additional 1 h. The solvent was evaporated, and the residue was partitioned between pH 7 aq phosphate buffer (0.4 M, 500 mL) and methylene chloride (250 mL). The aqueous layer was extracted with additional methylene chloride (×5), and the organic fractions were combined and dried. Evaporation of the solvent gave an orange oil. Chromatography (5% methanol/methylene chloride) gave **7** as a white solid (5.72 g, 93%): mp 113−114 °C (from MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (m, 6H), 1.48 (s, 9H), 1.55 (m, 2H), 2.38, (t, J = 7.9 Hz, 2H), 3.30 (s, 3H), 3.35 (t, J = 6.4 Hz, 2H), 3.91, (s, 3H), 4.96 (s, 2H), 6.51 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.1, 25.7, 27.1, 28.2, 29.29, 29.33, 53.9, 58.5, 72.6, 76.8, 81.1, 105.7, 115.1, 149.2, 152.2, 156.8, 162.7; MS (ESI) *m*/*z* 379 (100, M + 1); HRMS (ESI) calcd for $C_{19}H_{31}N_4O_4$ (M + 1) *m*/*z* 379.2345, found *m*/*z* 379.2346.

4-Amino-7-(*tert*-butyloxycarbonylamino)-5-methoxy-8-(6-methoxyhexyl)-1*H*-pyrido[4,3-*d*]pyrimidin-2-one (8). To a solution of **7** (4.50 g, 11.9 mmol) in dry methylene chloride (400 mL) was added *N*-(chlorocarbonyl) isocyanate (3.63 mL, 4.76 g, 45.1 mmol), and the reaction was stirred at room temperature for 70 min. Saturated aq sodium bicarbonate (47 mL) was added, and the resulting mixture was then poured into saturated brine (400 mL). The layers were separated, and the aqueous layer was washed with a 5% isopropyl alcohol/chloroform mixture (×4). The organic fractions were combined and dried, and the solvent was evaporated. The residue was dissolved in dry methanol (280 mL), and a solution of sodium methoxide prepared from sodium (2.30 g, 100 mmol) and methanol (200 mL) was added. The mixture was stirred at room temperature for 2 h. The solvent was evaporated, and the residue was partitioned between pH 7 aq phosphate buffer (0.4 M, 800 mL) and methylene chloride (400 mL). The layers were separated, and the aqueous layer was extracted with methylene chloride (×4). The organic fractions were combined and dried, and the solvent was evaporated to give a yellow solid. Chromatography (10% methanol/methylene chloride) gave **8** as a white solid (3.29 g, 66%): mp 215−216 °C dec (from MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.15 (br s, 6H), 1.31 (br s, 11H), 2.37 (s, 2H), 3.06, (s, 3H), 3.14 (t, J = 6.5 Hz, 3H), 3.95 (s, 3H), 7.49 (s, 1H), 7.91 (br s, 1H), 9.00 (s, 1H), 10.16 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.2, 25.6, 28.0, 28.2, 28.4, 29.0, 53.9, 57.8, 71.9, 79.1, 90.2, 110.0, 149.0, 150.9, 153.1, 155.9, 157.7, 162.6; MS (ESI) *m*/*z* 422 (100, M + 1); HRMS (ESI) calcd for $C_{20}H_{32}N_5O_5$ (M + 1) *m*/*z* 422.2403, found *m*/*z* 422.2399.

4,7-Diamino-8-(6-bromohexyl)-1*H*,6*H*-pyrido[4,3-*d*]pyrimidine-2,5-dione (2). A solution of **8** (0.500 g, 1.19 mmol) in 33% HBr−HOAc (25 mL) was heated at reflux for 4 h and then carefully poured into a mixture of saturated aq sodium bicarbonate (300 mL) and ethyl acetate (50 mL). The resulting precipitate was filtered and washed with water (×3) and ethyl acetate (×3). The combined filtrate and washings were separated, and the aqueous layer was extracted with ethyl acetate (×2). The combined organic fraction was dried, and the solvent was evaporated. The residue was combined with the solid from the filtration, and the mixture was chromatographed (20% methanol/methylene chloride) to give **2** as a tan solid (0.290 g, 69%): mp 170−171 °C dec (from DMSO); ^{1}H NMR (400 MHz, d_6-DMSO) δ 1.24 (m, 2H), 1.30 (m, 4H), 1.53 (quintet, J = 6.6 Hz, 2H), 2.35 (t, J = 6.3, 2H), 3.51 (t, J = 7.2 Hz, 2H), 6.51 (s, 2H), 7.58 (s, 1H), 8.71 (s, 1H), 9.73 (s, 1H), 10.93 (s, 1H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 21.2, 27.4, 27.7, 28.1, 32.3, 35.3, 85.0, 86.5, 151.8, 152.0, 157.0, 161.2, 164.7; MS (ESI) *m*/*z* 356 (85, M + 1).

Adamantan-1-ylacetic Acid 6-(4,7-Diamino-1*H*,6*H*-pyrido[4,3-*d*]pyrimidine-2,5-dion-8-yl) Hexyl Ester (9a). A solution of **2** (0.100 g, 0.281 mmol) and the sodium salt of adamantane-1-acetic acid (0.0670 g, 0.310 mmol) in DMF (20 mL) was heated at 120 °C for 18 h. The solvent was evaporated, and the brown solid residue was washed with water (×3) and ethyl acetate (×3). The crude product was recrystallized from DMSO to give **9a** as a white solid (0.113 g, 86%): mp 181−182 °C dec (from DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.30−1.40 (m, 8H), 1.52−1.60 (m, 12H), 1.88 (m, 2H), 1.97 (s, 3H), 2.35 (t, J = 6.4 Hz, 2H), 3.96 (t, J = 6.8 Hz, 2H), 6.40 (s, 2H), 7.40 (s, 1H), 8.69 (s, 1H), 9.66 (s, 1H), 10.72 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.9, 26.2, 28.7, 28.9, 29.0, 29.1, 32.7, 37.0, 42.5, 49.0, 63.2, 87.2, 87.4, 151.7, 153.4, 156.9, 161.0, 165.2, 171.8; MS (ESI) *m*/*z* 470 (100, M + 1); HRMS (ESI) calcd for $C_{25}H_{36}N_5O_4$ (M + 1) *m*/*z* 470.2767, found *m*/*z* 470.2761.

Ferrocenylacetic Acid 6-(4,7-Diamino-1*H*,6*H*-pyrido[4,3-*d*]-pyrimidine-2,5-dion-8-yl) Hexyl Ester (9b). A solution of **2** (0.100 g, 0.281 mmol) and the sodium salt of ferrocene acetic acid (0.0747 g, 0.281 mmol) in DMF (20 mL) was heated at 120 °C for 16 h. The solvent was evaporated, and the brown solid residue was washed with water (×3) and ethyl acetate (×3). The crude product was suspended in DMSO (10 mL), and the mixture was heated to reflux and filtered hot. The solvent was evaporated, and the resulting solid was recrystallized from DMSO to give **9b** as a brown solid (0.113 g, 78%): mp 215−216 °C dec (from DMSO); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.28 (m, 6H), 1.51 (m, 2H), 2.33 (m, 2H), 3.13 (s, 2H), 3.98 (t, J = 6.6 Hz, 2H), 4.07 (s, 7H), 4.13 (s, 2H), 6.46 (s, 2H), 7.44 (s, 1H), 8.68 (s 1H), 9.66 (s, 1H), 10.83 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.8, 26.3, 28.6, 28.8, 28.9, 35.5, 64.5, 68.1, 69.2, 69.3, 81.2, 86.0, 86.6, 151.8, 153.0, 156.7, 161.0, 165.2, 171.1; MS (ESI) *m*/*z* 520 (53, M + 1); HRMS (ESI) calcd for $C_{25}H_{30}FeN_5O_4$ (M + 1) *m*/*z* 520.1647, found *m*/*z* 520.1643.

4,7-Diamino-8-(6-methoxyhexyl)-1*H*,6*H*-pyrido[4,3-*d*]pyrimidine-2,5-dione (10). To a solution of **8** (0.050 g, 0.12 mmol) in acetonitrile (25 mL) were added sodium iodide (0.135 g, 0.901 mmol) and chlorotrimethylsilane (0.075 mL, 0.064 g, 0.59 mmol). The flask was protected from light, and the mixture was heated at reflux for 2 h. The reaction was poured into pH 7 aq phosphate buffer (0.4 M, 50 mL). The layers were separated, and the aqueous phase was extracted with methylene chloride (×4). The organic fractions were combined and dried, and the solvent was evaporated to give a white solid. Chromatography (25% methanol/methylene chloride) gave **10** as a white solid (0.032 g, 88%): mp 164−165 °C dec (from DMSO); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.29 (m, 6H), 1.46 (m, 2H), 2.37 (t, J = 6.5 Hz, 2H), 3.19 (s, 3H), 3.28 (t, J = 7.2 Hz, 2H), 6.60 (s, 2H), 7.52 (s, 1H), 8.73 (s, 1H), 9.71 (s, 1H), 10.90 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.2, 25.9, 28.4, 29.2, 30.8, 57.8, 71.9, 85.2, 86.1, 151.3, 152.3, 156.4, 160.5, 164.7; MS (ESI) *m*/*z* 308 (100, M + 1), 615 (37, 2M + 1); HRMS (ESI) calcd for $C_{14}H_{22}N_5O_3$ (M + 1) *m*/*z* 308.1723, found *m*/*z* 308.1711.

4,7-Diamino-8-(6-acetoxyhexyl)-1*H*,6*H*-pyrido[4,3-*d*]pyrimidine-2,5-dione (11). A solution of **8** (0.600 g, 1.42 mmol) in 33% HBr−HOAc (25 mL) was stirred at room temperature for 4 h and then carefully poured into a mixture of saturated aq sodium

bicarbonate (300 mL) and ethyl acetate (50 mL). The resulting precipitate was filtered and washed with water (×3) and ethyl acetate (×3). The solid was then recrystallized from DMSO to give **11** as a white solid (0.440 g, 92%): mp 178−179 °C dec (from DMSO); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.21−1.28 (m, 6H), 1.50 (m, 2H), 1.95, (s, 3H), 2.33 (t, J = 6.4 Hz, 2H), 3.93 (t, J = 6.5 Hz, 2H), 6.58 (s, 2H), 7.56 (s, 1H), 8.71 (s 1H), 9.72 (s, 1H), 10.94 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.8, 21.1, 25.6, 28.0, 28.2, 28.3, 63.9, 85.4, 85.8, 151.0, 152.4, 156.6, 160.4, 165.1, 170.5; MS (ESI) m/z 336 (100, M + 1), 671 (25, 2M + 1); HRMS (ESI) calcd for $C_{15}H_{22}N_5O_4$ (M + 1) m/z 336.1672, found m/z 336.1670.

4,7-Diamino-8-(6-hydroxyhexyl)-1*H*,6*H*-pyrido[4,3-*d*]pyrimidine-2,5-dione (3). A solution of **11** (0.100 g, 0.298 mmol) in 9 M NH_3 in methanol (50 mL) was stirred for 4 d. The solvent was evaporated, and the resulting solid was washed with water (×3) and methanol (×3). The crude product was recrystallized from DMSO to give **3** as a white solid (0.0808 g, 92%): mp 184−185 °C dec (from DMSO); ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.26 (m, 4H), 1.31 (m, 2H), 1.39 (quintet, J = 6.6 Hz, 2H), 2.37 (t, J = 6.3 Hz, 2H), 3.31 (m, 2H), 4.33 (t, J = 6.1 Hz, 1H), 6.47 (s, 2H), 7.49 (s, 1H), 8.71 (s, 1H), 9.69 (s, 1H), 10.84 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.9, 26.6, 29.0, 29.3, 33.5, 60.5, 86.1, 86.5, 151.2, 152.4, 156.5, 160.3, 164.9; MS (ESI) m/z 294 (100, M + 1), 587 (16, 2M + 1); HRMS (ESI) calcd for $C_{13}H_{20}N_5O_3$ (M + 1) m/z 294.1566, found m/z 294.1568.

11 from 3. A solution dicyclohexylcarbodiimide (0.0773 g, 0.375 mmol), 4-(dimethylamino)pyridine (8.0 mg, 0.065 mmol), and acetic acid (0.0195 mL, 0.0205 g, 0.341 mmol) in anhydrous DMF (10 mL) was stirred at room temperature for 10 min. A solution of **3** (0.100 g, 0.341 mmol) in anhydrous DMF (5 mL) was then added, and the reaction was stirred at room temperature for 12 h. The solvent was evaporated, and the resulting solid was chromatographed (25% methanol/methylene chloride) to give a white solid. The crude product was then recrystallized from DMSO to give **11** as a white solid (0.0833 g, 73%). The NMR spectra of this material were identical to those of an authentic sample of **11**.

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Supporting Information Available: High-field ^{1}H and ^{13}C NMR spectra for all new compounds (**2**, **3**, and **5**−**11**). This material is available free of charge via the Internet at http://pubs.acs.org.

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