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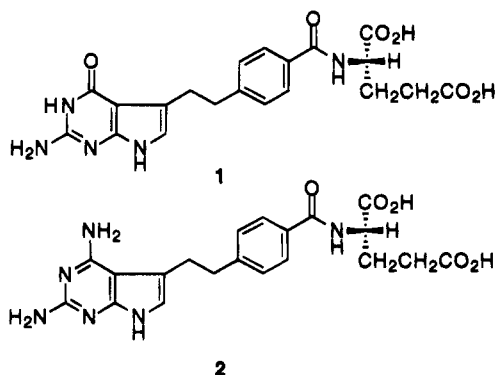
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Condensation of amidines with 2-amino-3-cyanofurans gives 2-substituted-4-aminopyrrolo[2,3-*d*]pyrimidines by a ring-opening, ring-recyclization sequence of reactions through which the starting furan 2-amino nitrogen becomes the pyrrole nitrogen of the final product and one of the amidine nitrogens becomes N-1 of the fused pyrimidine ring. 2,4-Diamino-5-[2-(4-carbethoxyphenyl)ethyl]pyrrolo[2,3-*d*]pyrimidine, a key intermediate in the synthesis of the DHFR inhibitor TNP-351, has been prepared in one step by reaction of ethyl 4-[2-(2-amino-3-cyanofuran-4-yl)ethyl]benzoate with guanidine.

There is intense current interest in pyrrolo[2,3-*d*]pyrimidines as folate antimetabolites. For example, *N*-{4-[2-(2-amino-3,4-dihydro-4-oxo-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)ethyl]benzoyl}-L-glutamic acid (LY231514, **1**) has been shown to be very efficiently converted intracellularly by the enzyme folylpolyglutamate synthetase (FPGS) to its polyglutamates, which then function as potent inhibitors of thymidylate synthase (TS) and thus block *de novo* DNA biosynthesis.¹ LY231514 exhibits potent *in vitro* and *in vivo* activity against a broad variety of solid tumors¹ and is now in phase II clinical trials. The corresponding 2,4-diamino derivative **2** (*N*-



{4-[2-(2,4-diamino-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)ethyl]benzoyl}-L-glutamic acid, TNP-351), prepared by Miwa and collaborators at Takeda Industries,² is representative of a new class of dihydrofolate reductase (DHFR) inhibitors which do not possess the 6-6 bicyclic system characteristic of the well-known pteridine and quinazoline

antifolates.³ Previous explorations by the Princeton/Lilly research groups of structure-activity requirements for TS inhibition have suggested that several of the inherent structural features of LY231514 appear to be mandatory for activity; these include the rigidity of the 6-5 fused ring system (open-chain versions are inactive), the positioning of the side chain at C-5 rather than C-6 (the latter is inactive),^{4a} and the hydrogen-bond-donating pyrrole NH grouping (the corresponding *N*-methyl derivative of LY231514 is inactive).^{4b} To explore the possible consequences of replacing the pyrrole NH by a hydrogen-bond-accepting oxygen atom, we attempted the preparation of furo[2,3-*d*]pyrimidine analogues of the above active antifolates LY231514 and TNP-351. The present paper describes the surprising results of this investigation.

It has been thoroughly documented that *o*-aminonitriles can be readily cyclized to annulated 2,4-diaminopyrimidine systems by reaction with guanidine.⁵ We first explored the possible application of this well-known methodology to the preparation of a model 2,4-diaminofuro[2,3-*d*]pyrimidine by the reaction of guanidine with 2-amino-3-cyano-4-methylfuran (**3a**), readily accessed by condensation of acetol (hydroxyacetone) with malononitrile.⁶ To our surprise, the product of this reaction was shown to be 2,4-diamino-5-methylpyrrolo[2,3-*d*]pyrimidine (**4a**) rather than the anticipated 2,4-diamino-5-methylfuro[2,3-*d*]pyrimidine. This unexpected ring transformation/ring annulation reaction turned out to be fairly general. Table 1 records the results of treating a variety of 2-amino-3-cyanofurans (all prepared by condensation of malononitrile with the respective α -hydroxy ketones) with guanidine and several related amidines. Although substituents at position 4 of the furan ring can apparently be accommodated, small alkyl groups lead to better results than an aryl substituent. However, the reaction

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Table 1. Conversion of 2-Amino-3-cyanofurans to Pyrrolo[2,3-*d*]pyrimidines

Entry	% yield(4)
a (R ₁ =Me, R ₂ =H, R ₃ =NH ₂)	67
b (R ₁ =Et, R ₂ =H, R ₃ =NH ₂)	66
c (R ₁ =Ph, R ₂ =H, R ₃ =NH ₂)	42
d (R ₁ =R ₂ =Me, R ₃ =NH ₂)	31
e (R ₁ =H, R ₂ =Ph, R ₃ =NH ₂)	NR
f (R ₁ =R ₂ =Ph, R ₃ =NH ₂)	NR
g (R ₁ =Me, R ₂ =H, R ₃ =CH ₃)	46
h (R ₁ =Me, R ₂ =H, R ₃ =Ph)	30
i (R ₁ =Me, R ₂ =H, R ₃ =Me ₂ N)	NR
j (R ₁ =Me, R ₂ =H, R ₃ =MeS)	NR

is sensitive to the presence and nature of substituents at position 5 and is blocked entirely by a 5-aryl substituent. Although some amidines other than guanidine (e.g., acetamidine and benzamidine) can be employed, some closely related amidines (*N,N*-dimethylguanidine, *S*-methyl-2-thiopseudourea) are ineffective.

We have successfully adapted this facile ring transformation/ring annulation sequence to an alternative and efficient synthesis of the DHFR inhibitor TNP-351. As outlined in Scheme 1, 3-(4-carbethoxyphenyl)propanal (**5**)⁷ was converted in one step to the α -hydroxy ketone **6** by reaction with formaldehyde and *N*-ethylbenzothiazolium bromide in the presence of triethylamine.⁸ Subsequent condensation with malononitrile gave the requisite furan *o*-aminonitrile precursor **7**. Reaction with guanidine in refluxing ethanol then yielded in one step 2,4-diamino-5-[2-(4-carbethoxyphenyl)ethyl]pyrrolo[2,3-*d*]pyrimidine (**8**), which was converted to the diethyl ester of **10**⁹ (TNP-351) by hydrolysis to the free benzoic acid followed by glutamate coupling utilizing the 2-chloro-4,6-dimethoxy-1,3,5-triazine/*N*-methylmorpholine methodology.¹⁰

Several plausible mechanisms for the above amidine-mediated ring transformation/ring annulation reactions can be suggested. For example, initial Michael addition of the amidine to the 2-position of the furan *o*-aminonitrile **3** (see Scheme 2) could be followed by furan ring cleavage to generate an open-chain carbonyl derivative (**11**), which then recycles to an intermediate pyrrole, thus incorporating the 2-amino group of the furan *o*-aminonitrile starting material as the pyrrole NH group. Subsequent intramolecular addition of the amidino substituent to the *o*-substituted nitrile group then completes the pyrimidine ring annulation to give **4**. Alternatively, deprotonation of the acidic 2-amino group of the starting furan *o*-aminonitrile **3** by the strongly basic amidine could be followed by C–O bond cleavage to generate an intermediate ketenimine which, by prototropic rearrangement, would lead to the substituted malononitrile **12**. Further reaction with the amidine in the usual way would lead to a 2-substituted-4,6-diaminopyrimidine carrying a β -carbonyl substituent at C-5; final ring closure would form the fused pyrrole ring.

Experiments are currently underway in an attempt to elucidate the reaction pathway involved in this intriguing transformation.

Experimental Section

2,4-Diamino-5-methylpyrrolo[2,3-*d*]pyrimidine (4a). To a solution of guanidine free base (from 22 mmol of guanidine hydrochloride and 22 mmol of NaOMe) in anhydrous EtOH (50 mL) was added aminonitrile **3a** (2.44 g, 22 mmol). The mixture was refluxed for 24 h, cooled, and acidified with AcOH. The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel with 5% MeOH/CH₂Cl₂ as the eluent. Fractions containing the product were combined and evaporated to give **4a** (2.20 g, 67%) as a light brown solid: mp 166–168 °C; ¹H NMR (DMSO-*d*₆) δ 2.20 (s, 3 H), 5.40–5.75 (br s, 2 H), 6.30 (s, 2 H), 6.40 (s, 1 H), 10.49 (s, 1 H); ¹³C NMR (DMSO-*d*₆, 75.6 MHz) δ 12.5, 96.3, 109.2, 115.2, 154.1, 158.7, 159.9; IR(KBr) ν_{\max} (cm⁻¹) 3505, 3359, 3129, 1632, 1588, 1552, 1447, 1400; EIMS *m/z* (relative intensity) 163 (M⁺, 100), 145 (18), 121 (27); HRMS calcd for C₇H₉N₅ 163.0858, found 163.0864.

2,4-Diamino-5-ethylpyrrolo[2,3-*d*]pyrimidine (4b). To a solution of guanidine free base (from 20 mmol of guanidine hydrochloride and 20 mmol of NaOMe) in anhydrous EtOH (50 mL) was added aminonitrile **3b** (1.52 g, 10 mmol). The mixture was refluxed for 36 h and cooled in an ice bath, and the precipitated solid was collected by filtration, washed with MeOH, and dried to give **4b** (0.72 g, 41%) as a white solid. The filtrate was evaporated in vacuo, and the residue was chromatographed on silica gel with 15% MeOH/CH₂Cl₂ as the eluent. Fractions containing the product were combined and evaporated to give an additional amount of **4b** (0.45 g, 25%, overall yield 66%) as a white solid: mp 215–216 °C; ¹H NMR (DMSO-*d*₆) δ 1.12 (t, 3 H, *J* = 7.3 Hz), 2.62 (q, 2 H, *J* = 7.3 Hz), 5.35 (br s, 2 H, exchangeable with D₂O), 5.96 (br s, 2 H, exchangeable with D₂O), 6.35 (s, 1 H), 10.34 (s, 1 H, exchangeable with D₂O); ¹³C NMR (DMSO-*d*₆, 75.6 MHz) δ 15.0, 19.8, 95.6, 113.8, 116.5, 154.2, 158.4, 159.8; IR(KBr) ν_{\max} (cm⁻¹) 3450, 3386, 3302, 3133, 1604, 1428, 1393, 1090, 794; EIMS *m/z* (relative intensity) 177 (M⁺, 100), 162 (60), 145 (22), 120 (15), 78 (37); HRMS calcd for C₈H₁₁N₅ 177.1014, found 177.0999. Anal. Calcd for C₈H₁₁N₅: C, 54.22; H, 6.26; N, 39.52. Found: C, 53.96; H, 6.29; N, 39.31.

2,4-Diamino-5-phenylpyrrolo[2,3-*d*]pyrimidine (4c). To a solution of guanidine free base (from 20 mmol of guanidine hydrochloride and 20 mmol of NaOMe) in anhydrous MeOH (15 mL) was added aminonitrile **3c** (1.84 g, 10 mmol). The mixture was refluxed for 24 h, cooled, and acidified with AcOH. The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel with 15% MeOH/CH₂Cl₂ as the eluent. Fractions containing the product were combined and evaporated to give **4c** (0.95 g, 42%) as a white solid: mp 220–222 °C; ¹H NMR (DMSO-*d*₆) δ 5.54 (br s, 4 H, exchangeable with D₂O), 6.76 (s, 1 H), 7.25 (m, 5 H), 10.94 (s, 1 H, exchangeable with D₂O); ¹³C NMR (DMSO-*d*₆, 75.6 MHz) δ 94.0, 116.3, 116.8, 126.3, 128.2 (\times 2), 129.1 (\times 2), 136.2, 154.6, 158.0, 160.1; IR(KBr) ν_{\max} (cm⁻¹) 3506, 3401, 3359, 3147, 1605, 1534, 1429, 759; EIMS *m/z* (relative intensity) 225 (M⁺, 100), 208 (11), 183 (25), 155 (14), 112 (12); HRMS calcd for C₁₂H₁₁N₅ 225.1014, found 225.1007. Anal. Calcd for C₁₂H₁₁N₅: C, 63.99; H, 4.92; N, 31.09. Found: C, 64.12; H, 4.94; N, 31.02.

2,4-Diamino-5,6-dimethylpyrrolo[2,3-*d*]pyrimidine (4d). To a solution of guanidine free base (from 10 mmol of guanidine hydrochloride and 10 mmol of NaOMe) in anhydrous MeOH (15 mL) was added aminonitrile **3d** (304 mg, 2 mmol). The mixture was refluxed for 96 h and cooled in an ice bath, and the precipitated solid was collected by filtration, washed with cold MeOH, and dried to give **4d** (0.11 g, 31%) as a white solid: mp 265–267 °C; ¹H NMR (DMSO-*d*₆) δ 2.04 (s, 3 H), 2.10 (s, 3 H), 5.26 (br s, 2 H, exchangeable with D₂O), 5.86 (br s, 2 H, exchangeable with D₂O), 10.26 (s, 1 H, exchangeable with D₂O); ¹³C NMR (DMSO-*d*₆, 75.6 MHz) δ 10.7, 10.8, 96.7, 103.8, 122.8, 153.1, 157.6, 159.2; IR(KBr) ν_{\max} (cm⁻¹) 3478, 3450, 3345, 3147, 1626, 1590, 1563, 1485, 1463, 1386, 1323,

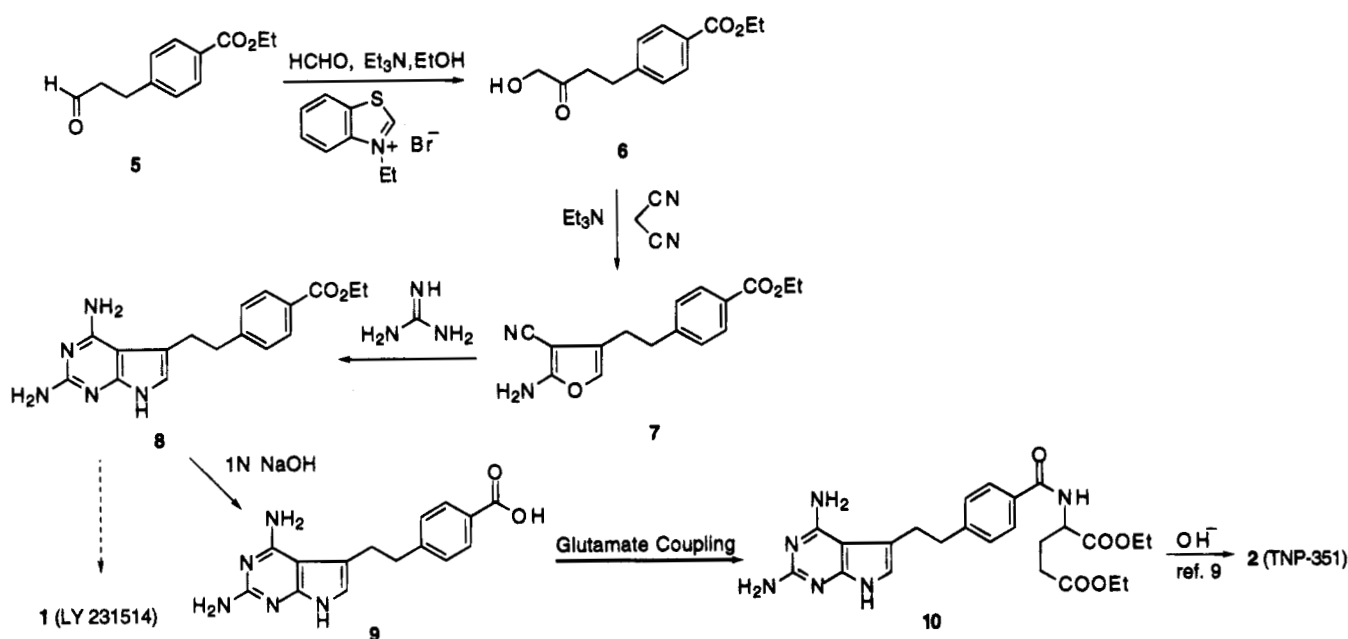
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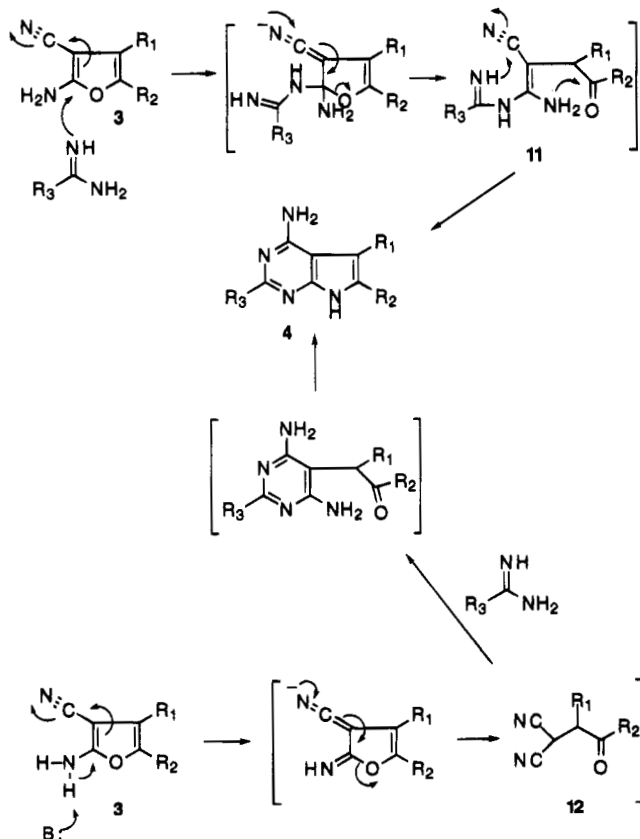
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Scheme 1



Scheme 2



795, 619; EIMS m/z (relative intensity) 177 (M^+ , 100), 159 (20), 134 (27); HRMS calcd for $C_8H_{11}N_5$ 177.1014, found 177.1018.

4-Amino-2,5-dimethylpyrrolo[2,3-*d*]pyrimidine (4g). To a solution of acetamidine free base (from 20 mmol of acetamidine hydrochloride and 20 mmol of NaOMe) in anhydrous MeOH (15 mL) was added aminonitrile **3a** (1.22 g, 10 mmol). The mixture was refluxed for 36 h and cooled in ice bath, and the solid was collected by filtration, washed with cold MeOH, dried, and recrystallized from MeOH/EtOAc to give **4g** (0.60 g, 37%) as a white solid. The filtrate was evaporated in vacuo, and the residue was chromatographed on silica gel with 15% MeOH/ CH_2Cl_2 as the eluent. Fractions containing the product

were combined and evaporated to give an additional amount of **4g** (0.15 g, 9%; overall yield 46%) as a white solid: mp 280 °C (decomposed with sublimation); 1H NMR (DMSO- d_6) δ 2.29 (s, 3 H), 2.35 (s, 3 H), 6.33 (s, 2 H, exchangeable with D_2O), 6.69 (s, 1 H), 10.89 (br s, 1 H, exchangeable with D_2O); ^{13}C NMR (DMSO- d_6 , 75.6 MHz) δ 12.3, 25.5, 100.1, 108.8, 118.1, 152.5, 157.9, 159.7; IR (KBr) ν_{max} (cm^{-1}) 3484, 3294, 3097, 1639, 1569, 1449, 1294, 1097, 801, 766; EIMS m/z (relative intensity) 162 (M^+ , 100), 145 (20), 120 (17), 69 (13); HRMS calcd for $C_8H_{10}N_4$ 162.0905, found 162.0902.

4-Amino-5-methyl-2-phenylpyrrolo[2,3-*d*]pyrimidine (4h). To a solution of benzamidine free base (from 10 mmol of benzamidine hydrochloride and 10 mmol of NaOMe) in anhydrous MeOH (7 mL) was added aminonitrile **3a** (0.61 g, 5 mmol). The mixture was refluxed for 50 h and cooled in an ice bath, and the solid was filtered, washed with cold MeOH, and dried to give **4h** (0.19 g, 17%) as a white solid. The filtrate was evaporated in vacuo, and the residue was chromatographed on silica gel with 15% MeOH/ CH_2Cl_2 as the eluent. Fractions containing the product were combined and evaporated to give an additional amount of **4h** (0.15 g, 13%; overall yield 30%) as a white solid: mp 290–292 °C; 1H NMR (DMSO- d_6) δ 2.35 (s, 3 H), 6.48 (s, 2 H, exchangeable with D_2O), 6.83 (s, 1 H), 7.40 (m, 3 H), 8.31 (dd, 2 H, $J = 6, 2$ Hz), 11.21 (br s, 1 H, exchangeable with D_2O); ^{13}C NMR (DMSO- d_6 , 75.6 MHz) δ 12.3, 100.4, 109.2, 119.6, 127.5 ($\times 2$), 128.2 ($\times 2$), 129.1, 139.5, 152.6, 158.0, 158.1; IR (KBr) ν_{max} (cm^{-1}) 3492, 3302, 3105, 1654, 1639, 1562, 1456, 1315, 766, 703; EIMS m/z (relative intensity) 224 (M^+ , 6), 206 (1), 170 (1), 141 (2), 121 (2), 104 (2), 78 (100); HRMS calcd for $C_{13}H_{12}N_4$ 224.1062 found 224.1055. Anal. Calcd for $C_{13}H_{12}N_4$: C, 69.62; H, 5.39; N, 24.98. Found: C, 69.35; H, 5.37; N, 24.60.

Ethyl 4-(4-Hydroxy-3-oxobutyl)benzoate (6). A mixture of aldehyde **5**⁷ (1.1 g, 5 mmol), paraformaldehyde (150 mg, 5 mmol), *N*-ethylbenzothiazolium bromide (230 mg, 0.9 mmol), and Et_3N (90 mg, 0.9 mmol) in EtOH (10 mL) was heated at 70 °C for 16 h. The reaction mixture was concentrated in vacuo, and the residue was chromatographed on silica gel with 15% EtOAc/hexanes as the eluent. Fractions containing the product were combined and evaporated to give **6** (730 mg, 58%) as a colorless oil which solidified upon standing: mp 51–52 °C; 1H NMR ($CDCl_3$, 300 MHz) δ 1.38 (t, 3 H, $J = 7.2$ Hz), 2.75 (t, 2 H, $J = 7.5$ Hz), 3.03 (t, 2 H, $J = 7.5$ Hz), 3.05 (s, 1 H), 4.20 (s, 2 H), 4.35 (q, 2 H, $J = 7.2$ Hz), 7.24 (d, 2 H, $J = 8.2$ Hz), 7.95 (d, 2 H, $J = 8.2$ Hz); EIMS m/z (relative intensity) 236 (M^+ , 19), 205 (36), 191 (41), 177 (46), 163 (100), 149 (24), 133 (81), 105 (24), 91 (14), 77 (18); HRMS calcd for $C_{13}H_{16}O_4$,

236.1049, found 236.1048. Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.29; H, 6.70.

Ethyl 4-[2-(2-Amino-3-cyanofur-4-yl)ethyl]benzoate (7). To a solution of hydroxy ketone **6** (2.36 g, 10 mmol) in MeOH (30 mL) at 25 °C was added a mixture of malononitrile (0.66 g, 10 mmol) and Et_3N (1.01 g, 10 mmol) in MeOH (10 mL), and the resulting solution was stirred at 25 °C for 10 h. The solid was collected by filtration, washed with a small amount of CH_2Cl_2 , and dried to give **7** (2.17 g, 76%) as a white solid. A small sample was recrystallized from CH_2Cl_2 : mp 195–197 °C; 1H NMR ($CDCl_3$, 300 MHz) δ 1.39 (t, 3 H, $J = 7.2$ Hz), 2.71 (t, 2 H, $J = 7.6$ Hz), 2.95 (t, 2 H, $J = 7.6$ Hz), 4.36 (q, 2 H, $J = 7.2$ Hz), 4.73 (br s, 2 H), 6.44 (s, 1 H), 7.24 (d, 2 H, $J = 8.2$ Hz), 7.96 (d, 2 H, $J = 8.2$ Hz); EIMS m/z (relative intensity) 284 (M^+ , 30), 238 (100), 211 (17), 194 (13), 163 (44), 135 (33), 118 (60), 107 (27), 90 (25), 77 (20); HRMS calcd for $C_{16}H_{16}N_2O_3$ 284.1161, found 284.1158. Anal. Calcd for $C_{16}H_{16}N_2O_3$: C, 67.60; H, 5.67; N, 9.85. Found: C, 67.85; H, 5.71; N, 10.14.

Ethyl 4-[2-(2,4-Diaminopyrrolo[2,3-d]pyrimidin-5-yl)ethyl]benzoate (8). To a solution of guanidine free base (3 mmol, from 285 mg of guanidine hydrochloride and 162 mg of NaOMe) in anhydrous EtOH (50 mL) was added aminonitrile **7** (568 mg, 2 mmol), and the mixture was heated under reflux for 30 h. The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel with 5% CH_3OH/CH_2Cl_2 as the eluent. Fractions containing the product were combined and evaporated to give **8** (360 mg, 56%) as a light brown solid: mp 202–204 °C; 1H NMR ($DMSO-d_6$, 300 MHz) δ 1.27 (t, 3 H, $J = 7.0$ Hz), 2.93 (m, 4 H), 4.24 (q, 2 H, $J = 7.0$ Hz), 5.38 (br s, 2 H, exchangeable with D_2O), 6.02 (br s, 2 H, exchangeable with D_2O), 6.32 (s, 1 H), 7.34 (d, 2 H, $J = 8.1$ Hz), 7.81 (d, 2 H, $J = 8.1$ Hz), 10.36 (s, 1 H, exchangeable with D_2O); EIMS m/z (relative intensity) 325 (M^+ , 40), 311 (3), 280 (4), 252 (2), 238 (3), 162 (100), 145 (11), 120 (7); HRMS calcd for $C_{17}H_{19}N_5O_2$ 325.1538, found 325.1543. Anal. Calcd for $C_{17}H_{19}N_5O_2$: C, 62.76; H, 5.89; N, 21.52. Found: C, 62.48; H, 5.80; N, 21.11.

4-[2-(2,4-Diaminopyrrolo[2,3-d]pyrimidin-5-yl)ethyl]benzoic Acid (9). A solution of ester **8** (654 mg, 2 mmol) in 0.5 N NaOH (6 mL) and MeOH (20 mL) was heated under reflux for 15 h. The reaction mixture was cooled, acidified with glacial HOAc, and filtered. The residue was washed with

water and dried to give **9** (560 mg, 89%) as a white solid: mp > 300 °C (dec); 1H NMR ($DMSO-d_6$, 300 Hz) δ 2.92 (m, 4 H), 5.45 (br s, 2 H, exchangeable with D_2O), 6.10 (s, 2 H, exchangeable with D_2O), 6.35 (s, 1 H), 7.32 (d, 2 H, $J = 8.0$ Hz), 7.81 (d, 2 H, $J = 8.0$ Hz), 10.40 (s, 1 H, exchangeable with D_2O); HRFABMS calcd for $C_{15}H_{16}N_5O_2$ (MH^+) m/z 298.1304, found 298.1246.

Diethyl N-[4-[2-(2,4-Diaminopyrrolo[2,3-d]pyrimidin-5-yl)ethyl]benzoyl]-L-glutamate (10). To a suspension of acid **9** (148 mg, 0.5 mmol) in DMF (10 mL) at 25 °C was added *N*-methylmorpholine (NMM, 0.062 mL, 0.57 mmol) followed by 2-chloro-4,6-dimethoxy-1,3,5-triazine (100 mg, 0.57 mmol), and the resulting solution was stirred at 25 °C for 1.5 h. NMM (0.062 mL, 0.57 mmol) was added to the solution followed by diethyl L-glutamate (140 mg, 0.59 mmol), the resulting mixture was stirred at 25 °C for 4 h and concentrated in vacuo (0.5 mmHg), and the residue was dissolved in CH_2Cl_2 (50 mL). The CH_2Cl_2 solution was washed with 5% $NaHCO_3$, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed on silica gel with 3% $MeOH/CH_2Cl_2$ as the eluent. Fractions containing the product were combined and evaporated to give a gummy residue which was triturated with ether/hexanes. The resulting solid was collected by filtration and dried to give **10** (150 mg, 62%) as a white solid: mp 84–87 °C; 1H NMR ($CDCl_3$) δ 1.17 (t, 3 H, $J = 7.1$ Hz), 1.24 (t, 3 H, $J = 7.1$ Hz), 2.10–2.52 (m, 4 H), 2.79 (br s, 4 H), 4.06 (q, 2 H, $J = 7.1$ Hz), 4.15 (q, 2 H, $J = 7.1$ Hz), 4.75 (m, 1 H), 5.25 (br s, 2 H), 5.46 (br s, 2 H), 6.28 (s, 1 H), 7.01 (d, 2 H, $J = 7.8$ Hz), 7.60 (d, 3 H, 2-Ar and 1-NH, $J = 7.8$ Hz), 10.05 (s, 1 H); ^{13}C NMR ($DMSO-d_6$, 75.6 MHz) δ 14.3 ($\times 2$), 25.9, 27.8, 30.4, 35.9, 52.2, 60.2, 60.8, 95.7, 113.8, 114.8, 127.6 ($\times 2$), 128.6 ($\times 2$), 131.4, 145.8, 154.3, 158.3, 159.8, 166.8, 172.1, 172.4; IR (KBr) ν_{max} (cm^{-1}) 3373 (broad), 2985, 1725, 1605, 1577, 1541, 1203, 1098, 1020; EIMS m/z (relative intensity) 482 (M^+ , 8), 436 (6), 162 (100), 145 (7), 118 (6), 84 (18); HRMS calcd for $C_{24}H_{30}N_6O_5$ 482.2277, found 482.2295. Anal. Calcd for $C_{24}H_{30}N_6O_5$: C, 59.74; H, 6.27; N, 17.42. Found: C, 59.55; H, 6.08; N, 17.19.

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