× 4 ion-exchange resin ($H^+$ form) contained in a column (0.4 × 2 cm) fashioned from a blue pipet cone. The column was washed with 3 × 0.5 mL of water, and the combined eluants were counted for radioactivity with use of Aquasol-2 (15 mL).

**Inhibition Studies.** DAP-epimerase, partially purified as described above, was incubated in 50 mM TrisHCl (pH 7.8) with various concentrations of **3** and **2a–c** at 25 °C. At the time intervals indicated in the various figures (Figures 1, 2, and 8), aliquots were removed and diluted 5–10-fold into the assay reaction mix, and the remaining enzyme activity was determined.

**Acknowledgment.** The authors thank Dr. F. Piriou for NMR experiments and Anne Czermak and Jean-Paul François for technical assistance with the synthesis.

# Synthesis and Antiviral Activity of Some Acyclic and C-Acyclic Pyrrolo[2,3-*d*]pyrimidine Nucleoside Analogues

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A series of acyclic and C-acyclic 7-deazapurine nucleosides have been synthesized and tested for antiviral activity. Reaction of the sodium salt of 2-amino-3,4-bis(aminocarbonyl)-5-(methylthio)pyrrole (**6**) with an appropriate electrophile gave pyrrole nucleosides which served as common intermediates to both the 7-deazaadenosine and the 7-deazaguanosine series. Several of these 5- and 5,6-substituted pyrrolo[2,3-*d*]pyrimidine nucleosides have shown activity against HIV virus in preliminary in vitro screens.

Pyrrolo[2,3-*d*]pyrimidine nucleosides have been the subject of a number of scientific studies since the report of the pronounced biological activity of some of these nucleosides.[1] In fact, the antiviral activity of several of the naturally occurring pyrrolo[2,3-*d*]pyrimidine nucleosides, and of some of their analogues, has been well documented.[2] These natural products are commonly referred to as the 7-deazapurines and some representative examples of this class of compounds are illustrated in Chart I.[3]

As part of our continuing efforts in the synthesis of acyclic nucleosides as potential antiviral agents,[4] we were interested in exploring the possibility that some acyclic 7-deazapurine analogues bearing C-5, or C-5 and C-6 substituents, may also have antiviral activity. We,[5] along with others,[6] found that replacing the furanose ring of guanosine with an acyclic carbohydrate [i.e. (1,3-dihydroxy-2-propoxy)methyl] resulted in a modified nucleoside **5** which possesses pronounced activity against the human herpes simplex viruses 1 and 2. We observed that varying the nature of the heterocyclic base has a pronounced effect on the antiviral activity of the acyclic nucleoside[7] and were interested in determining whether antiviral activity is retained when the (1,3-dihydroxy-2-propoxy)methyl group is employed in combination with the 7-deazapurine skeleton.[8,9] While none of the compounds of this series are active against herpes viruses, we were pleased to discover that compounds **55** and **67** in the (1,3-dihydroxy-2-propoxy)methyl series (Tables IV and V) show activity against the HIV virus. These results encouraged us to extend our synthetic efforts towards other acyclic and C-acyclic pyrrolo[2,3-*d*]pyrimidine analogues. We report here the synthesis and preliminary antiviral (HIV) screening results of a series of new 7-deazapurine acyclonucleoside analogues.

**Chart I.** Nucleoside Analogues

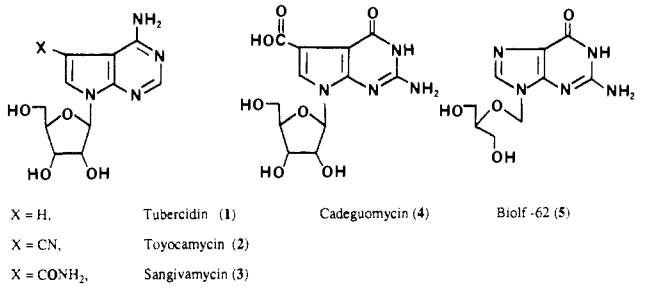
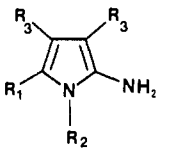
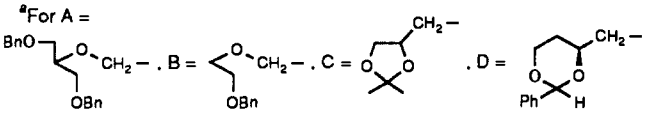



Table I. Substituted Pyrroles



| compd | $R_2$[a] | $R_1$ | $R_3$ | yield, % |
|---|---|---|---|---|
| 11 | A | $SCH_3$ | $CONH_2$ | 32 |
| 12 | B | $SCH_3$ | $CONH_2$ | 32 |
| 13 | C | $SCH_3$ | $CONH_2$ | 62 |
| 14 | D | $SCH_3$ | $CONH_2$ | 51 |
| 15 | A | H | $CONH_2$ | 75 |
| 16 | B | H | $CONH_2$ | 76 |
| 17 | C | H | $CONH_2$ | 73 |
| 18 | D | H | $CONH_2$ | 54 |
| 19 | A | $SCH_3$ | CN | 51 |
| 20 | B | $SCH_3$ | CN | 53 |
| 21 | C | $SCH_3$ | CN | 60 |
| 22 | D | $SCH_3$ | CN | 59 |
| 23 | A | H | CN | 50 |
| 24 | B | H | CN | 52 |
| 25 | C | H | CN | 51 |
| 26 | D | H | CN | 42 |

[a] For A =  . B =  . C =  . D = 

## Results and Discussion

A number of syntheses of pyrrolo[2,3-*d*]pyrimidine nucleosides and their analogues have been published over the past 20 years. Some of the synthetic approaches to the natural products themselves have relied on the construction of the pyrrolo[2,3-*d*]pyrimidine ring as a first stage, followed by subsequent attachment of the carbohydrate,[10] while others have involved pyrrole *N*-nucleosides as a key

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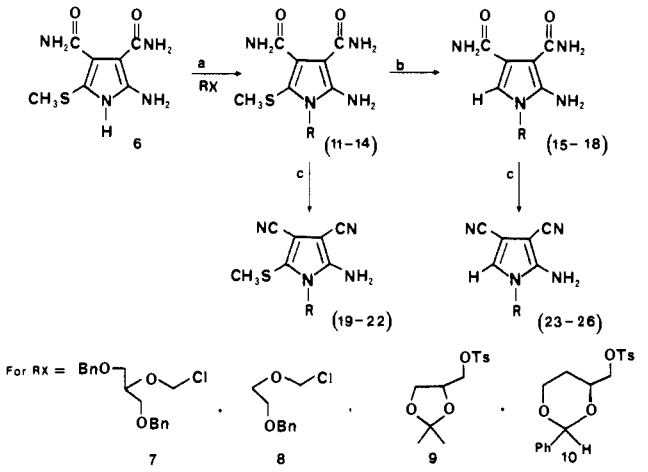
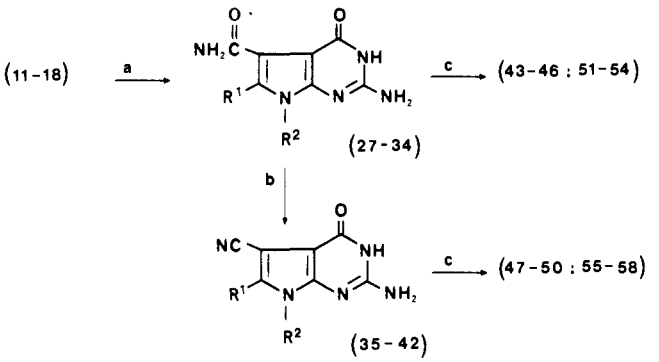
**Scheme I**[a]



[a] (a) NaH/DMF. (b) Ra-Ni/EtOH. (c) Py/TsCl.

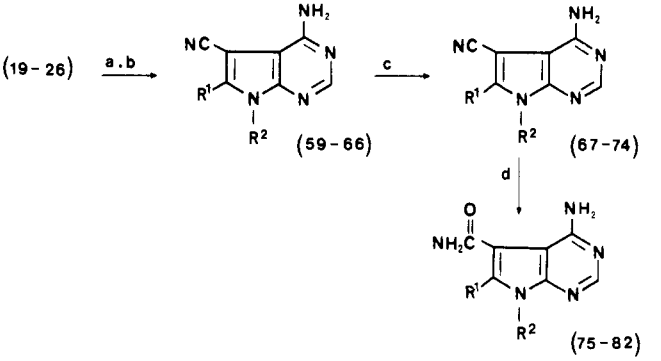
**Scheme II**[a]



[a] (a) $CS_2$/MeOH/NaOH; $H_2O_2$; $NH_3$. (b) Py/TsCl. (c) HOAc/$H_2O$ or $BCl_3$.

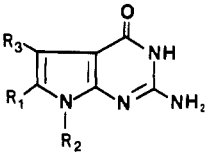
intermediate.[11] Procedures which have been applied specifically for acyclic or C-acyclic 7-deazapurines include those relying on a condensation of a preformed deazapurine with an appropriate electrophile [e.g. compounds

**Scheme III**[a]



[a] (a) $HC(OEt)_3$. (b) $NH_3$. (c) HOAc/$H_2O$ or $BCl_3$. (d) $NH_4OH/H_2O_2$.

**Table II.** Protected Acyclic 7-Deazaguanine Analogues



| compd | $R_2$[a] | $R_1$ | $R_3$ | yield, % |
|---|---|---|---|---|
| 27 | A | $SCH_3$ | $CONH_2$ | 43 |
| 28 | B | $SCH_3$ | $CONH_2$ | 54 |
| 29 | C | $SCH_3$ | $CONH_2$ | 28 |
| 30 | D | $SCH_3$ | $CONH_2$ | 31 |
| 31 | A | H | $CONH_2$ | 76 |
| 32 | B | H | $CONH_2$ | 56 |
| 33 | C | H | $CONH_2$ | 35 |
| 34 | D | H | $CONH_2$ | 47 |
| 35 | A | $SCH_3$ | CN | 75 |
| 36 | B | $SCH_3$ | CN | 76 |
| 37 | C | $SCH_3$ | CN | 78 |
| 38 | D | $SCH_3$ | CN | 77 |
| 39 | A | H | CN | 71 |
| 40 | B | H | CN | 60 |
| 41 | C | H | CN | 74 |
| 42 | D | H | CN | 85 |

[a] See footnote Table I for definitions of A, B, C, and D.


(1) For a general reference to these compounds see: Suhadolnik, P. K. *Nucleosides as Biological Probes*; John Wiley and Sons: New York, 1979.

(2) For some recent references to antiviral activity of pyrrolo[2,3-*d*]pyrimidines see the following papers and their cited references: (a) DeClercq, E.; Balzarini, J.; Madej, D.; Hansske, F.; Robins, M. J. *J. Med. Chem.* **1987**, *30*, 481. (b) Bergstorm, D. E.; Brattesani, A. J.; Ogawa, M. K.; Reddy, P. A.; Schweickert, M. J.; Balzarini, J.; DeClercq, E. *J. Med. Chem.* **1984**, *27*, 285. (c) Turk, S. R.; Shipman, C.; Nassiri, R.; Genzlinger, G.; Krawczyk, S. H.; Townsend, L. B.; Drach, J. C. *Antimicrob. Agents Chemother.* **1984**, *31*, 544. (d) DeClercq, E.; Bernaerts, R.; Bergstrom, D. E.; Robins, M. J.; Montgomery, J. A.; Holy, A. *Antimicrob. Agents Chemother.* **1986**, *29*, 482. (e) O'Brien, W. J.; Taylor, J. L.; O'Malley, T. P.; Ritch, P. S. *Cur. Eye Res.* **1987**, *6*, 255.

(3) For isolation papers see: Tubercidin [Suzuki, S.; Matumo, S. *J. Antibiot., Ser. A.* **1957**, *10*, 201.], Toyocamycin [Ohkuma, K. *Ibid.* **1960**, *13*, 361. Nishimura, H.; Katagiri, K. K.; Sata, K.; Mayama, M.; Shimaoka, N. *Ibis.* **1956**, *9*, 60.], Sangivamycin [Rao, K. V.; Renn, D. W. *Antimicrob. Agents Chemother.* **1963**, *77*], Cadeguomycin [Tanaka, N.; Wu, R. T.; Okabe, T.; Yamashita, H.; Shimazu, A.; Nishimura, T. *J. Antibiot.* **1982**, *35*, 272. Wu, R. T.; Okabe, T.; Namikoshi, M.; Okuda, S.; Nishimura, T.; Tanaka, N. *Ibid.* **1982**, *35*, 279.]

(4) For a review of the chemistry and antiviral activity of acyclonucleosides see: (a) Chu, C. K.; Cutler, S. J. *J. Heterocyclic Chem.* **1986**, *23*, 289. (b) Remy, R. J.; Secrist, J. A., III. *Nucleosides Nucleotides* **1985**, *4*, 411.

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(7) (a) Ogilvie, K. K.; Hamilton, R. G.; Gillen, M. F.; Radatus, R. K.; Smith, K. O.; Galloway, K. S. *Can. J. Chem.* **1984**, *62*, 16. (b) Ogilvie, K. K.; Nguyen-Ba, N.; Gillen, M. F.; Radatus, B. K.; Cheriyan, U. O.; Hanna, H. R.; Smith, K. O.; Galloway, K. S. *Can. J. Chem.* **1984**, *62*, 241.

(8) A portion of this work was presented by N. Nguyen-Ba at the 70th Annual Canadian Chemical Conference, Quebec City, June 7-11, 1987; Abstract ORG-51-F.

(9) Gupta, P. K.; Daunert, S.; Nassiri, M. R.; Wotring, L. L.; Drach, J. C.; Townsend, L. B. *J. Med. Chem.* **1989**, *32*, 402.

(10) For examples of synthetic approaches to pyrrolo[2,3-*d*]-pyrimidine nucleosides which rely on the contruction of the deazapurine ring prior to glycosylation see: (a) Taylor, E. C.; Hendess, R. W. *J. Am. Chem. Soc.* **1965**, *87*, 1995. (b) Tolman, R. L.; Robins, R. K.; Townsend, L. B. *Ibid.* **1969**, *91*, 2102. (c) Winkeler, H.-D.; Seela, F. *J. Org. Chem.* **1983**, *48*, 3119. (d) Ramasamy, K.; Imamura, N.; Robins, R. K.; Revankar, G. R. *Tetrahedron Lett.* **1987**, *28*, 5107. (e) Kazimierczuk, Z.; Revankar, G. R.; Robins, R. K. *Nucleic Acids Res.* **1984**, *12*, 1179. (f) Ramasamy, K.; Robins, R. K.; Revankar, G. R. *J. Chem. Soc., Chem. Commun.* **1989**, 560.

(11) Ramasamy, K.; Robins, R. K.; Revankar, G. *Tetrahedron* **1986**, *42*, 5869.

9,[12] 7,[13] and (2-acetoxyethoxy)methyl bromide[14]] or those which proceed via the intermediacy of substituted pyrroles[15] or substituted pyrimidines.[16]

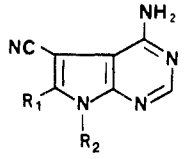
Our synthesis of a series of new C-5 and C-5,-6 substituted acyclic 7-deazapurines nucleosides involves using the same pyrrole nucleoside intermediate (Scheme I and Table I) as a common synthon to both the 7-deazaadenosine (Scheme III) *and* the 7-deazaguanosine (Scheme II) analogues.[17] The construction of these key intermediates (**11–14**) simply involves the treatment of the sodium salt of pyrrole **6**[18] with an appropriate electrophile (**7–10**) in DMF. These reaction conditions are similar to those developed and extensively employed by the R. K. Robins group[11] for other pyrrole substrates. We were unable to use the recommended reaction solvent ($CH_3CN$) due to the low solubility of 2-amino-3,4-bis(aminocarbonyl)-5-(methylthio)pyrrole (**6**) and instead, used DMF. In general the condensation reaction between **6** and the electrophiles (**7–10**) proceed in modest to moderate yields (30–60%) with the yields for the chloromethyl ether condensations being lower than for the tosylate condensations. The starting materials however are inexpensive and are easily accessible via published literature procedures, and the condensation products (**11–14**) are easily purified by using standard flash chromatography techniques.

Removal of the methyl thio group was carried out at an early stage of the synthesis in an attempt to circumvent experimental problems such as those encountered by Taylor and Hendess[10a] in their synthesis of the aglycone of toyocamycin. Desulfurization of **11–14** using freshly prepared Raney nickel[19] afforded compounds **15–18**. Compounds **11–14** and **15–18** then served as immediate precursors for the C-5,6 substituted and the C-5 substituted 7-deazaguanine analogues (Scheme II).[20] Access to the 7-deazaadenine analogues was gained by first dehydrating the carboamide functionalities to the corresponding dinitrile compounds **19–22** and **23–26**.[17] These transformations were easily verified by $^1H$ NMR and, in the preparation of the dicarbonitrile compounds, by the combination of $^1H$ NMR with IR and/or $^{13}C$ NMR.

Direct transformation of **11–14** and **15–18** to the protected C-5,-6 substituted and C-5 substituted 7-deazaguanines **27–30** and **31–34**, was accomplished by using a literature procedure.[17] This method involved treatment of the pyrroles, **11–14** and **15–18**, with carbon disulfide in methanolic sodium hydroxide. Direct oxidation of the crude cyclized product with hydrogen peroxide, followed by treatment with ammonia, affords **27–34** in yields ranging from 30–75% yield after purification. The carboamide functional group was transformed to the corresponding carbonitrile[17] to give compounds **35–38** and **39–42** (Table II).

A sample of each of the 16 compounds **27–42** was deprotected and tested for biological activity (Table IV). Boron trichloride in dichloromethane was successfully employed for debenzylation, and the acetal protecting

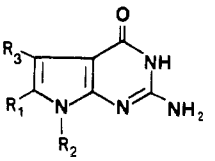
Table III. Protected Acyclic 7-Deazaadenine Analogues



| compd | $R_2$[a] | $R_1$ | yield, % |
|---|---|---|---|
| **59** | A | $SCH_3$ | 91 |
| **60** | B | $SCH_3$ | 91 |
| **61** | C | $SCH_3$ | 91 |
| **62** | D | $SCH_3$ | 86 |
| **63** | A | H | 90 |
| **64** | B | H | 90 |
| **65** | C | H | 94 |
| **66** | D | H | 91 |

[a] See footnote Table I for definitions of A, B, C, and D.

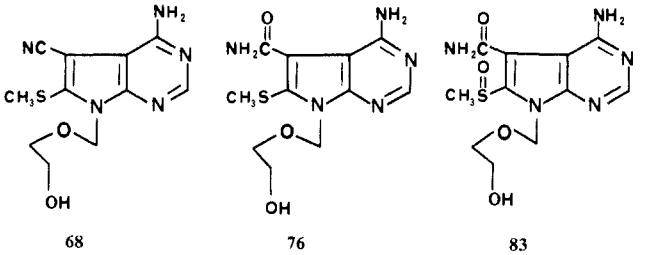
Table IV. 7-Deazaguanine Nucleoside Analogues



| compd | $R_1$ | $R_2$ | $R_3$ | activity, HIV: $IC_{50}$, μM[a] |
|---|---|---|---|---|
| **43** | $SCH_3$ | $(HOCH_2)_2CHOCH_2$ | $CONH_2$ | - |
| **51** | H | $(HOCH_2)_2CHOCH_2$ | $CONH_2$ | - |
| **47** | $SCH_3$ | $(HOCH_2)_2CHOCH_2$ | CN | - |
| **55** | H | $(HOCH_2)_2CHOCH_2$ | CN | 3 |
| **44** | $SCH_3$ | $HOCH_2CH_2OCH_2$ | $CONH_2$ | - |
| **52** | H | $HOCH_2CH_2OCH_2$ | $CONH_2$ | - |
| **48** | $SCH_3$ | $HOCH_2CH_2OCH_2$ | CN | - |
| **56** | H | $HOCH_2CH_2OCH_2$ | CN | - |
| **45** | $SCH_3$ | (*RS*)-$HOCH_2CHOHCH_2$ | $CONH_2$ | - |
| **53** | H | (*RS*)-$HOCH_2CHOHCH_2$ | $CONH_2$ | - |
| **49** | $SCH_3$ | (*RS*)-$HOCH_2CHOHCH_2$ | CN | - |
| **57** | H | (*RS*)-$HOCH_2CHOHCH_2$ | CN | - |
| **46** | $SCH_3$ | (*S*)-$HOCH_2CH_2CHOHCH_2$ | $CONH_2$ | - |
| **54** | H | (*S*)-$HOCH_2CH_2CHOHCH_2$ | $CONH_2$ | - |
| **50** | $SCH_3$ | (*S*)-$HOCH_2CH_2CHOHCH_2$ | CN | - |
| **58** | H | (*S*)-$HOCH_2CH_2CHOHCH_2$ | CN | - |

[a] A dash indicates that $IC_{50} > 200$ μM.

**Chart II.** Compounds Obtained from Exposure of **68** to Ammonium Hydroxide–Hydrogen Peroxide



**68** **76** **83**


(12) (a) LaMontagne, M. P.; Smith, D. C.; Wu, G. S. *J. Heterocycl. Chem.* **1983**, *20*, 295. (b) Seela, F.; Kehne, A. *Liebigs Ann. Chem.* **1982**, 1940.

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(14) (a) Seela, F.; Kehne, A.; Winkeler, H.-D. *Liebigs. Ann. Chem.* **1983**, 137. (b) Pudlo, J. S.; Saxena, N. K.; Nassiri, M. R.; Turk, S. R.; Drach, J. C.; Townsend, L. B. *J. Med. Chem.* **1988**, *31*, 2086.

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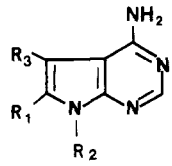
**Table V.** 7-Deazaadenine Nucleoside Analogues



| compd | $R_1$ | $R_2$ | $R_3$ | activity, HIV: $IC_{50}$, $\mu M$[a] |
|---|---|---|---|---|
| **67** | $SCH_3$ | $(HOCH_2)_2CHOCH_2$ | CN | 20 |
| **71**[b] | H | $(HOCH_2)_2CHOCH_2$ | CN | - |
| **75** | $SCH_3$ | $(HOCH_2)_2CHOCH_2$ | $CONH_2$ | - |
| **79**[b] | H | $(HOCH_2)_2CHOCH_2$ | $CONH_2$ | - |
| **68** | $SCH_3$ | $HOCH_2CH_2OCH_2$ | CN | - |
| **72**[b] | H | $HOCH_2CH_2OCH_2$ | CN | 46 |
| **76** | $SCH_3$ | $HOCH_2CH_2OCH_2$ | $CONH_2$ | - |
| **80**[b] | H | $HOCH_2CH_2OCH_2$ | $CONH_2$ | - |
| **69** | $SCH_3$ | (*RS*)-$HOCH_2CHOHCH_2$ | CN | - |
| **73** | H | (*RS*)-$HOCH_2CHOHCH_2$ | CN | 197 |
| **77** | $SCH_3$ | (*RS*)-$HOCH_2CHOHCH_2$ | $CONH_2$ | - |
| **81** | H | (*RS*)-$HOCH_2CHOHCH_2$ | $CONH_2$ | - |
| **70** | $SCH_3$ | (*S*)-$HOCH_2CH_2CHOHCH_2$ | CN | 100 |
| **74** | H | (*S*)-$HOCH_2CH_2CHOHH_2$ | CN | - |
| **78** | $SCH_3$ | (*S*)-$HOCH_2CH_2CHOHCH_2$ | $CONH_2$ | - |
| **82** | H | (*S*)-$HOCH_2CH_2CHOHCH_2$ | $CONH_2$ | - |

[a] A dash indicates that $IC_{50} > 200$ $\mu M$. [b] An alternate synthesis of compounds **72**, **80**, **71**, and **79** has been reported by L. B. Townsend et al.[9,22]

groups were removed by brief exposure to 80% aqueous acetic acid.

Conversion of compounds **19–26** to the 7-deazaadenine analogues was accomplished by using a literature procedure[10a] which relies on the intermediacy of imidate esters. A neat mixture of the aminopyrrole in an excess of triethyl orthoformate was stirred under reflux conditions until such time as the reaction was judged to be complete by TLC (28–48 h). Evaporation of the excess reagent left a crude imidate ester to which was added absolute ethanol saturated with ammonia. Displacement of the ethoxy group by ammonia and subsequent cyclization afforded the 7-deazapurine ring system. In general this process was highly efficient and yields of the products (**59–66**) were in the order of 90% (Table III).

Deprotection of **59–66** with either boron trichloride in methylene chloride or with aqueous acetic acid gave compounds **67–74** (Table V). Conversion to the corresponding amides **75–82** was effected by brief treatment of the nitrile with aqueous ammonium hydroxide and hydrogen peroxide.[10a] The reaction times were kept to a minimum (ca. 30–45 min) so as to minimize exposure to the oxidative conditions. No problems were encountered with the C-5 substituted analogues (**71–74**) or with three of the four C-5,-6 substituted anallogues. In the case of **68**, however, we observed oxidation of the methylthio group in addition to the desired conversion of the amide to a nitrile (Chart II).

When **68** was exposed to $NH_4OH/H_2O_2$ treatment (45 min) and the solvent evaporated under reduced pressure at 40 °C, the major reaction product was not the desired compound **76**. The $^1H$ NMR spectrum of the major product showed a downfield shift of the methyl signal from the anticipated chemical shift. In addition, the two protons of the $NCH_2O$ methylene were no longer magnetically equivalent, and were observed as two doublets with a geminal coupling of ca. 10 Hz. This data suggests that the compound isolated was most likely **83** and not **76**. High-resolution chemical-ionization mass spectra and $^{13}C$ NMR spectra supported this conclusion. Purification of **83** was difficult due to its low solubility and to similarities in the $R_f$ of **76** and **83**. However, preparative TLC allowed for the separation of a sufficient amount of pure **83** for characterization.

When attempts to convert **68** to **76** by an alternate procedure,[21] using a dilute aqueous solution of sodium hydroxide, led to decomposition of starting material we reexamined the $NH_4OH/H_2O_2$ reaction conditions. A sufficiently large sample of **76** (so as to permit characterization and biological testing of the compound) was obtained by using a combination of brief treatment (25 min) with $NH_4OH/H_2O_2$ and freeze drying of the reaction mixture. Flash chromatography allowed separation of the starting material from the reaction products and preparative TLC was used to isolate a sample of pure **76**.

Spectral data ($^1H$ NMR, $^{13}C$ NMR, UV, high-resolution MS, and/or elemental analysis) of the fully deprotected acyclic and C-acyclic 7-deazapurine nucleosides analogues are included in the experimental section and are consistent with the structures shown in Tables IV and V.

## Biological Evaluation of the New Analogues

Samples of all new compounds were submitted to Syntex Research, Mountain View, CA for biological testing. Samples were tested in an antiviral screen (with emphasis on HSV i.e. HSV-1 and HSV-2) as well as in a specific test for HIV.

Biological activity was recorded as $IC_{50}$s (inhibitory concentration). None of the compounds showed activity against HSV-1 and HSV-2 at levels below 200 $\mu M$. However, several compounds (**55**, **67**, **70**, **72**, and **73**) showed activity against HIV below this level (Tables IV and V). Compounds **55** and **67** are particularly interesting showing $IC_{50}$s of 3 and 20 $\mu M$, respectively. Their toxicity to ALEC cells are approximately 400 and 800 $\mu M$, respectively, leading to therapeutic ratios ($Tox/IC_{50}$) of approximately 133 for compound **55** and approximately 40 for compound **67**. DHPG (Biolf-62) was used as the reference compound for the herpes simplex test ($IC_{50} = 32$ $\mu M$) and AZT was used as the reference compound for the HIV test ($IC_{50} = 0.002–0.01$ $\mu M$).

## Conclusions

Synthetic procedures have been developed for the preparation of a series of acyclic and C-acyclic 7-deazapurine nucleosides. Several of these compounds, particularly in the 7-deazaadenine analogue series, have shown interesting activity against HIV.

## Experimental Section

**General Procedures.** Melting points were determined on a Fisher-Jones apparatus or a Gallenkamp block and are uncorrected. Commercial thin-layer chromatography (TLC) plates (silica gel Merck 60 $F_{254}$) were used. TLC plates were examined under ultraviolet radiation (254 nm), and the silica plates were heated after being dipped in a solution (100 mL of 10% $H_2SO_4$ in $H_2O$) of ammonium molybdate (2.5 g) and ceric sulfate (1.0 g). Infrared (IR) spectra were recorded on a Analect FT, AQS-18 spectrophotometer with a MAP-67 data system. Nuclear magnetic resonance (NMR) spectra were recorded on Varian XL-200 and XL-300 instruments. The chemical shift values are expressed in parts per million relative to the standard chemical shift of the solvent ($CDCl_3$ or DMSO-$d_6$). The following abbreviations are used with respect to NMR spectra: s = singlet; d = doublet; t = triplet; b = broad; $J$ = coupling constant; $\delta$ = chemical shift. Low- and high-resolution mass spectra were obtained with Du Pont 21-492 B, Vacuum Generators ZAB-2F and Hewlett-Packard

(21) Watanabe, S.; Ueda, T. *Nucleosides Nucleotides* **1982**, *1*, 191.
(22) Gupta, P. K.; Townsend, L. B. *Abstracts of Papers*, Third Chemical Congress of North America, Toronto, Canada, June 5–10, 1988. American Chemical Society: Washington, DC, 1988; Medicinal Chemistry Abstract 18.

5984A mass spectrometers. Ultraviolet (UV) spectra obtained on a Hewlett-Packard 8451-A and on a Cary 17 instrument. Microanalyses were performed by Canadian Microanalytical Services of Vancouver B.C. Elemental analysis of the target compounds were obtained whenever quantities were sufficient. The analyses agreed with the calculated values within 0.4%. In all other cases high-resolution mass spectra were obtained and purity was verified by chromatographic analyses (HPLC and TLC). HPLC analysis was carried out by direct injection of an aqueous solution of the nucleoside analogue (0.2 mg/mL) in a 10 μL injection loop on a high-performance liquid chromatograph (Varian model 2510, Walnut Creek, USA) using a prepacked Ultrasphere XL-ODS column (4.6 mm × 70 mm, sphere size 3.0 μm, Beckman). A flow rate of 5.0 mL/min was applied and the elution was monitored continuously at 254 nm via a UV-visible variable wavelength detector. Water and acetonitrile (both containing 0.05% trifluoroacetic acid) were used as eluants. The concentrations of the solvents varied depending on the compound being analyzed and on the type of run (gradient elution or isocratic) and ranged from 97:3 $H_2O$–$CH_3CN$ to 80:20 $H_2O$–$CH_3CN$.

**Biological Testing.** Samples for testing were supplied to Syntex Research. The protocol employed for *HIV testing* is as follows: Alex cells were preinfected with HIV for 3 h at 37 °C. Test samples were added to the infected cells in 3- or 5-fold dilutions, out four places for screening and eight places for confirmation. The test plates were incubated in the $CO_2$ at 37 °C for 8 days with a medium/sample change on day 4. Uninfected cells were exposed to the varying test dilutions to evaluate cytotoxicity. Reverse transcriptase levels were assayed on day 8 to determine if antiviral activity was present. The protocol for the *antiviral testing* is as follows: One day old confluent monolayers of HEp-2 cells (for herpes and $PI_3$ viruses) and MA-104 cells (for RSV) were preinfected for 1.5 h at 37 °C with HSV-2 (G and Lovelace strains), $PI_3$ (C243 strain), and RSV (long). Test samples were added to the infected cells in 3-fold dilutions out seven places and incubated at 37 °C for 72 h. Uninfected cells with test sample dilutions, but without virus, were used to evaluate cytotoxicity. A backtitration of the virus was preformed to make sure the amount of virus used was corrected. At the end of the 72-h incubation period the cells were evaluated for toxicity and/or virus presence by visual inspection for CPE.

**1-[[1,3-Bis(benzyloxy)-2-propoxy]methyl]-2-amino-3,4-bis(aminocarbonyl)-5-(methylthio)pyrrole (11).** Sodium hydride (8.22 g, 60% dispersion in oil, 0.21 mol) was added to a solution of 2-amino-3,4-bis(aminocarbonyl)-5-(methylthio)pyrrole (**6**) (40.0 g, 0.187 mol) in dry DMF (400 mL) in small portions under a nitrogen atmosphere at room temperature. The mixture was stirred for an additional 5 min after addition of the last portion of NaH before a solution of chloroethyl ether **7** (73.2 g, 90% purity as estimated by NMR, 0.21 mmol) in DMF was slowly added. The reaction mixture was stirred for 3 h at room temperature, then poured into 1 L of cold water, and extracted with chloroform (3 × 500 mL). The combined organic layers were washed with water (2 × 500 mL) and dried over anhydrous $Na_2SO_4$ and the solvent evaporated under reduced pressure to afford an oily residue. Chromatography on silica gel using first 1:1 hexane–ethyl acetate followed by 95:5 ethyl acetate–methanol afforded 29.3 g of **11** (31.5% yield): mp 139–141 °C; $R_f$ = 0.49 [TLC, silica, 95:5 ethyl acetate–methanol]. $^1H$ NMR [$CDCl_3$, 200 MHz]: δ 9.85 (b, 1 H, –CONH–), 8.05 (b, 1 H, –CONH–), 7.33 (m, 10 H, 2 × Ph), 6.36 (b, 2 H, $NH_2$), 5.80 (b, 1 H, –CONH–), 5.30 (b, 1 H, –CONH–), 4.51 (s, 4 H, 2 × $CH_2Ph$), 3.93 (m, 1 H, –CH–), 3.53 (d, 4 H, $J$ = 6 Hz, 2 × $CH_2OBn$), 2.21 (s, 3 H, $SCH_3$). Upon $D_2O$ exchange, the signal at 6.36 disappeared, and upon irradiation of the signal at 3.93, the signal at 3.53 collapsed to a singlet. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 168.5, 167.3, 148.1, 138.1, 128.2, 127.51, 127.46, 123.0, 115.2, 94.5, 75.4, 72.4, 71.1, 69.8, 21.0. UV (MeOH) $\lambda_{max}$: 304, 268.

**2-Amino-3,4-bis(aminocarbonyl)-5-(methylthio)-1-[[2-(benzyloxy)ethoxy]methyl]pyrrole (12).** Procedure as per compound **11**, i.e. pyrrole **6** (10 g, 46.7 mmol), sodium hydride (2.4 g, 60% dispersion in oil, 60 mmol), and chloromethyl ether **8** (13 g, 90%, 59 mmol) in a total of 130 mL of dry DMF gave 5.7 g of **12** (32% yield): mp 156–158 °C; $R_f$ = 0.38 [TLC, silica, 95:5 ethyl acetate–methanol]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 8.10 (b, 1 H, –CONH–), 7.76 (b, 1 H, –CONH–), 7.72 (b, 1 H, –CONH–), 7.29 (m, 5 H, Ph), 6.63 (b, 3 H, $NH_2$ and 1 –CONH–), 5.35 (s, 2 H, –$NCH_2O$–), 4.45 (s, 2 H, $CH_2Ph$), 3.60 (m, 4 H, –$CH_2CH_2$–), 2.19 (s, 3 H, $SCH_3$). UV (MeOH) $\lambda_{max}$: 304, 268 nm.

**2-Amino-3,4-bis(aminocarbonyl)-5-(methylthio)-1-[(*RS*)-2,3-*O*-isopropylidene-2,3-dihydroxypropyl]pyrrole (13).** Procedure as per **11** with the following exceptions: after the addition of the sodium hydride (1.96 g, 60% dispersion in oil, 49 mmol) to a solution of **6** (10 g, 46.7 mmol) in DMF (100 mL), a solution of tosylate **9** (14.7 g, 51.3 mmol) in DMF (50 mL) was added, and the total reaction mixture was stirred at 100 °C for 18 h. After this time period the reaction was cooled, the DMF evaporated under reduced pressure, and the remaining residue taken up in $CHCl_3$ (1 L). The chloroform extract was then washed with water, dried, and evaporated to dryness. Purification was as per **11** to give 9.5 g (62% yield) of **13** as a foam: $R_f$ = 0.33 [TLC, silica, 95:5 ethyl acetate–methanol]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 8.25 (b, 1 H, –CONH–), 7.74 (b, 2 H, –$CONH_2$–), 6.63 (b, 1 H, –CONH–), 6.45 (b, 2 H, $NH_2$), 4.34 (m, 1 H, –CH–), 4.07 (m, 3 H), 3.70 (m, 1 H), 2.19 (s, 3 H, $SCH_3$), 1.35 (s, 3 H, $CH_3$), 1.23 (s, 3 H, $CH_3$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 168.6, 167.4, 147.7, 122.2, 115.7, 109.0, 94.8, 74.1, 66.2, 44.5, 26.3, 25.2, 21.0. UV (MeOH) $\lambda_{max}$: 304, 268.

**2-Amino-3,4-bis(aminocarbonyl)-5-(methylthio)-1-[(*S*)-2,4-*O*-benzylidene-2,4-dihydroxybutyl]pyrrole (14).** Procedure as per compound **13**. Pyrrole **6** (7 g, 3.3 mmol), sodium hydride (1.37 g, 60% dispersion in oil, 3.4 mmol), and tosylate **10** (13 g, 3.7 mmol) in a total of 80 mL of DMF gave 6.3 g of **14** (51% yield) as a foam: $R_f$ = 0.36 [TLC, silica, 95:5 ethyl acetate–methanol]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 8.25 (b, 1 H, –CONH–), 7.72 (b, 2 H, $CONH_2$), 7.35 (m, 5 H, Ph), 6.63 (b, 1 H, –CONH–), 6.43 (b, 2 H, $NH_2$), 5.49 (s, 1 H, –OCHO–), 4.10 (m, 5 H), 2.12 (s, 3 H, $SCH_3$), 1.59 (m, 2 H, –$CH_2$–). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 168.8, 167.7, 148.0, 138.5, 128.9, 128.2, 126.2, 122.1, 116.2, 100.5, 94.8, 75.4, 65.9, 46.3, 28.1, 21.1. UV (MeOH) $\lambda_{max}$: 304, 268.

**[[1,3-Bis(benzyloxy)-2-propoxy]methyl]-2-amino-3,4-bis(aminocarbonyl)pyrrole (15).** Freshly prepared Raney nickel[19] [from 100 g of 50% aluminum nickel alloy (commercially available from Aldrich)] was added to a hot solution of compound **11** (15 g, 30 mmol) in absolute ethanol (1 L). The mixture was stirred at reflux (ca. 2 h) until no more of the starting material could be detected by TLC. The hot mixture was filtered through Celite, and the residue was extracted twice with boiling ethanol (2 × 500 mL). The combined filtrates were concentrated under vacuum. A white solid precipitated out from the concentrated solution, and 9.53 g of pure **15** was obtained after filtration and drying (75% yield): mp 140–142 °C; $R_f$ = 0.5 [TLC, silica, 9:1 ethyl acetate–methanol]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 9.80 (b, 1 H, –CONH–), 7.56 (b, 1 H, –CONH–), 7.29 (m, 10 H, 2 × Ph), 7.15 (s, 1 H, H-5), 7.05 (b, 1 H, –CONH–), 6.53 (b, 1 H, —CONH–), 6.38 (s, 2 H, $NH_2$), 5.28 (s, 2 H, –$NCH_2O$–), 4.45 (s, 4 H, 2 × $CH_2Ph$), 3.91 (m, 1 H, –CH–), 3.48 (m, 4 H, 2 × $CH_2OBn$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 168.08, 167.98, 147.4, 138.1, 128.2, 127.5, 119.7, 113.8, 93.9, 75.5, 74.1, 72.3, 69.6. UV (MeOH) $\lambda_{max}$: 292, 270 (s) nm.

**2-Amino-3,4-bis(aminocarbonyl)-1-[(2-(benzyloxy)ethoxy)methyl]pyrrole (16).** Procedure as per **15** with the following exceptions: Raney nickel (2 tsp) was added to a hot solution of **12** (10.3 g, 27.2 mmol) in ethanol (750 mL), and after 2 h at reflux the reaction mixture was filtered and evaporated. Recrystallization of the crude product from ethanol–ether gave 6.94 g of **16** (76% yield): mp dec at 105 °C; $R_f$ = 0.32 [TLC, silica, 95:5 ethyl acetate–methanol]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 9.75 (b, 1 H, –CONH–), 7.56 (b, 1 H, –CONH–), 7.30 (m, 5 H, Ph), 7.11 (s, 1 H, H-5), 7.03 (b, b, 1 H, –CONH–), 6.50 (b, 1 H, –CONH–), 6.46 (b, 2 H, $NH_2$), 5.18 (s, 2 H, –$NCH_2O$–), 4.55 (s, 2 H, $CH_2Ph$), 3.52 (m, 4 H, –$CH_2CH_2$–). UV (MeOH) $\lambda_{max}$: 290 nm.

**2-Amino-3,4-bis(aminocarbonyl)-1-[(*RS*)-2,3-*O*-isopropylidene-2,3-dihydroxypropyl]pyrrole (17).** Procedure as per **16** with the following exceptions: Raney nickel (2 tsp) was added to a hot solution of compound **13** (6 g, 18 mmol) in ethanol (300 mL). The crude reaction product was purified by flash chromatography (9:1 chloroform–methanol as eluting solvent), rather than recrystallization, to give 3.8 g of **17** (73% yield): mp dec at $T$ > 210 °C; $R_f$ = 0.45 [TLC, silica, 9:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 9.85 (b, 1 H, –CONH–), 7.53 (b,

1 H, -CONH-), 7.01 (s, 1 H, H-5), 7.01 (b, 1 H, -CONH-), 6.50 (b, 1 H, -CONH-), 6.35 (b, 2 H, $NH_2$), 4.28 (m, 1 H, -CH-), 4.00 (m, 1 H), 3.82 (m, 2 H), 3.64 (m, 1 H), 1.31 (s, 3 H, $CH_3$), 1.24 (s, 3 H, $CH_3$). UV (MeOH) $\lambda_{max}$: 292 nm.

**2-Amino-3,4-bis(aminocarbonyl)-1-[(*S*)-2,4-*O*-benzylidene-2,4-dihydroxybutyl]pyrrole (18).** Procedure as per 17 with the following exceptions: treatment of 14 (1.4 g, 3.6 mmol) with Raney nickel (2 tsp) in hot ethanol (100 mL) for 18 h gave, after purification by column chromatography, some recovered starting material 14 (0.257 g, 18% recovery) together with the desired product 18 (0.670 g, 54% yield) as an off-white foam: $R_f$ = 0.45 [TLC, silica, 9:1 methylene chloride–methanol]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 9.82 (b, -CONH-), 7.50 (b, -CONH-), 7.36 (m, Ph), 7.06 (s, 1 H, H-5), 7.02 (b, 1 H, -CONH-), 6.50 (b, -CONH-), 6.36 (s, $NH_2$), 5.53 (s, 1 H, -OCHO-), 4.18 (m, 2 H), 4.08 (m, 3 H), 1.60 (m, 2 H). The signals at 7.50 and 7.36 together integrate to 6 H, and those at 6.50 and 6.36, to 3 H. The signal at 6.36 exchanges in $D_2O$. $^{13}C$ NMR [$CDCl_3$, 75.4 MHz]: $\delta$ 168.47, 168.45, 148.4, 137.6, 129.3, 128.5, 125.9, 119.3, 101.5, 76.69, 60.3, 50.2, 27.9.

**[[1,3-Bis(benzyloxy)-2-propoxy]methyl]-2-amino-3,4-dicyano-5-(methylthio)pyrrole (19).** According to the procedure of ref 17, a mixture of compound 11 (3 g, 6 mmol) and tosyl chloride (3.45 g, 18 mmol) in a total of 40 mL of dry distilled pyridine was stirred at room temperature for 24 h. The mixture was poured into ice-water (200 mL), and after the mixture was stirred for 15 min, it was extracted with chloroform (3 × 300 mL). The combined organic extracts were washed with water (2 × 200 mL) and dried over $Na_2SO_4$, and the solvent was evaporated under reduced pressure. Flash chromatography of the crude product allowed separation of the desired product 19 from minor reaction components. 19 (1.42 g, 51% yield) was obtained as a white crystalline compound: mp 92–94 °C; $R_f$ = 0.49 [TLC, silica, 1:1 hexane–ethyl acetate]. $^1H$ NMR [$CDCl_3$, 200 MHz): $\delta$ 7.35 (m, 10 H, 2 × Ph), 5.46 (s, 2 H, $-NCH_2O-$), 4.79 (b, 2 H, $NH_2$), 4.51 (s, 4 H, 2 × $CH_2Ph$), 3.95 (m, 1 H, -CH-), 3.53 (d, 4 H, 2 × $CH_2OBn$), 2.27 (s, 3 H, $SCH_3$). IR (KBr): 2220, 2200 $cm^{-1}$ (2 × CN).

**2-Amino-3,4-dicyano-5-(methylthio)-1-[(2-(benzyloxy)-ethoxy)methyl]pyrrole (20).** Procedure as per compound 19. Compound 12 (3 g, 7.9 mmol) and tosyl chloride (4.5 g, 24 mmol) in pyridine (60 mL) gave, after workup and purification by flash chromatography, compound 20 (1.44 g, 53% yield) as an oil: $R_f$ = 0.42 [TLC, silica, 2:3 hexane–ethyl acetate]. $^1H$ NMR [$CDCl_3$, 200 MHz): $\delta$ 7.32 (m, 5 H, Ph), 5.04 (s, 2 H, $-NCH_2O-$), 4.78 (b, 2 H, $NH_2$), 4.52 (s, 2 H, $CH_2Ph$), 3.67 (s, 4 H, $-CH_2CH_2-$), 2.33 (s, 3 H, $SCH_3$). IR (Nujol): 2228, 2206 $cm^{-1}$ (2 × CN). UV (MeOH) $\lambda_{max}$: 296, 255 nm.

**2-Amino-3,4-dicyano-5-(methylthio)-1-[(*RS*)-2,3-*O*-isopropylidene-2,3-dihydroxypropyl]pyrrole (21).** Procedure as per compound 19. Compound 13 (3.4 g, 10.3 mmol) and tosyl chloride (6.0 g, 31 mmol) in pyridine (80 mL) gave, after workup and purification by flash chromatography, 1.84 g of 21 (60% yield): mp 145–146 °C; $R_f$ = 0.55 [TLC, silica, 2:3 hexane–ethyl acetate]. $^1H$ NMR [$CDCl_3$, 200 MHz]: $\delta$ 4.93 (b, 2 H, $NH_2$), 4.32–4.25 (m, 2 H), 4.20–4.13 (m, 1 H), 4.06–3.96 (m, 1 H), 3.66–3.58 (m, 1 H), 2.37 (s, 3 H, $SCH_3$), 1.38 (s, 3 H, $CH_3$), 1.35 (s, 3 H, $CH_3$). IR (KBr): 2229, 2207 $cm^{-1}$ (2 × CN). UV (MeOH) $\lambda_{max}$: 297, 254 nm.

**2-Amino-3,4-dicyano-5-(methylthio)-1-[(*S*)-2,4-*O*-benzylidene-2,4-dihydroxybutyl]pyrrole (22).** Procedure as per compound 19. Compound 14 (3 g, 7.7 mmol) and tosyl chloride (4.5 g, 24 mmol) in pyridine (60 mL) gave, after workup and purification, 1.60 g of 22 (59% yield) as a foam: $R_f$ = 0.51 [TLC, silica, 3:7 hexane–ethyl acetate]. $^1H$ NMR [$CDCl_3$, 200 MHz]: $\delta$ 7.78 (s, 5 H, Ph), 5.47 (s, 1 H, -OCHO-), 4.72 (b, 2 H, $NH_2$), 4.20 (m, 5 H), 2.39 (s, 3 H, $SCH_3$), 1.80 (m, 2 H, $CH_2$). IR (Nujol): 2228, 2208 $cm^{-1}$ (2 × CN). UV (MeOH) $\lambda_{max}$: 297, 254 nm.

**[[1,3-Bis(benzyloxy)-2-propoxy]methyl]-2-amino-3,4-dicyanopyrrole (23).** Procedure as per compound 19. Compound 15 (3 g, 6.6 mmol) and tosyl chloride (3.8 g, 20 mmol) in pyridine (80 mL) gave, after workup and purification by flash chromatography, compound 23 (1.40 g, 50% yield) as an oil: $R_f$ = 0.44 [TLC, silica, 1:1 hexane–ethyl acetate]. $^1H$ NMR [$CDCl_3$, 200 MHz]: $\delta$ 7.35 (m, 10 H, 2 × Ph), 6.65 (s, 1 H, H-5), 5.26 (s, 2 H, $-NCH_2O-$), 4.55 (b, 2 H, $NH_2$), 4.49 (s, 4 H, 2 × $CH_2Ph$), 3.85 (m, 1 H, -CH-), 3.53 (d, 4 H, $J$ = 5.4 Hz, 2 × $CH_2OBn$). IR (Nujol): 2226, 2212 $cm^{-1}$ (2 × CN).

**2-Amino-3,4-dicyano-1-[[2-(benzyloxy)ethoxy]methyl]-pyrrole (24).** Procedure as per compound 19. Compound 16 (3 g, 9.0 mmol) and tosyl chloride (5.2 g, 27 mmol) in 60 mL of pyridine gave, after workup and purification by flash chromatography and by recrystallization from ethanol–acetate, 1.40 g of 24 (52% yield): mp 64–66 °C; $R_f$ = 0.47 [TLC, silica, 3:7 hexane–ethyl acetate]. $^1H$ NMR [$CDCl_3$, 200 MHz]: $\delta$ 7.35 (nm, 5 H, Ph), 6.70 (s, 1 H, H-5), 5.19 (s, 2 H, $-NCH_2O-$), 4.52 (b, 2 H, $NH_2$), 4.49 (s, 2 H, $CH_2Ph$), 3.65 (s, 4 H, $-CH_2CH_2-$). IR (KBr): 2228, 2206 $cm^{-1}$ (2 × CN).

**2-Amino-3,4-dicyano-1-[(*RS*)-2,3-*O*-isopropylidene-2,3-dihydroxypropyl]pyrrole (25).** Procedure as per compound 19. Compound 17 (2 g, 7.1 mmol) and tosyl chloride (4.0 g, 21 mmol) in pyridine (70 mL) gave, after workup and purification by flash chromatography and by recrystallization from ethanol–acetate, 890 mg of 25 (51% yield): mp 178–180 °C; $R_f$ = 0.47 [TLC, silica, 3:7 hexane–ethyl acetate]. $^1H$ NMR [$CDCl_3$, 200 MHz]: $\delta$ 7.17 (s, 1 H, H-5), 6.51 (b, 2 H, $NH_2$), 4.25 (m, 1 H, -CH-), 3.99 (m, 2 H), 3.88 (m, 2 H), 1.29 (s, 3 H, $-CH_3$), 1.22 (s, 3 H, $CH_3$). IR (KBr): 2229, 2202 $cm^{-1}$ (2 × CN).

**2-Amino-3,4-dicyano-1-[(*S*)-2,4-*O*-benzylidene-2,4-dihydroxybutyl]pyrrole (26).** Procedure as per compound 19. Compound 18 (0.5314 g, 1.543 mmol) and tosyl chloride (0.936 g, 4.91 mmol) in pyridine (20 mL) gave, after workup and flash chromatography, 0.2006 g of compound 26 (42% yield) as a foam: $R_f$ = 0.13 [TLC, silica, 2:3 hexane–ethyl acetate]. $^1H$ NMR [$CDCl_3$, 300 MHz]: $\delta$ 7.40 (s, 5 H, Ph), 6.74 (s, 1 H, H-5), 5.50 (s, 1 H, -OCHO-), 4.54 (s, 2 H, $NH_2$), 4.33 (ddd, 1 H, $J$ = 3.9, 5.1, 11.7 Hz), 4.22 (m, 1 H), 4.08–3.83 (m, 3 H), 1.84 (m, 1 H), 1.59 (m, 1 H). $^{13}C$ NMR [$CDCl_3$, 75.4 MHz]: $\delta$ 147.5, 137.3, 129.5, 128.6, 125.7, 124.5, 114.0, 113.7, 101.6, 92.7, 76.62, 66.1, 51.3, 27.4.

**2-Amino-5-(aminocarbonyl)-6-(methylthio)-7-[[1,3-bis-(benzyloxy)-2-propoxy]methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (27).** To a sample of compound 11 (1.716 g, 3.44 mmol) was added sodium hydroxide (0.89 g, 22.2 mmol) and dry methanol (40 mL). The mixture was stirred at room temperature for ca. 30 min under dry conditions until all the NaOH had been consumed and was then transferred to a stainless steel reaction vessel. The flask was rinsed with an additional 10 mL of methanol, and the washings were transferred to the bomb. $CS_2$ (1.5 mL, 1.90 g, 24.9 mmol) was added, and the bomb was then sealed and heated in an oil bath at 145 °C overnight. The vessel was cooled to 0 °C before opening and transferring the bright orange solution to a round-bottom flask. The methanol was evaporated under reduced pressure, and to the residue was added a 1:1 mixture of methanol–water (40 mL). This mixture was cooled to 0 °C, and $H_2O_2$ (5.3 mL, 30% in $H_O$, 45.9 mmol) was added dropwise over 20 min. The reaction mixture was stirred at 0 °C for 2 h and then saturated with ammonia (bubbled $NH_3$ through the cooled solution for 20 min). The mixture was then transferred back into the bomb and the vessel sealed and heated at 120 °C overnight. Evaporation of the methanol under reduced pressure, followed by evaporation of the water on a lyopholizer (so as to circumvent the difficulties encountered with foaming and bumping of the aqueous slurry) gave a pale orange solid. DMF (ca. 150 mL) was added, and the insoluble material was filtered off and discarded. Silica gel was added to the filtrate and the solvent evaporated so as to effect adsorption of the compounds onto the silica gel. The silica gel was loaded onto a prepacked column of silica gel (5 × 20 cm), and the column was eluted with 10% methanol in ethyl acetate followed by 20% methanol in ethyl acetate. A second chromatography using 5% methanol in ethyl acetate as the eluting solvent, followed by recrystallization from ethanol gave 777 mg of 27 (1.48 mmol, 43% yield) as a white crystalline solid: mp 153–155 °C; $R_f$ = 0.42 [TLC, silica, 9:1 ethyl acetate–methanol]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.98 (s, 1 H, NH), 9.89 (s, b, 1 H, -CONH-), 7.26 (m, 10 H, 2 × Ph), 7.03 (s, b, 1 H, -CONH-), 6.55 (s, b, 2 H, $NH_2$), 5.64 (s, 2 H, $-NCH_2O-$), 4.41 (s, 4 H, 2 × $CH_2Ph$), 4.06 (m, 1 H, -CH-), 3.54–3.34 [m, 4 H, $-CH_2O$; overlapping dd at 3.48 ($J$ = 4.5, 10.5 Hz) and 3.38 ($J$ = 5.9, 10.6 Hz)], 2.35 (s, 3 H, $SCH_3$). Upon $D_2O$ exchange the signals at 10.98 and 6.55 disappear and those at 9.89 and 7.03 are diminished in intensity. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 163.5, 159.7, 153.0, 152.0, 138.2, 130.3, 128.2, 127.3, 117.2, 96.9, 76.3, 72.2,

70.2, 69.7, 19.4. MS (low-resolution CI, $NH_3$) $m/z$: 524 [100, M ($C_{26}H_{29}N_5O_3S$) + H]. UV (MeOH) $\lambda_{max}$ ($\epsilon$): 312 (8360), 284 (10700), 236 (17900).

**2-Amino-5-(aminocarbonyl)-6-(methylthio)-7-[(2-(benzyloxy)ethoxy)methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (28).** Procedure as per compound **27**. Compound **12** (1 g, 2.6 mmol), sodium hydroxide (0.634 g, 15.8 mmol), methanol (50 mL), and $CS_2$ (1.206 g, 15.8 mmol) were used in the first step. MeOH–$H_2O$ (1:1, 70 mL) and hydrogen peroxide (3 mL), 30% in $H_2O$, 26.4 mmol) were used for the subsequent steps. After flash chromatography, 576 mg of **28** (54% yield) was obtained: mp 221–224 °C. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 11.00 (b, 1 H, –NH–), 9.88 (b, 1 H, –CONH–), 7.27 (m, 5 H, Ph), 7.05 (b, 1 H, –CONH–), 6.58 (b, 2 H, $NH_2$), 5.52 (s, 2 H, $-NCH_2O-$), 4.41 (s, 2 H, $CH_2Ph$), 3.50 (m, 4 H, $-CH_2CH_2-$), 2.34 (s, 3 H, $SCH_3$). UV (MeOH) $\lambda_{max}$ = 310, 280, 233 nm.

**2-Amino-5-(aminocarbonyl)-6-(methylthio)-7-[(*RS*)-2,3-*O*-isopropylidene-2,3-dihydroxypropyl]pyrrolo[2,3-*d*]pyrimidin-4-one (29).** Procedure as per compound **27**. Compound **13** (1.49 g, 4.54 mmol), sodium hydroxide (1.08 g, 27.0 mmol), MeOH (40 mL), and $CS_2$ (2.0 mL, 2.5 g, 33 mmol) were used in the first step. MeOH–$H_2O$ (1:1, 40 mL) and hydrogen peroxide (6.3 mL, 30% in $H_2O$, 1.9 g, 55 mmol) were used in subsequent steps. After flash chromatography, 445 mg of pure **29** (1.26 mmol, 28% yield) and 209 mg of a slightly impure sample of **29** were obtained: mp 254–256 °C dec; $R_f$ = 0.56 [TLC, silica, 20% MeOH in $CHCl_3$]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.93 (s, 1 H, NH), 9.91 (s, 1 H, –CONH–), 6.99 (s, 1 H, –CONH–), 6.53 (s, 2 H, $NH_2$), 4.30 (m, 3 H) 3.95 (dd, 1 H, $J$ = 6.2, 8.6 Hz), 3.82 (dd, 1 H, $J$ = 4.9, 8.5 Hz), 2.37 (s, 3 H, $SCH_3$), 1.34 (s, 3 H, $CH_3$), 1.20 (s, 3 H, $CH_3$). The signals at 10.93, 9.91, 6.99, and 6.53 exchange with $D_2O$. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 163.5, 159.6, 152.7, 151.4, 130.9, 116.1, 108.9, 97.0, 73.8, 66.4, 44.6, 26.5, 25.1, 19.4. MS [high-resolution EI] $m/z$: 353.1183, $M^+$, calcd for M ($C_{14}H_{19}N_5O_4S$), 353.1158. UV (MeOH) $\lambda_{max}$ ($\epsilon$) = 316 (7420), 282 (9140), 242 (17400).

**2-Amino-5-(aminocarbonyl)-6-(methylthio)-7-[(*S*)-2,4-*O*-benzylidene-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidin-4-one (30).** Procedure as per compound **27**. Compound **14** (2.5 g, 6.4 mmol), sodium hydroxide (1.56 g, 39 mmol), methanol (40 mL) and $CS_2$ (2.6 mL, 3.3 g, 43 mmol) were used in the first step. MeOH–$H_2O$ (1:1, 40 mL) and hydrogen peroxide (9.2 mL, 30% in $H_2O$, 2.76 g, 81 mmol) were used in subsequent steps. Purification of the reaction products by column chromatography gave 821 mg of compound **30** (1.98 mmol, 31% yield) as a pale pink solid: mp 238–240 °C dec; $R_f$ = 0.54 [TLC, silica, 20% MeOH in $CH_2Cl_2$]. $^1H$ NMR [DMSO-$d_6$, 300 MHz]: $\delta$ 10.95 (s, 1 H, NH), 9.933 (d, 1 H, $J$ = 1.2 Hz, –CONH–), 7.34 (m, 5 H, Ph), 6.978 (d, 1 H, $J$ = 2.0 Hz, –CONH–), 6.58 (s, 2 H, $NH_2$), 5.47 (s, 1 H, –OCHO–), 4.33 (dd, 1 H, $J$ = 9.1, 15.4 Hz), 4.25 (m, 2 H), 4.15 (m, 1 H), 3.89 (m, 1 H), 2.33 (s, 3 H, $SCH_3$), 1.75 (m, 1 H), 1.42 (m, 1 H). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 163.5, 159.6, 152.7, 151.6, 138.5, 131.1, 128.5, 127.9, 126.1, 116.0, 100.1, 96.9, 74.7, 65.8, 45.7, 28.4, 19.4. MS [low-resolution EI] $m/z$: nonvolatile. UV (MeOH) $\lambda_{max}$ ($\epsilon$) = 314 (6500), 284 (8000), 240 (15000).

**2-Amino-5-(aminocarbonyl)-7-[[1,3-bis(benzyloxy)-2-propoxy]methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (31).** Procedure as per compound **27**. Compound **15** (3 g, 6.63 mmol), sodium hydroxide (1.33 g, 33 mmol), methanol (45 mL), and $CS_2$ (2.5 g, 33 mmol) were used in the first step. MeOH–$H_2O$ (1:1, 50 mL) and 30% $H_2O_2$ in $H_2O$ (7.6 mL, 66 mmol) were used for the subsequent steps. After flash chromatography 2.41 g of **31** (76% yield) was obtained: mp dec at $T$ > 230 °C; $R_f$ = 0.39 [TLC, silica, 9:1 $CH_2Cl_2$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.93 (b, 1 H, NH), 9.52 (b, 1 H, –CONH–), 7.46 (s, 1 H, H-6), 7.25 (m, 10 H, 2 × Ph), 7.08 (b, 1 H, –CONH–), 6.48 (b, 2 H, $NH_2$), 5.46 (s, 2 H, $-NCH_2O-$), 4.39 (s, 4 H, 2 × $CH_2Ph$), 4.05 (m, 1 H, –CH–), 3.40 (m, 4 H, 2 × $CH_2OBn$). UV (MeOH) $\lambda_{max}$ = 294, 269 nm.

**2-Amino-5-(aminocarbonyl)-7-[(2-(benzyloxy)ethoxy)-methoxy]pyrrolo[2,3-*d*]pyrimidin-4-one (32).** Procedure as per compound **27**. Compound **16** (1.5 g, 4.52 mmol), sodium hydroxide (1.084 g, 27.12 mmol), methanol (70 mL), and $CS_2$ (2.06 g, 27.12 mmol) were used in the first step. MeOH–$H_2O$ (1:1, 80 mL) and 30% $H_2O_2$ (6.14 mL, 30% in $H_2O$, 54.2 mmol) were used in subsequent steps. After flash chromatography 903 mg of compound **32** (56% yield) was obtained: mp dec at $T$ > 230 °C; $R_f$ = 0.28 [TLC, silica, 9:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.97 (s, 1 H, NH), 9.545 (d, 1 H, $J$ = 2.8 Hz, –CONH–), 7.46 (s, 1 H, H-6), 7.28 (m, 5 H, Ph), 7.13 (d, 1 H, $J$ = 2.8 Hz, –CONH–), 6.53 (b, 2 H, $NH_2$), 5.38 (s, 2 H, $-NCH_2O-$), 4.43 (s, 2 H, $CH_2Ph$), 3.61–3.49 (m, 4 H, $-CH_2CH_2-$). UV (MeOH) $\lambda_{max}$ = 294, 260 nm.

**2-Amino-5-(aminocarbonyl)-7-[(*RS*)-2,3-*O*-isopropylidene-2,3-dihydroxypropyl]pyrrolo[2,3-*d*]pyrimidin-4-one (33).** Procedure as per compound **27**. Compound **17** (1.09 g, 3.86 mmol), sodium hydroxide 0.961 g, 24.0 mmol), methanol (48 mL), and $CS_2$ (1.4 mL, 1.8 g, 23.3 mmol) were used in the first step. MeOH–$H_2O$ (1:1, 50 mL) and 30% $H_2O_2$ (4.4 mL, 1.38 g, 38.8 mmol) were used for subsequent steps. After flash chromatography 414 mg of compound **33** (1.35 mmol, 35% yield) was obtained as a very pale pink solid: mp 266–270 °C dec; $R_f$ = 0.15 [TLC, silica, 9:1 $CH_2Cl_2$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.89 (s, 1 H, NH), 9.50 (b*, 1 H, –CONH–), 7.35 (s, 1 H, H-6), 7.05 (b*, 1 H, –CONH–), 6.47 (s, 2 H, $NH_2$), 4.37 (m, 1 H), 4.38–3.90 (m, 3 H, contains a dd at 3.96 with $J$ = 6.4, 8.4 Hz ("1 H")), 3.69 (dd, 1 H, $J$ = 5.8, 8.5 Hz), 1.32 (s, 3 H, $CH_3$), 1.23 (s, 3 H, $CH_3$). The amide NH signals* appear to be doublets with small coupling constants (ca. 2 Hz) whose values were not well resolved. Upon $D_2O$ exchange the signals at 10.89 and 6.47 disappear. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 163.9, 160.1, 152.7, 151.6, 126.9, 113.7, 108.9, 95.9, 73.9, 66.1, 46.6, 26.6, 25.1. MS [low-resolution EI] $m/z$: 307 ($M^+$, 3.4). UV (MeOH) $\lambda_{max}$ ($\epsilon$) = 298 (8920), 274 (8160), 234 (19000).

**2-Amino-5-(aminocarbonyl)-7-[(*S*)-2,4-*O*-benzylidene-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidin-4-one (34).** Procedure as per compound **27**. Compound **18** (975 mg, 2.83 mmol), sodium hydroxide (0.71 g, 17.8 mmol), methanol (30 mL), and $CS_2$ (20 mmol) were used in the first step. MeOH–$H_2O$ (1:1, 30 mL) and 30% $H_2O_2$ (4.1 mL, 1.23 g, 36 mmol) were used in subsequent steps. After flash chromatography, 486 mg of **34** (1.315 mmol, 46.5% yield) was obtained as an off-white solid: mp 278–281 °C dec; $R_f$ = 0.54 [TLC, silica, 4:1 $CH_2Cl_2$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.86 (s, 1 H, NH), 9.48 (d, 1 H, $J$ = 2.8 Hz, –CONH–), 7.34 (m, 6 H, Ph + H-6), 7.05 (d, 1 H, $J$ = 2.8 Hz, –CONH–), 6.47 (s, 2 H, $NH_2$), 5.50 (s, 1 H, –OCHO–), 4.40–4.00 (m, 4 H), 4.00–3.80 (m, 1 H, –CH–), 1.82–1.2 (m, 2 H, $-CH_2-$). Upon prolonged exposure to $D_2O$ the signals at 10.86, 9.48, 7.05, and 6.47 disappeared. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 164.0, 160.2, 152.7, 151.8, 138.6, 128.6, 128.0, 127.1, 126.0, 113.7, 100.0, 95.9, 74.6, 65.7, 48.1, 28.1. MS [high-resolution EI] $m/z$: 369.1367, calcd for M ($C_{18}H_{19}N_5O_4$), 369.1436. UV (MeOH) $\lambda_{max}$ ($\epsilon$) = 298 (7900), 272 (7310), 236 (15800).

**2-Amino-5-cyano-6-(methylthio)-7-[[1,3-bis(benzyloxy)-2-propoxy]methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (35).** According to the procedure of ref 17, a mixture of compound **27** (345 mg, 0.659 mmol) and tosyl chloride (188 mg, 0.986 mmol) in dry pyridine (16 mL) was stirred at room temperature overnight under an argon atmosphere. Water was added (ca. 50 mL), and the mixture was extracted with $CHCl_3$ (3 × ca. 50 mL). The combined extracts were washed with water, dried over anhydrous $Na_2SO_4$, and concentrated to ca. 50 mL). Silica gel was added, and the solvent was evaporated so as to effect adsorption of the compounds onto the silica gel. The gel was loaded onto a prepared column (3 × 20 cm of silica gel packed with 5% MeOH in EtOAc) and eluted with 5% MeOH in EtOAc to afford 249.6 mg of **35** (0.4936 mmol, 75% yield) as a white foam. Recrystallization from ethanol provided a white crystalline solid: mp 132–133 °C; $R_f$ = 0.45 [TLC, silica, 5% MeOH in EtOAc]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.87 (s, 1 H, NH), 7.27 (m, 10 H, 2 × Ph), 6.64 (s, b, 2 H, $NH_2$), 5.55 (s, 2 H, $-NCH_2O-$), 4.41 (s, 4 H, 2 × $CH_2Ph$), 4.09 (m, 1 H, –CH–), 3.54–3.34 (m, 4 H, 2 × $-CH_2-$ overlapping dd at 3.49 ($J$ = 4.4, 10.5 Hz) and 3.39 ($J$ = 6.0, 10.5 Hz)), 2.39 (s, 3 H, $SCH_3$). Upon $D_2O$ exchange the signals at 10.87 and 6.63 disappear. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 156.6, 154.3, 152.2, 138.2, 133.7, 128.2, 127.4, 127.2, 114.5, 99.3, 94.3, 76.8, 72.2, 71.1, 69.6, 20.0. MS [low-resolution CI, $NH_3$] $m/z$: 506 (100), M ($C_{26}H_{27}N_5O_4S$) + H. UV (MeOH) $\lambda_{max}$ ($\epsilon$) = 307 (11000)*, 284 (13100), 232 (19000) nm. The $\lambda$ and $A$ values for the shoulder peak* were determined by extrapolation.

**2-Amino-5-cyano-6-(methylthio)-7-[(2-(benzyloxy)ethoxy)methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (36).** Procedure

as per compound **35**. Compound **28** (1.3 g, 3.22 mmol) and tosyl chloride (921 mg, 4.83 mmol) in pyridine (45 mL) gave, after workup and flash chromatography, 944 mg of **36** (76% yield): mp 183–184 °C. $^1$H NMR [DMSO-$d_6$, 200 MHz]: δ 10.87 (s, 1 H, NH), 7.30 (m, 5 H, Ph), 6.25 (b, 2 H, $NH_2$), 5.58 (s, 2 H, $-NCH_2O-$), 4.51 (s, 2 H, $CH_2Ph$), 3.75–3.57 (m, 4 H, $-CH_2CH_2-$), 2.48 (s, 3 H, $SCH_3$). IR (KBr): 2238 cm$^{-1}$ (CN). UV (MeOH) $\lambda_{max}$ = 305, 280, 230 nm.

**2-Amino-5-cyano-6-(methylthio)-7-[(*RS*)-2,3-*O*-isopropylidene-2,3-dihydroxypropyl]pyrrolo[2,3-*d*]pyrimidin-4-one (37).** Procedure as per compound **35**. Compound **29** (322 mg, 0.939 mmol) and tosyl chloride (280 mg, 1.468 mmol) in pyridine (20 mL) gave, after workup and flash chromatography, 245 mg of **37** (0.731 mmol, 78% yield) as a very pale pink solid: mp 269–271 °C dec; $R_f$ = 0.35 [TLC, silica, 9:1 $CHCl_3$–MeOH]. $^1$H NMR [DMSO-$d_6$, 200 MHz]: δ 10.85 (s, 1 H, NH), 6.62 (s, 2 H, $NH_2$), 4.43 (m, 1 H), 4.18 (m, 2 H), 4.00 (dd, $J$ = 8.8, 6.4 Hz, 1 H), 3.84 (dd, $J$ = 8.7, 5.2 Hz, 1 H), 2.44 (s, 3 H, $SCH_3$), 1.33 (s, 3 H, $CH_3$), 1.21 (s, 3 H, $CH_3$). Upon $D_2O$ exchange the signals at 10.85 and 6.62 disappear. $^{13}$C NMR [DMSO-$d_6$, 75.4 MHz]: δ 156.6, 154.0, 151.5, 134.4, 114.7, 109.0, 99.6, 92.7, 73.4, 66.3, 45.7, 26.4, 25.0, 19.9. UV (MeOH) $\lambda_{max}$ (ε) = 310 (10000), 282 (12100), 236 (21600).

**2-Amino-5-cyano-6-(methylthio)-7-[(*S*)-2,4-*O*-benzylidene-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidin-4-one (38).** Procedure as per compound **35**. Compound **30** (436.8 mg, 1.05 mmol) and tosyl chloride (292 mg, 1.652 mmol) in pyridine (20 mL) gave, after workup and flash chromatography, 320 mg of **38** (0.805 mmol, 76.6% yield) as a very pale pink solid: mp 233–234 °C; $R_f$ = 0.35 [TLC, silica, 9:1 $CH_2Cl_2$–MeOH]. $^1$H NMR [DMSO-$d_6$, 200 MHz]: δ 10.83 (s, 1 H, NH), 7.31 (s, 5 H, Ph), 6.64 (s, 2 H, $NH_2$), 5.46 (s, 1 H, –OCHO–), 4.40–4.10 (m, 4 H), 3.88 (m, 1 H), 2.33 (s, 3 H, $SCH_3$), 1.9–1.4 (m, 2 H). $^{13}$C NMR [DMSO-$d_6$, 75.4 MHz]: δ 156.6, 154.1, 151.7, 138.4, 134.6, 128.6, 127.9, 126.0, 114.7, 100.1, 99.6, 92.7, 74.3, 65.7, 46.9, 28.4, 19.9. MS [high-resolution EI] $m/z$: 397.1125, M$^+$; calcd for M ($C_{19}H_{19}N_5O_3S$), 397.1208. UV (MeOH) $\lambda_{max}$ (ε) = 310 (7850), 282 (9860), 238 (16700).

**2-Amino-5-cyano-7-[[1,3-bis(benzyloxy)-2-propoxy]methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (39).** Procedure as per compound **35**. Compound **31** (1.001 g, 2.096 mmol) and tosyl chloride (780 mg, 4.095 mmol) in pyridine (40 mL) gave, after workup and flash chromatography, 749 mg of **39** (71% yield): mp 158–160 °C. $^1$H NMR [DMSO-$d_6$, 200 MHz]: δ 10.81 (b, 1 H, NH), 7.81 (s, 1 H, H-6), 7.30 (m, 10 H, 2 × Ph), 6.57 (b, 2 H, $NH_2$), 5.45 (s, 2 H, $-NCH_2O-$), 4.41 (s, 4 H, 2 × $CH_2Ph$), 4.01 (m, 1 H, –CH–), 3.43 (m, 4 H, 2 × $CH_2OBn$). IR (KBr): 2232 cm$^{-1}$ (CN).

**2-Amino-5-cyano-7-[(2-(benzyloxy)ethoxy)methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (40).** Procedure as per compound **35**. Compound **32** (1 g, 2.8 mmol) and tosyl chloride (800 mg, 4.2 mmol) in pyridine (65 mL) gave, after workup and flash chromatography, 570 mg of **40** (60% yield): mp 129–131 °C; $R_f$ = 0.40 [TLC, silica, 9:1 $CHCl_3$–MeOH]. $^1$H NMR [DMSO-$d_6$, 200 MHz]: δ 10.64 (s, 1 H, NH), 7.80 (s, 5 H, H-6), 7.26 (m, 5 H, Ph), 6.69 (b, 2 H, $NH_2$), 5.33 (s, 2 H, $-NCH_2O-$), 4.41 (s, 2 H, $CH_2Ph$), 3.62–3.36 (m, 4 H, $-CH_2CH_2-$). IR (KBr) 2225 cm$^{-1}$ (CN).

**2-Amino-5-cyano-7-[(*RS*)-2,3-*O*-isopropylidene-2,3-dihydroxypropyl]pyrrolo[2,3-*d*]pyrimidin-4-one (41).** Procedure as per compound **35**. Compound **33** (235 mg, 0.765 mmol) and tosyl chloride (225 mg, 1.18 mmol) in pyridine (25 mL) gave, after workup and flash chromatography, 164 mg of **41** (0.567 mmol, 74% yield): mp 263–265 °C dec; $R_f$ = 0.28 [TLC, silica, 9:1 $CHCl_3$–MeOH]. $^1$H NMR [DMSO-$d_6$, 200 MHz]: δ 10.77 (s, b, 1 H, NH), 7.65 (s, 1 H, H-6), 6.54 (s, 2 H, $NH_2$), 4.38 (m, 1 H), 4.06 (m, 2 H), 3.97 (dd, 1 H, $J$ = 6.4, 8.6 Hz), 3.72 (dd, 1 H, $J$ = 5.3, 8.6 Hz), 1.30 (s, 3 H, $CH_3$), 1.23 (s, 3 H, $CH_3$). Upon $D_2O$ exchange the signals at 10.77 and 6.54 disappear. $^{13}$C NMR [DMSO-$d_6$, 75.4 MHz]: δ 157.3, 153.8, 150.9, 130.9, 115.5, 108.9, 98.6, 84.8, 73.5, 66.0, 47.0, 26.5, 25.1. MS [high-resolution EI] $m/z$: 289.1175, calcd for M ($C_{13}H_{15}N_5O_3$), 289.1175. UV (MeOH) $\lambda_{max}$ (ε) = 290 (9340), 270 (11400), 234 (22700).

**2-Amino-5-cyano-7-[(*S*)-2,4-*O*-benzylidene-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidin-4-one (42).** Procedure as per compound **35**. Compound **34** (296.9 mg, 0.8037 mmol) and tosyl chloride (242 mg, 1.269 mmol and 150 mg, 0.787 mmol) in pyridine (15 mL) gave, after workup and flash chromatography, 241.5 mg of **42** (0.6873 mmol, 85% yield) as a very pale pink solid: mp 227–232 °C; $R_f$ = 0.49 [TLC, silica, 4:1 $CH_2Cl_2$–MeOH]. $^1$H NMR [DMSO-$d_6$, 200 MHz]: δ 10.76 (s, b, 1 H, NH), 7.66 (s, 1 H, H-6), 7.35 (m, 5 H, Ph), 6.56 (s, b, 2 H, $NH_2$), 5.51 (s, 1 H, –OCHO–), 4.30–4.05 (m, 4 H), 4.00–3.80 (m, 1 H), 1.80–1.20 (m, 2 H). Upon $D_2O$ exchange the signals at 10.76 and 6.56 disappear. $^{13}$C NMR [DMSO, 75.4 MHz]: δ 157.3, 153.8, 151.0, 138.5, 131.0, 128.6, 128.0, 125.9, 115.5, 99.9, 98.6, 84.7, 74.2, 65.7, 48.5, 28.0. UV (MeOH) $\lambda_{max}$ (ε) = 290 (8050), 270 (9980), 236 (16700).

**4-Amino-5-cyano-6-(methylthio)-7-[[1,3-bis(benzyloxy)-2-propoxy]methyl]pyrrolo[2,3-*d*]pyrimidine (59).** The procedure of ref 10a was followed, i.e. a mixture of compound **19** (930 mg, 2.01 mmol) and triethyl orthoformate (30 mL) was stirred at reflux until all of the starting material had reacted (ca. 48 h). The volatile material was evaporated at reduced pressure, and the residue was dissolved in ethanol (30 mL, absolute) which had previously been saturated with ammonia. The reaction mixture was stirred at room temperature for 4 h and then concentrated to ca. 5 mL under reduced pressure. The precipitate was filtered and washed with a little ethanol to give, after drying, 896 mg of **59** (91% yield): mp 93–95 °C; $R_f$ = 0.55 [TLC, silica, ethyl acetate]. $^1$H NMR [$CDCl_3$, 200 MHz]: δ 8.24 (s, 1 H, H-2), 7.29 (m, 10 H, –2 × Ph), 6.92 (b, 2 H, $NH_2$), 5.75 (s, 2 H, $-NCH_2O-$), 4.36 (s, 4 H, 2 × $CH_2Ph$), 4.01 (m, 1 H, –CH–), 3.44 (d, 4 H, 2 × $CH_2OBn$), 2.51 (s, 3 H, $SCH_3$). IR (KBr) 2220 cm$^{-1}$ (CN). UV (EtOH) $\lambda_{max}$ = 297, 230 nm.

**4-Amino-5-cyano-6-(methylthio)-7-[(2-(benzyloxy)ethoxy)methyl]pyrrolo[2,3-*d*]pyrimidine (60).** Procedure as per compound **59**. Compound **20** (1 g, 3.37 mmol) gave 980 mg of **60** after recrystallization from ethanol (91% yield): mp 119–121 °C; $R_f$ = 0.37 [TLC, silica, ethyl acetate]. $^1$H NMR [$CDCl_3$, 200 MHz]: δ 8.34 (s, 1 H, H-2), 7.28 (m, 5 H, Ph), 5.76 (s, 2 H, $-NCH_2O-$), 5.58 (b, 2 H, $NH_2$), 4.48 (s, 2 H, $CH_2Ph$), 3.62 (m, 4 H, $-CH_2CH_2-$), 2.63 (s, 3 H, $SCH_3$). IR (KBr) 2224 cm$^{-1}$ (CN). UV (MeOH) $\lambda_{max}$ = 295 nm.

**4-Amino-5-cyano-6-(methylthio)-7-[(*RS*)-2,3-*O*-isopropylidene-2,3-dihydroxypropyl]pyrrolo[2,3-*d*]pyrimidine (61).** Procedure as per **59**. Compound **21** (600 mg, 2.05 mmol) gave 596 mg of **61** after recrystallization from ethanol (91% yield): mp 190–191 °C; $R_f$ = 0.56 [TLC, silica, 95:5 EtOAc–MeOH]. $^1$H NMR [$CDCl_3$, 200 MHz]: δ 8.31 (s, 1 H, H-2), 5.68 (b, 2 H, $-NH_2$), 4.55 (m, 1 H, –CH–), 4.45 (d, 1 H, $J$ = 5.2 Hz, $-NCH_2-$), 4.13–4.06 (m, 1 H)), 3.88–3.81 (m, 1 H), 2.66 (s, 3 H, $SCH_3$), 1.40 (s, 3 H, $CH_3$), 1.28 (s, 3 H, $CH_3$). IR (KBr) 2217 cm$^{-1}$ (CN). UV (MeOH) $\lambda_{max}$ = 295 nm.

**4-Amino-5-cyano-6-(methylthio)-7-[(*S*)-2,4-*O*-benzylidene-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidine (62).** Procedure as per **59**. Compound **22** (800 mg, 2.26 mmol) gave 740 mg of **62** after recrystallization from ethanol (86% yield): mp 166–167 °C; $R_f$ = 0.49 [TLC, silica, 95:5 EtOAc–MeOH]. $^1$H NMR [$CDCl_3$, 200 MHz]: δ 8.34 (s, 1 H, H-2), 7.35 (m, 5 H, Ph), 5.58 (b, 2 H, $NH_2$), 5.37 (s, 1 H, –CH–), 4.40 (m, 4 H), 3.94 (m, 1 H), 2.50 (s, 3 H, $SCH_3$), 1.87 (m, 2 H). IR (KBr) 2236 cm$^{-1}$ (CN). UV (MeOH) $\lambda_{max}$ = 295 nm.

**4-Amino-5-cyano-7-[[1,3-bis(benzyloxy)-2-propoxy]methyl]pyrrolo[2,3-*d*]pyrimidine (63).** Procedure as per **59**. Compound **23** (450 mg, 1.08 mmol) gave 431 mg of **63** (90% yield): mp 107–109 °C; $R_f$ = 0.55 [TLC, silica, EtOAc]. $^1$H NMR [$CDCl_3$, 200 MHz]: δ 8.36 (s, 1 H, H-2), 7.62 (s, 1 H, H-6), 7.29 (m, 10 H, 2 × Ph), 5.75 (s, 2 H, $-NCH_2O-$), 5.53 (b, 2 H, $NH_2$), 4.44 (s, 4 H, 2 × $CH_2Ph$), 3.97 (m, 1 H, –CH–), 3.50 (m, 4 H, 2 × $CH_2OBn$). IR (KBr) 2223 cm$^{-1}$ (CN). UV (MeOH) $\lambda_{max}$ = 278, 230.

**4-Amino-5-cyano-7-[[2-(benzyloxy)ethoxy]methyl]pyrrolo[2,3-*d*]pyrimidine (64).** Procedure as per **59**. Compound **24** (1 g, 3.37 mmol) gave 980 mg of **64** (90% yield): mp 144–146 °C; $R_f$ = 0.63 [TLC, silica, 95:5 EtOAc–MeOH]. $^1$H NMR [$CDCl_3$, 200 MHz]: δ 8.37 (s, 1 H, H-2), 7.65 (s, 1 H, H-6), 7.30 (m, 5 H, –Ph), 5.66 (s, 2 H, $-NCH_2O-$), 5.53 (b, 2 H, $NH_2$), 4.51 (s, 2 H, $CH_2Ph$), 4.51 (s, 2 H, $CH_2Ph$), 3.62 (m, 4 H, $-CH_2CH_2-$). IR (KBr) 2226 cm$^{-1}$ (CN). UV (MeOH) $\lambda_{max}$ 278, 230 nm.

**4-Amino-5-cyano-7-[(*RS*)-2,3-*O*-isopropylidene-2,3-dihydroxypropyl]pyrrolo[2,3-*d*]pyrimidine (65).** Procedure as per **59**. Compound **25** (400 mg, 1.62 mmol) gave 417 mg of **65** (94% yield): mp 195–196 °C; $R_f$ = 0.50 [TLC, silica, 95:5 EtOAc–MeOH]. $^1$H NMR [$CDCl_3$, 200 MHz]: δ 8.33 (s, 1 H, H-2), 7.66 (s, 1 H, H-6), 5.69 (b, 2 H, $NH_2$), 4.44 (m, 2 H), 4.24 (m, 1

H), 4.09 (m, 1 H), 3.65 (m, 1 H), 1.39 (s, 3 H, $CH_3$), 1.32 (s, 3 H, $CH_3$). IR (KBr) 2220 $cm^{-1}$ (CN). UV (MeOH) $\lambda_{max}$ = 280, 232 nm.

**4-Amino-5-cyano-7-[(*S*)-2,4-*O*-benzylidene-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidine (66).** Procedure as per **59**. Compound **26** (184.7 mg, 0.5989 mmol) gave 183.2 mg of **66** (0.5462 mmol, 91% yield) after purification by flash chromatography:mp 204–205 °C; $R_f$ = 0.35 [TLC, silica, 9:1 $CH_2Cl_2$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 8.24 (s, 1 H, H-2 or H-6), 8.16 (s, 1 H, H-6 or H-2), 7.34 (s, 5 H, Ph), 6.80 (s, b, 2 H, $NH_2$), 5.49 (s, 1 H, –OCHO–), 4.32 (m, 3 H), 4.14 (m, 1 H), 3.92 (m, 1 H), 1.57 (m, 2 H, $-CH_2-$). Upon $D_2O$ exchange the signal at 6.80 disappeared. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 157.0, 153.5, 150.1, 138.5, 135.4, 128.6, 128.0, 126.0, 115.6, 100.9, 99.9, 81.4, 74.3, 65.7, 48.7, 28.0. MS [high-resolution EI] $m/z$: 335.1458, $M^+$; calcd for M ($C_{18}H_{17}N_5O_2$), 335.1382. UV (MeOH) $\lambda_{max}$ ($\epsilon$) = 282 (12800), 238 (10600).

**2-Amino-5-(aminocarbonyl)-6-(methylthio)-7-[(1,3-dihydroxy-2-propoxy)methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (43).** Boron trichloride (3.2 mL, 1 M in $CH_2Cl_2$, 3.2 mmol) was added via syringe to a cooled (–78 °C) solution of compound **27** (206.0 mg, 0.3934 mmol) in methylene chloride (30 mL), and the mixture was stirred at –78 °C for 4 h under an argon atmosphere, before addition of 1:1 MeOH–$CH_2Cl_2$ (15 mL) to quench the reaction. After 5 min, an excess of triethylamine was added, and the cooling bath was removed. The reaction mixture was warmed to room temperature over 30 min before evaporating the solvents under reduced pressure. Water was added to aid in the coevaporation of the higher boiling liquids. Chloroform was added to the resulting white solid, and the insoluble material (**43**) was filtered off and washed repeatedly with chloroform. Evaporation of the chloroform extract and examination of the dried material by $^1H$ NMR showed it to be triethylamine hydrochloride. The crude product (**43**) was purified by flash chromatography (2 × 15 cm) by using dry-loading techniques (DMF–silica gel) to apply the sample to the prepared column. Elution with 20% MeOH–$CH_2Cl_2$ followed by 25% MeOH–$CH_2Cl_2$ afforded 85.4 mg of **43** (0.249 mmol, 63% yield): $R_f$ = 0.16 [TLC, silica, 1:4 MeOH–$CH_2Cl_2$]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.97 (s, 1 H, NH), 9.88 (s, b, 1 H, CONH), 7.01 (s, b, 1 H, CONH), 6.55 (s, b, 2 H, $NH_2$), 5.62 (s, 2 H, $-NCH_2O-$), 4.50 (t, 2 H, $J$ = 5.3 Hz, OH), 3.62 (m, 1 H, –CH–), 3.52–3.36 (m, 2 H, $-CH_2-$), 3.34–3.18 (m, "2H", $CH_2(+H_2O)$), 2.39 (s, 3 H, $SCH_3$). Upon $D_2O$ exchange the signals at 10.97, 9.88, 7.01, 6.55, and 4.50 are significantly reduced in intensity. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 163.6, 159.6, 153.1, 151.1, 130.4, 117.0, 96.9, 79.9, 70.2, 60.8, 19.4. Recrystallization from water–ethanol provided a sample for biological testing:mp 260–263 °C dec. MS [high-resolution FAB, glycerol] $m/z$: 344.10287, calcd for M ($C_{12}H_{17}N_5O_3S$) + H, 344.10287. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [311 (5300)*, 280 (7470), 240 (14200)]; pH = 7 [309 (6200)*, 280 (8560), 240 (13200)]; pH = 13 [314 (6750), 238 (15300)]. The $\lambda$ and $A$ values for shoulder* peaks were determined by extrapolation.

**2-Amino-5-(aminocarbonyl)-6-(methylthio)-7-[(2-hydroxyethoxy)methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (44).** Procedure as per compound **43**. Compound **28** (250 mg, 0.62 mmol) and $BCl_3$(4 mL, 1 M in $CH_2Cl_2$, 4 mmol) in $CH_2Cl_2$ (100 mL) gave, after workup (30 mL 1:1 $CH_2Cl_2$–MeOH, 5 mL $Et_3N$) and flash chromatography, 143 mg of **44** (74% yield): mp 255–258 °C; $R_f$ = 0.40 [TLC, silica, 4:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 11.01 (s, 1 H, NH), 9.88 (s, 1 H, –CONH–), 7.07 (s, 1 H, –CONH–), 6.60 (b, 2 H, $NH_2$), 5.54 (s, 2 H, $-NCH_2O-$), 4.64 (t, 1 H, OH), 3.45 (s, 4 H, $-CH_2CH_2-$), 2.39 (s, 3 H, $SCH_3$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 163.4, 159.6, 153.0, 152.1, 130.3, 117.1, 96.7, 70.5, 70.1, 59.9, 19.4. Anal. ($C_{11}H_{15}N_5O_4S$) C, H, N.

**2-Amino-5-cyano-6-(methylthio)-7-[[1,3-dihydroxy-2-propoxy]methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (47).** Procedure as per compound **43**. Compound **35** (131.0 mg, 0.2591 mmol) and $BCl_3$ (2.1 mL, 1 M in $CH_2Cl_2$, 2.1 mmol) in $CH_2Cl_2$ (20 mL) gave, after workup (10 mL 1:1 MeOH–$CH_2Cl_2$, 2 mL $Et_3N$) and flash chromatography, 66.2 mg of **47** (0.2036 mmol, 79% yield): $R_f$ = 0.33 [TLC, silica, 4:1 $CH_2Cl_2$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 11.01 (s, 1 H, NH), 6.82 (s, b, 2 H, $NH_2$), 5.53 (s, 2 H, $-NCH_2O-$), 4.57 (t, 2 H, $J$ = 5.7 Hz, OH), 3.63 (m, 1 H, –CH–), 3.44 (m, 2 H, $-CH_2-$), 3.36–3.20 (m, "2" H, $CH_2$ + $H_2O$ peak), 2.46 (s, 3 H, $SCH_3$). Upon $D_2O$ exchange the signals at 11.01, 6.82, and 4.57 disappear. The $H_2O$ signal exchanges and a HOD signal is now observed at a slightly lower field; the signal at 3.36–3.20 is now clearly seen as a 2 H dd ($J$ = 5.7, 11.4 Hz) and the corresponding signal at 3.44 is now partially obscured by the HOD signal. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 156.6, 154.5, 152.2, 133.8, 114.6, 99.2, 94.0, 80.4, 70.9, 60.7, 20.2. MS [High-resolution FAB, glycerol] $m/z$: 326.09293, calcd for M ($C_{12}H_{15}N_5O_4S$) + H, 326.0923010. UV ($H_2O$) $\delta_{max}$ ($\epsilon$): pH = 1 [308 (6100), 282 (6700), 234 (12000)]; pH = 7 [308 (6250), 282 (6660), 234 (12100)]; pH = 13 [312 (6830), 234 (14100)]. Recrystallization from ethanol–water afforded a slightly gelatinous solid which dried to a white powder: mp dec at $T$ > 220 °C.

**2-Amino-5-cyano-6-(methylthio)-7-[(2-hydroxyethoxy)methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (48).** Procedure as per compound **43**. Compound **36** (600 mg, 1.55 mmol) and $BCl_3$ (9 mL, 1 M in $CH_2Cl_2$, 9 mmol) in dichloromethane (100 mL) gave, after workup (50 mL 1:1 MeOH–$CH_2Cl_2$, 10 mL $Et_3N$) and flash chromatography, 285 mg of **48** (62% yield): mp 283–286 °C; $R_f$ = 0.47 [TLC, silica, 4:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.90 (b, 1 H, NH), 6.67 (b, 2 H, $NH_2$), 5.43 (s, 2 H, $-NCH_2O-$), 4.63 (t, 1 H, OH), 3.44 (m, 4 H, $CH_2CH_2$), 2.44 (s, 3 H, $SCH_3$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 156.58, 154.32, 152.32, 133.75, 114.40, 99.10, 94.10, 71.38, 70.48, 59.85, 20.06. IR (KBr) 2233 $cm^{-1}$ (CN). anal. ($C_{11}H_{13}N_5O_3S$) C, H, N. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [306 (10100), 280 (11420), 232 (19400)], pH = 7 [306 (11100), 280 (12300), 232 (20800)], pH = 13 [310 (12000), 232 (24100)].

**2-Amino-5-(aminocarbonyl)-7-[(1,3-dihydroxy-2-propoxy)methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (51).** Procedure as per **43**. Compound **31** (477 mg, 1 mmol) and $BCl_3$ (8 mL, 1 M in $CH_2Cl_2$, 8 mmol) in $CH_2Cl_2$ (100 mL) gave, after workup (50 mL 1:1 MeOH–$CH_2Cl_2$, 10 mL $Et_3N$) and recrystallization, 226 mg of **51** (76% yield): mp = dec at $T$ > 280 °C; $R_f$ = 0.21 [TLC, silica, 3:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 10.93 (b, 1 H, NH), 9.51 (d, 1 H, $J$ = 2.8 Hz, –CONH–), 7.43 (s, 1 H, H-6), 7.07 (b, 1 H, $J$ = 2.8 Hz, –CONH–), 6.49 (b, 2 H, $NH_2$), 5.43 (s, 2 H, $-NCH_2O-$), 4.55 (t, 2 H, OH), 3.53 (, 1 H, –CH–), 3.40 (m, 4 H, 2 × $CH_2OH$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 163.9, 160.2, 153.0, 152.0, 126.4, 114.5, 96.1, 79.7, 72.7, 60.8. Anal. ($C_{11}H_{15}N_5O_5 \cdot {}^1/_2\,H_2O$) C, H, N. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [296 (8200), 270 (8010), 232 (19040)], pH = 7 [296 (8270), 270 (7060), 232 (18470)], pH = 14 [294 (6010), 232 (19390).

**2-Amino-5-(aminocarbonyl)-7-[(2-hydroxyethoxy)methyl]pyrrolo[2,3-*d*]pyrimidin-4-one (52).** Procedure as per **43**. Compound **32** (357 mg, 1 mmol) and $BCl_3$ (8 mL, 1 M in $CH_2Cl_2$, 8 mmol) in methylene chloride (150 mL) gave, after workup (50 mL 1:1 MeOH–$CH_2Cl_2$, 10 mL $Et_3N$) and recrystallization from ethanol–water, 203 mg (76% yield) of compound **52**: mp dec at $T$ > 230 °C; $R_f$ = 0.27 [TLC, silica, $CHCl_3$–MeOH (4:1)]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.93 (b, 1 H, NH), 9.51 (d, 1 H, $J$ = 2.2 Hz, CONH), 7.42 (s, 1 H, H-6), 7.09 (d, 1 H, $J$ = 2.3 Hz, –CONH–), 6.50 (b, 2 H, $NH_2$), 5.34 (s, 2 H, $-NCH_2O-$), 4.63 (t, 1 H, OH), 3.41 (s, 4 H, $-CH_2CH_2-$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 163.9, 160.2, 153.0, 152.1, 126.4, 114.5, 96.1, 73.4, 70.2, 59.9. Anal. ($C_{10}H_{13}N_5O_4 \cdot {}^1/_5H_2O$) C, H, N. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [294 (7000), 268 (6800), 230 (15200)], pH = 7 [296 (8150), 270 (7300), 230 (16600)], pH = 13 [292 (6300), 256 (7850), 232 (16700)].

**2-Amino-5-cyano-7-[(1,3-dihydroxy-2-propoxy)methyl]-pyrrolo[2,3-*d*]pyrimidin-4-one (55).** Procedure as per **43**. Compound **39** (1.1 g, 2.4 mmol) and $BCl_3$ (19 mL, 1 M in $CH_2Cl_2$, 19 mmol) in methylene chloride (200 mL) gave, after workup (100 mL 1:1 $CH_2Cl_2$, 20 mL $Et_3$) and recrystallization from ethanol–water, 460 mg of **55** (69% yield): mp 242–244 °C; $R_f$ = 0.25 [TLC, silica; 3:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 10.78 (b, 1 H, NH), 7.78 (s, 1 H, H-6), 6.55 (b, 2 H, $NH_2$), 5.42 (s, 2 H, $-NCH_2O-$), 4.57 (t, 2 H, 2 × OH), 3.50 (m, 1 H, –CH–), 3.35 (m, 4 H, 2 × $CH_2OH$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 157.3, 154.0, 151.0, 130.3, 115.3, 98.6, 85.8, 80.2, 73.1, 60.8. IR (KBr) 2233 $cm^{-1}$ (CN). Anal. ($C_{11}H_{13}N_5O_4 \cdot {}^1/_5H_2O$) C, H, N. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [290 (8990), 268 (10870), 230 (22840)], pH = 7 [290 (9150), 268 (9150), 230 (22940)], pH = 13 [288 (8930), 270 (7880), 228 (27880)].

**2-Amino-5-cyano-7-[(2-hydroxyethoxy)methyl]pyrrolo-[2,3-*d*]pyrimidin-4-one (56).** Procedure as per **43**. Compound

40 (400 mg, 1.18 mmol) and $BCl_3$ (7 mL, 1 M in $CH_2Cl_2$, 7 mmol) in methylene chloride (100 mL) gave, after workup (30 mL 1:1 MeOH–$CH_2Cl_2$, 10 mL $Et_3N$) and flash chromatography, 203 mg (69% yield) of **56**: mp 242–245 °C; $R_f$ = 0.43 [TLC, silica, 4:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 10.86 (b, 1 H, NH), 7.80 (s, 1 H, H-6), 6.56 (b, 2 H, $NH_2$), 5.32 (s, 2 H, $-NCH_2O-$), 4.62 (t, 2 H, OH), 3.42 (s, 4 H, $-CH_2CH_2-$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 157.3, 154.1, 151.2, 130.5, 115.3, 98.7, 86.0, 73.7, 70.5, 59.9. Anal. ($C_{10}H_{11}N_5O_3$) C, H, N. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [288 (8030), 266 (9800), 228 (19 800)], pH = 7 [290 (8700), 266 (10 400), 230 (20 800)], pH = 13 [286 (8700), 268 (7860), 228 (23 100)].

**4-Amino-5-cyano-6-(methylthio)-7-[(1,3-dihydroxy-2-propoxy)methyl]pyrrolo[2,3-*d*]pyrimidine (67).** Procedure as per **43**. Compound **59** (700 mg, 1.43 mmol) and $BCl_3$ (9 mL, 1 M in $CH_2Cl_2$) in $CH_2Cl_2$ (75 mL) gave, after workup and recrystallization from ethanol, 349 mg of **67** (79% yield): mp 171–173 °C; $R_f$ = 0.50 [TLC, silica, 3:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 8.23 (s, 1 H, H-2), 6.92 (s, 2 H, $NH_2$), 5.73 (s, 2 H, $-NCH_2O-$), 4.56 (t, 2 H, 2 × OH), 3.63 (m, 1 H, –CH–), 3.30 (m, 4 H, 2 × $CH_2OH$), 2.60 (s, 3 H, $SCH_3$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 156.0, 154.1, 151.0, 140.5, 114.8, 101.2, 89.2, 80.68 71.1, 60.7, 19.2. Anal. ($C_{11}H_{13}N_5O_3$) C, H, N. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [300 (16 170), 238 (18 650)], pH = 7 [302 (15 900), 236 (16 450)], pH = 13 [302 (15 330), 236 (15 710)].

**4-Amino-5-cyano-6-(methylthio)-7-[(2-hydroxyethoxy)methyl]pyrrolo[2,3-*d*]pyrimidine (68).** Procedure as per **43**. Compound **60** (420 mg, 1.13 mmol) and $BCl_3$ (5 mL, 1 M in $CH_2Cl_2$, 5 mmol) in methylene chloride (75 mL) gave, after workup (20 mL 1:1 MeOH–$CH_2Cl_2$, 7 mL $Et_3N$) and flash chromatography, 225 mg of **68** (71%): mp 197–198 °C; $R_f$ = 0.58 [TLC, silica, 4:1 EtOAc–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 8.23 (s, 1 H, H-2), 6.95 (s, 2 H, $NH_2$), 5.64 (s, 2 H, $-NCH_2O-$), 4.63 (t, 1 H, OH), 3.46 (m, 4 H, $-CH_2CH_2-$), 2.58 (s, 3 H, $SCH_3$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 156.4, 154.5, 151.5, 140.6, 115.3, 101.4, 89.8, 71.9, 71.1, 60.1, 19.5. IR (KBr) 2229 $cm^{-1}$ (CN). Anal. ($C_{11}H_{13}N_5O_2S$) C, H, N. UV ($H_2O$) $\delta_{max}$ (ε): pH = 1 [300 (12 080)], pH = 7 [302 (10 430)], pH = 13 [302 (11 250)].

**4-Amino-5-cyano-7-[(1,3-dihydroxy-2-propoxy)methyl]pyrrolo[2,3-*d*]pyrimidine (71).** Procedure as per compound **43**. Compound **63** (321 mg, 0.724 mmol) and $BCl_3$ (5 mL, 1 M in $CH_2Cl_2$, 5 mmol) in methylene chloride (40 mL) gave, after workup (10 mL of 1:1 MeOH–$CH_2Cl_2$, 3 mL $Et_3N$) and flash chromatography 139 mg of **71** (75% yield): mp 185–187 °C; $R_f$ = 0.41 [TLC, silica, 3:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 8.30 (s, 1 H, H-6 or H-2), 8.22 (s, 1 H, H-2 or H-6), 6.58 (s, 2 H, $NH_2$), 5.64 (s, 2 H, $-NCH_2O-$), 4.59 (t, $J$ = 5.5 Hz, 2 H, 2 × OH), 3.53 (m, 1 H, –CH–), 3.30 (m, 4 H, 2 × $CH_2OH$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 156.9, 153.7, 150.2, 134.7, 115.3, 100.8, 82.6, 80.6, 73.2, 60.8. IR (KBr) 2220 $cm^{-1}$ (CN). Anal. ($C_{11}H_{13}N_5O_3$) C, H, N. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [274 (13 270), 236 (17 980)], pH = 7 [286 (11 940)*, 278 (15 940), 230 (12 300)], pH = 13 [286 (11 850)*, 278 (14 750), 230 (11 550)]. The $A$ and λ values for the shoulder peaks* were determined by extrapolation.

**4-Amino-5-cyano-7-[(2-hydroxyethoxy)methyl]pyrrolo[2,3-*d*]pyrimidine (72).** Procedure as per compound **43**. Compound **64** (500 mg, 1.54 mmol) and $BCl_3$ (7 mL, 1 M in $CH_2Cl_2$, 7 mmol) in methylene chloride (75 mL) gave, after workup (30 mL 1:1 MeOH–$CH_2Cl_2$, 7 mL $Et_3N$) and flash chromatography, 274 mg of **72** (76% yield): mp 185–186 °C; $R_f$ = 0.51 [TLC, silica, 4:1 EtOAc–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 8.33 (s, 1 H, H-6 or H-2), 8.22 (s, 1 H, H-2 or H-6), 6.87 (s, 2 H, $NH_2$), 5.55 (s, 2 H, $-NCH_2O-$), 4.65 (t, 1 H, OH), 3.42 (m, 4 H, $-CH_2CH_2-$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 157.0, 153.8, 150.3, 134.7, 115.2, 100.8, 82.8, 73.7, 70.8, 59.8. IR (KBr) 2227 $cm^{-1}$ (CN). Anal. ($C_{10}H_{11}N_5O_2$) C, H, N. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [274 (11 760), 234 (14 620)], pH = 7 [278 (10 050), 230 (10 050)], pH = 13 [278 (13 750), 230 (11 800)].

**2-Amino-5-(aminocarbonyl)-6-(methylthio)-7-[(*RS*)-2,3-dihydroxypropyl]pyrrolo[2,3-*d*]pyrimidin-4-one (45).** A mixture of compound **29** (171 mg, 0.487 mmol) and 80% aqueous acetic acid (5 mL) was stirred at 80 °C for 4 h. The solvents were evaporated, and DMF and silica gel were added to the remaining residue. The DMF was evaporated and the silica gel loaded onto a prepared column of silica gel. Elution with 4:1 $CHCl_3$–MeOH afforded 88.3 mg of **45** (0.282 mmol, 58% yield). Recrystallization from water provided a sample for biological testing: mp 274–277 °C with dec; $R_f$ = 0.35 [TLC, silica, 4:1 EtOAc–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 10.90 (s, 1 H, NH), 9.93 (s, b, 1 H, –CONH–), 6.93 (s, b, 1 H, –CONH–), 6.51 (s, 2 H, $NH_2$), 4.84 (d, $J$ = 5.15 Hz, 1 H, OH), 4.64 (t, $J$ = 5.03 Hz, 1 H, OH), 4.14 (m, 2 H), 3.82 (m, 1 H), 3.28 (m, 2 H + "$H_2O$"), 2.36 (s, 3 H, $SCH_3$). Upon $D_2O$ exchange the signals at 10.90, 6.51, 4.84, and 4.64 disappear and the multiplet at 3.28 is now clearly seen. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 163.8, 159.7, 152.6, 151.5, 131.6, 115.8, 97.0, 70.1, 64.0, 45.1, 19.4. MS [high-resolution CI, $NH_3$] $m/z$: 314.092 16, calcd for M($C_{11}H_{15}N_5O_4S$) + $H^+$, 314.092 30. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [316 (7000), 277 (8700)*, 244 (21 000)], pH = 7 [316 (7600), 280 (9300), 242 (19 000)], pH = 13 [318 (8800), 242 (19 800)]. The λ and $A$ values for the shoulder peak were determined by extrapolation.

**2-Amino-5-(aminocarbonyl)-6-(methylthio)-7-[(*S*)-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidin-4-one (46).** Procedure as per **45**. Compound **30** (303.7 mg, 0.731 mmol) and 80% HOAc in $H_2O$ gave, after purification by flash chromatography, 180.9 mg of **46** (0.552 mmol, 76% yield). Recrystallization from $H_2O$ gave a sample for biological testing: mp 244–247 °C; $R_f$ = 0.15 [TLC, silica, 4:1 $CH_2Cl_2$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 300 MHz]: δ 10.92 (s, b, 1 H, NH), 9.975 (d, b, $J$ = 1.8 Hz, 1 H, –CONH–), 6.945 (d, b, $J$ = 1.8 Hz, 1 H, –CONH–), 6.50 (s, b, 2 H, $NH_2$), 4.81 (d, $J$ = 5.3 Hz, 1 H, OH), 4.33 (t, $J$ = 5.1 Hz, 1 H, OH), 4.27–3.86 (m, 3 H), 3.46 (m, 2 H), 2.36 (s, 3 H, $SCH_3$), 1.42 (m, 2 H). Upon $D_2O$ exchange the signals at 10.92, 6.50, 4.81, and 4.33 disappear. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 163.7, 159.7, 152.5, 151.4, 131.4, 115.8, 97.0, 66.2, 57.6, 47.9, 37.6, 19.4. MS [high-resolution CI, $NH_3$] $m/z$: meas. 328.108 03, calcd for M ($C_{12}H_{17}N_5O_4S$) + $H^+$, 328.107 93. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [316 (5640), 276 (7200)*, 240 (16 900)], pH = 7 [316 (6140), 280 (7390), 244 (16 200)], pH = 13 [318 (7330), 244 (16 600)]. The λ and $A$ values for the shoulder peak* were found by extrapolation.

**2-Amino-5-cyano-6-(methylthio)-7-[(*RS*)-2,3-dihydroxypropyl]pyrrolo[2,3-*d*]pyrimidin-4-one (49).** Procedure as per **45**. Compound **37** (177.3 mg, 0.5286 mmol) and aqueous acetic acid gave, after chromatography and recrystallization from water, 95.6 mg of **49** (0.324 mmol, 61% yield): mp 280–285 °C with dec; $R_f$ = 0.44 [TLC, silica, 3:1 $CH_2Cl_2$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 10.80 (s, b, 1 H, NH), 6.59 (s, 2 H, $NH_2$), 4.96 (d, $J$ = 4.8 Hz, 1 H, OH), 4.72 (t, $J$ = 5.5 Hz, 1 H, OH), 4.08 (d, $J$ = 6.0 Hz, 2 H), 3.94 (m, 1 H), 3.34 (m, "2" H + $H_2O$ signal at 3.32), 2.43 (s, 3 H, $SCH_3$). Upon $D_2O$ exchange the signals at 10.80, 6.59, 4.96, and 4.72 disappear, and the multiplet at 3.34 is now clearly seen as a 2 H multiplet. $^{13}C$ NMR [DMSO-$d_6$, 200 MHz]: δ 156.6, 153.8, 151.6, 134.9, 114.9, 99.6, 92.4, 69.4, 63.9, 46.4, 19.8. MS [high-resolution, EI] $m/z$: meas. 295.0737, calcd for M ($C_{11}H_{13}N_5O_3S$), 295.0739. Anal. ($C_{11}H_{13}N_5O_3$) C, H, N. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [310 (9730), 280 (10 130), 240 (22 060)], pH = 7 [312 (10 360), 280 (10 520), 242 (23 140)], pH = 13 [314 (11 470), 240 (24 570)].

**2-Amino-5-cyano-6-(methylthio)-7-[(*S*)-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidin-4-one (50).** Procedure as per **45**. Compound **38** (150.8 mg, 0.3795 mmol) and aqueous acetic acid gave, after chromatography, 91.4 mg of **50** (0.295 mmol, 78% yield). Recrystallization from water provided an analytical sample: mp 275–278 °C with dec; $R_f$ = 0.26 [TLC, silica, 4:1 $CH_2Cl_2$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 300 MHz]: δ 10.82 (s, b, 1 H, NH), 6.59 (s, b, 2 H, $NH_2$), 4.89 (d, $J$ = 5.1 Hz, 1 H, OH), 4.38 (t, $J$ = 5.1 Hz, 1 H, OH), 4.02 (m, 3 H), 3.49 (m, 2 H), 2.43 (s, 3 H, $SCH_3$), 1.46 (m, 2 H). Upon $D_2O$ exchange the signals at 10.82, 6.59, 4.89, and 4.38 disappear. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 156.7, 153.8, 151.6, 134.7, 115.0, 99.6, 92.4, 65.6, 57.4, 49.2, 37.6, 19.9. MS [high resolution CI, $NH_3$] $m/z$: meas. 310.097 30, calcd for M ($C_{12}H_{15}N_5O_3S$) + $H^+$, 310.097 40. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [310 (9080), 282 (9490), 244 (19 400)], pH = 7 [312 (9040), 282 (9180), 244 (20 200)], pH = 13 [314 (10 600), 242 (21 100)].

**2-Amino-5-(aminocarbonyl)-7-[(*RS*)-2,3-dihydroxypropyl]pyrrolo[2,3-*d*]pyrimidin-4-one (53).** Procedure as per **45**. Compound **33** (147 mg, 0.480 mmol) in aqueous acetic acid gave, after chromatography and recrystallization from water, 43.8 mg of compound **53** (0.164 mmol, 34% yield): mp 295–298 °C with dec; $R_f$ = 0.10 [TLC, silica, 4:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 10.84 (s, 1 H, NH), 9.51 (s, b, 1 H, –CONH–)*, 7.30 (s, 1 H, H-6), 6.98 (s, b, 1 H, –CONH–), 6.44 (s,

2 H, $NH_2$), 4.97 (d, $J$ = 5.0 Hz, 1 H, OH), 4.72 (t, $J$ = 5.6 Hz, 1 H, OH), 4.10 (m, 1 H), 3.78 (m, 2 H), 3.30 (m, 2 H). The amide NH signals* appear to be coupled although the $J$ values could not be resolved at 200 MHz. Upon $D_2O$ exchange the signals at 10.84, 6.44, 4.98, and 4.72 disappear and those at 9.51 and 6.98 decrease in intensity. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 164.1, 160.1, 152.5, 151.6, 127.6, 113.2, 95.9, 70.1, 63.5, 47.3. MS [high-resolution CI, $NH_3$] $m/z$: meas. 268.104 56, calcd for M ($C_{10}H_{13}N_5O_4$) + $H^+$, 268.104 58. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [296 (6690), 272 (6300)*, 236 (15 600)], pH = 7 [298 (7790), 273* (6300), 236 (16 600)], pH = 13 [296 (6400), 260 (8600)*, 236 (15 900)]. The $\lambda$ and $A$ values for the shoulder peaks* were determined by extrapolation.

**2-Amino-5-(aminocarbonyl)-7-[(*S*)-2,4-dihydroxybutyl]-pyrrolo[2,3-*d*]pyrimidin-4-one (54).** Procedure as per **45**. Compound **34** (157.1 mg, 0.4251 mmol) and aqueous acetic acid gave, after recrystallization from water–ethanol, 105.5 mg of **54** (0.375 mmol, 88% yield): mp 276–278 °C with dec; $R_f$ = 0.24 [TLC, silica, 7:3 $CH_2Cl_2$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.84 (s, b, 1 H, NH), 9.50 (d, b, $J$ = 3.0 Hz, 1 H, –CONH–), 7.31 (s, 1 H, H-6), 7.005 (d, b, $J$ = 2.9 Hz, 1 H, –CONH–), 6.43 (s, b, 2 H, $NH_2$), 4.87 (d, $J$ = 4.2 Hz, 1 H, OH), 4.39 (t, $J$ = 5.1 Hz, 1 H, OH), 3.88 (m, 3 H), 3.48 (m, 2 H)8 1.42 (m, 2 H). Upon $D_2O$ exchange the signals at 10.84, 6.43, 4.87, and 4.39 disappear. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 164.2, 160.2, 152.5, 151.6, 127.5, 113.2, 95.9, 66.3, 57.5, 50.3, 37.6. MS [high-resolution CI, $NH_3$] $m/z$: meas. 282.120 13, calcd for M ($C_{11}H_{15}N_5O_4$) + $H^+$, 282.120 23. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [296 (6900), 274 (6900)*, 238 (16 100)], pH = 7 [298 (8100), 273 (6500)*, 240 (16 800)], pH = 13 [296 (6870), 260 (9200)*, 240 (16 300)]. The $\lambda$ and $A$* values for the shoulder peaks* were determined by extrapolation.

**2-Amino-5-cyano-7-[(*RS*)-2,3-dihydroxypropyl]pyrrolo-[2,3-*d*]pyrimidin-4-one (57).** Procedure as per **45**. Compound **41** (163 mg, 0.563 mmol) and aqueous acetic acid gave, after chromatography and recrystallization, 93.7 mg of **57** (0.376 mmol, 67% yield): mp 276–278 °C with dec; $R_f$ = 0.21 [TLC, silica, 4:1 $CH_2Cl_2$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.74 (s, b, 1 H, NH), 7.59 (s, 1 H, H-6), 6.51 (s, 2 H, $NH_2$), 5.02 (d, $J$ = 5.0 Hz, 1 H, OH), 4.75 (t, $J$ = 5.6 Hz, 1 H, OH), 4.10 (apparent d, $J$ = 10.0 Hz, 1 H), 3.90–3.53 (m, 2 H), 3.42–3.20 (m, "2" H + $H_2O$ peak at 3.32). Upon $D_2O$ exchange the signals at 10.74, 6.51, 5.02, and 4.75 disappear, and some of the remaining signals are altered. The multiplet at 3.42–3.20 is now clearly seen, and the apparent doublet at 4.10 is observed as a dd ($J$ = 12.4, 2.3 Hz). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 157.4, 153.7, 150.8, 131.4, 115.7, 98.7, 84.3, 69.7, 63.5, 47.8. MS [high-resolution CI, $NH_3$] $m/z$: meas. 250.093 93, calcd for M ($C_{10}H_{11}N_5O_3$) + $H^+$, 250.094 01. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [292 (9630), 270 (10 800), 234 (26 700)], pH = 7 [292 (10 800), 270 (11 100), 234 (28 200)], pH = 13 [290 (9930), 232 (27 400)].

**2-Amino-5-cyano-7-[(*S*)-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidin-4-one (58).** Procedure as per **45**. Compound **42** (143.8 mg, 0.4091 mmol) and aqueous acetic acid gave, after chromatography, 82.9 mg of **58** (0.3148 mmol, 77% yield) as a white solid. Recrystallization from water–ethanol afforded a gelatinous material which dried to give a brittle solid: mp 243–244 °C; $R_f$ = 0.40 [TLC, silica, 7:3 $CH_2Cl_2$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 10.73 (s, b, 1 H, NH), 7.60 (s, 1 H, H-6), 6.50 (s, b, 2 H, $NH_2$), 4.92 (d, $J$ = 5.1, 1 H, OH), 4.40 (t, $J$ = 5.1 Hz, 1 H, OH), 4.10–3.75 (m, 3 H), 3.50 (m, 2 H), 1.60–1.20 (m, 2 H). Upon $D_2O$ exchange the signals at 10.73, 6.50, 4.92, and 4.40 disappeared. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 157.6, 153.9, 150.9, 131.3, 115.8, 98.7, 84.3, 66.1, 57.4, 50.7, 37.5. MS [high-resolution CI, $NH_3$] $m/z$: meas. 264.109 78, calcd for M ($C_{11}H_{13}N_5O_3$) + $H^+$, 264.109 68. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [292 (6210), 270 (6990), 234 (16 300)], pH = 7 [294 (5930), 270 (6230), 236 (15 400)], pH = 13 [290 (6590), 236 (15 300)].

**4-Amino-5-cyano-6-(methylthio)-7-[(*RS*)-2,3-dihydroxypropyl]pyrrolo[2,3-*d*]pyrimidine (69).** Procedure as per **45**. Compound **61** (400 mg, 1.25 mmol) and aqueous acetic acid gave, after recrystallization from water–ethanol, 304 mg of **69** (87% yield): mp 196–198 °C; $R_f$ = 0.52 [TLC, silica, 4:1 EtOAc–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 8.20 (s, 1 H, H-2), 6.86 (s, 2 H, $NH_2$), 4.98 (d, 1 H, OH, exchanges in $D_2O$), 4.80 (t, 1 H, OH, exchanges in $D_2O$), 4.27 (m, 2 H, $-NCH_2-$), 3.93 (m, 1 H, –CH–), 3.38 (m, 2 H, $-CH_2-$), 2.57 (s, 3 H, $SCH_3$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 155.9, 153.5, 150.4, 141.5, 115.2, 101.6, 87.4, 69.4, 63.98 46.9, 19.1. IR (KBr): 2207 $cm^{-1}$ (CN). Anal. ($C_{11}H_{13}N_5O_2S$) C, H, N. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [302 (14 700), 242 (18 200)], pH = 7 [302 (15 100), 240 (15 800)], pH = 13 [302 (15 300), 240 (14 200)].

**4-Amino-5-cyano-6-(methylthio)-7-[(*S*)-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidine (70).** Procedure as per **45**. Compound **62** (500 mg, 1.31 mmol) and aqueous acetic acid gave, after recrystallization from water–ethanol, 319 mg of **70** (83% yield): mp 157–159 °C; $R_f$ = 0.45 [TLC, silica, 4:1 EtOAc–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 8.15 (s, 1 H, H-2), 6.86 (s, 2 H, $NH_2$), 4.88 (d, 1 H, OH), 4.37 (t, 1 H, OH), 4.18 (d, $J$ = 6.4 Hz, 2 H, $-NCH_2-$), 4.02 (m, 1 H, –CH–), 3.47 (m, 2 H, $-CH_2-$), 2.55 (s, 3 H, $SCH_3$), 1.49 (m, 2 H, $-CH_2-$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 155.9, 153.5, 150.4, 141.3, 115.2, 101.6, 87.3, 65.7, 49.4, 37.6, 19.1. IR (KBr): 2232 $cm^{-1}$ (CN). Anal. ($C_{12}H_{15}N_5O_2S \cdot {}^1/_2H_2O$) C, H, N. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [304 (12 600), 244 (16 000)], pH = 7 [302 (13 000), 242 (12 600)], pH = 13 [302 (13 200), 242 (12 800)].

**4-Amino-5-cyano-7-[(*RS*)-2,3-dihydroxypropyl]pyrrolo-[2,3-*d*]pyrimidine (73).** Procedure as per **45**. Compound **65** (300 mg, 1.1 mmol) and aqueous acetic acid gave, after recrystallization from ethanol, 228 mg of **73** (89% yield): mp 206–208 °C; $R_f$ = 0.49 [TLC, silica, 4:1 EtOAc–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 8.19 (s, 1 H, H-6 or H-2), 8.09 (s, 1 H, H-2 or H-6), 6.78 (b, 2 H, $NH_2$), 5.05 (d, 1 H, OH), 4.80 (t, 1 H, OH), 4.32 (m, 1 H, $-CH_2N-$), 3.92 (m, 1 H, $-CH_2N-$), 3.81 (m, 1 H, –CH–), 3.36 (m, 2 H, $CH_2O$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 156.9, 153.2, 149.9, 135.7, 115.7, 101.0, 80.8, 69.7, 63.5, 48.1. IR (KBr): 2223 $cm^{-1}$ (CN). Anal. ($C_{10}H_{11}N_5O_2$) C, H, N. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [276 (11 700), 236 (17 500)], pH = 7 [280 (14 700), 234 (11 900)], pH = 13 [280 (14 100), 234 (11 100)].

**4-Amino-5-cyano-7-[(*S*)-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidine (74).** Procedure as per **45**. Compound **66** (175.4 mg, 0.523 mmol) and aqueous acetic acid gave, after chromatography, 116.5 mg of **74** (0.4711 mmol, 90% yield). Recrystallization from ethanol–water provided a sample for biological testing: mp 195–196 °C; $R_f$ = 0.33 [TLC, silica, 4:1 $CH_2Cl_2$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 8.20 (s, 1 H, H-6 or H-2), 8.12 (s, 1 H, H-6 or H-2), 6.78 (s, b, 2 H, $NH_2$), 4.95 (d, $J$ = 5.4 Hz, 1 H, OH), 4.40 (t, $J$ = 5.1 Hz, 1 H, OH), 4.20 (dd, $J$ = 3.7, 13.0 Hz, 1 H), 4.12–3.82 (m, 2 H), 3.49 (m, 2 H), 1.47 (m, 2 H, $-CH_2-$). Upon $D_2O$ exchange the signals at 6.78, 4.95, and 4.40 disappear. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 156.9, 153.3, 150.0, 135.6, 115.8, 101.0, 80.98 66.0, 57.3, 50.9, 37.5. MS [high-resolution EI] $m/z$: meas. 247.113, calcd for $C_{11}H_{13}N_5O_2$, 247.1069. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 :278 (12 300), 240 (19 600)], pH = 7 [282 (14 100), 236 (12 300)], pH = 13 [282 (14 700), 236 (12 600)].

**4-Amino-5-(aminocarbonyl)-6-(methylthio)-7-[(1,3-dihydroxy-2-propoxy)methyl]pyrrolo[2,3-*d*]pyrimidine (75).** Aqueous hydrogen peroxide (30%, 0.3 mL) was added to a mixture of compound **67** (70 mg, 0.22 mmol) suspended in aqueous ammonium hydroxide (10 mL, 28% $NH_4OH$). The mixture was stirred at room temperature; after 15 min the solution became clear, and after 30 min the reaction was judged to be complete by TLC. The mixture was evaporated to dryness under reduced pressure, and recrystallization of the resulting solid from ethanol–water afforded 61 mg of **75** (82% yield): mp dec at $T$ > 185 °C; $R_f$ = 0.42 [TLC, silica, 3:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 8.15 (b, 1 H, –CONH–), 8.12 (s, 1 H, H-2), 7.98 (b, 1 H, –CONH–), 5.79 (s, 2 H, $-NCH_2O-$), 4.56 (t, 2 H, 2 × OH), 3.68 (m, 1 H, –CH–), 3.37 (m, 4 H, 2 × $CH_2$), 2.46 (s, 3 H, $SCH_3$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: $\delta$ 166.0, 157.6, 153.8, 151.1, 130.2, 115.5, 101.2, 80.2, 70.5, 60.7, 20.5. MS [high-resolution CI, $NH_3$] $m/z$: meas. 328.106 991 4, calcd for M ($C_{12}H_{17}N_5O_4S$) + $H^+$, 328.107 951 1. UV ($H_2O$) $\lambda_{max}$ ($\epsilon$): pH = 1 [290 (10 600), 234 (11 100)], pH = 7 [298 (9400)], pH = 13 [296 (9600)].

**4-Amino-5-(aminocarbonyl)-6-(methylthio)-7-[(*RS*)-2,3-dihydroxypropyl]pyrrolo[2,3-*d*]pyrimidine (77).** Procedure as per **75**. Compound **69** (100 mg, 0.35 mmol), aqueous ammonium hydroxide (20 mL, 28%), and aqueous hydrogen peroxide (0.5 mL, 30%) gave 91 mg of **77** (86% yield): mp 238–240 °C; $R_f$ = 0.33 [TLC, silica, 4:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: $\delta$ 8.16 (s, 1 H, –CONH–), 8.08 (s, 1 H, H-2), 7.91 (s, 1 H, –CONH–), 4.97 (d, 1 H, OH), 4.77 (t, 1 H, OH), 4.32 (m, 2 H,

–$NCH_2$–), 3.96 (m, 1 H, –CH–), 3.33 (m, 2 H, –$CH_2O$–), 2.40 (s, 3 H, $SCH_3$). $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 166.1, 157.6, 153.2, 150.5, 131.2, 113.9, 101.6, 69.8, 64.0, 46.0, 20.3. Anal. ($C_{11}H_{15}N_5O_3S$) C, H, N. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [296 (11900), 244 (14300)], pH = 7 [302 (11200), 250 (10050)], pH = 13 [302 (11700), 248 (10400)].

**4-Amino-5-(aminocarbonyl)-6-(methylthio)-7-[(*S*)-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidine (78).** Procedure as per **75**. Compound **70** (150 mg, 0.51 mmol), aqueous ammonium hydroxide (20 mL, 28%), and aqueous hydrogen peroxide (0.5 mL, 30%) gave 134 mg of **78** (84% yield): mp 196–198 °C; $R_f$ = 0.27 [TLC, silica, 4:1 $CHCl_3$–MeOH]: δ 8.16 (s, 1 H, –CONH–), 8.08 (s, 1 H, H-2), 7.93 (s, 1 H, –CONH–), 4.88 (d, 1 H, OH), 4.35 (t, 1 H, =OH), 4.25 (m, 2 H, –$CH_2N$–), 4.08 (m, 1 H, –CH–), 3.47 (m, 2 H, –$CH_2O$–), 2.39 (s, 3 H, $SCH_3$), 1.46 (m, 2 H, –$CH_2$–). The 4-amino-group appears as a low broad signal from 7–9 ppm. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 166.1, 157.5, 153.2, 150.5, 130.8, 113.8, 101.6, 65.9, 57.5, 48.7, 37.7, 20.3. Anal. ($C_{12}H_{17}N_5O_3S \cdot {}^1/_5H_2O$) C, H, N. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [296 (11200), 242 (14200)], pH = 7 [302 (11600), 250 (10800)], pH = 13 [302 (11200), 248 (10200)].

**4-Amino-5-(aminocarbonyl)-7-[(1,3-dihydroxy-2-propoxy)methyl]pyrrolo[2,3-*d*]pyrimidine (79).** Procedure as per **75**. Compound **71** (263 mg, 0.999 mmol), aqueous ammonium hydroxide (20 mL, 28%), and aqueous hydrogen peroxide (1 mL, 30%) gave 231 mg of **79** (82% yield): mp dec at $T > 210$ °C; $R_f$ = 0.20 [TLC, silica, 3:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 8.09 (s, 1 H, H-6 or H-2), 8.06 (s, 1 H, H-2 or H-6), 7.91 (b, 1 H, –CONH–), 7.33 (b, 1 H, –CONH–), 5.61 (s, 2 H, –$NCH_2O$–), 4.49 (t, 2 H, 2 × OH, exchanges in $D_2O$), 3.50 (m, 1 H, –CH–), 3.40 (m, 4 H, 2 × $CH_2OH$). The 4-amino group appeared as a low broad signal from 7–9 ppm. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 166.4, 158.1, 153.1, 150.8, 127.8, 110.6, 80.0, 72.7, 60.7. Anal. ($C_{11}H_{15}N_5O_4$) C, H, N. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [276 (12600), 232 (15350)], pH = 7 [280 (13510), 229 (12320)], pH = 13 [280 (12970), 232 (10920)].

**4-Amino-5-(aminocarbonyl)-7-[(2-hydroxyethoxy)methyl]pyrrolo[2,3-*d*]pyrimidine (80).** Procedure as per **75**. Compound **72** (70 mg, 0.3 mmol), aqueous ammonium hydroxide (20 mL, 28%), and aqueous hydrogen peroxide (0.5 mL, 30%) gave 62 mg of **80** (83% yield) mp 228–230 °C; $R_f$ = 0.29 [TLC, silica, 4:1 EtOAc–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 8.10 (s, 1 H, H-6 or H-2), 8.06 (s, 1 H, H-2 or H-6), 7.94 (b, 1 H, –CONH–), 7.35 (b, 1 H, –CONH–), 5.54 (s, 2 H, –$NCH_2O$–), 4.64 (t, 1 H, OH), 3.43 (m, 4 H, –$CH_2CH_2$–). The 4-amino group appeared as a low broad signal from 7–9 ppm. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 166.4, 158.1, 153.2, 151.0, 1227.9, 111.0, 100.6, 73.3, 70.5, 59.9. Anal. ($C_{10}H_{13}N_5O_3 \cdot {}^1/_5H_2O$) C, H, N. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [274 (11160), 228 (11900)], pH = 7 [278 (12700), 228 (9500)], pH = 13 [278 (12250), 232 (8250)].

**4-Amino-5-(aminocarbonyl)-7-[(*RS*)-2,3-dihydroxypropyl]pyrrolo[2,3-*d*]pyrimidine (81).** Procedure as per **75**. Compound **73** (100 mg, 0.43 mmol), aqueous ammonium hydroxide (20 mL, 28%), and aqueous hydrogen peroxide (0.5 mL, 30%) gave 94 mg of **81** (87% yield): mp 232–234 °C; $R_f$ = 0.20 [TLC, silica, 4:1 $CHCl_3$–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ, 8.10 (s, 1 H, H-6 or H-2), 8.06 (s, 1 H, H-2 or H-6), 7.94 (b, 1 H, –CONH–), 7.35 (b, 1 H, –CONH–), 4.97 (d, 1 H, OH), 4.77 (t, 1 H, OH), 4.32 (m, 2 H, –$CH_2N$–), 3.96 (m, 1 H, –CH–), 3.33 (d, 2 H, $CH_2OH$). The 4-amino group appeared as a low broad signal from 7–9 ppm. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 166.5, 158.0, 152.5, 150.5, 129.3, 109.2, 100.7, 70.0, 63.4, 47.7. Anal. ($C_{10}H_{13}N_5O_3$) C, H, N. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [278 (8500), 234 (9300)], pH = 7 [280 (10000), 232 (700)], pH = 13 [280 (10000), 234 (6400)].

**4-Amino-7-[(*S*)-2,4-dihydroxybutyl]pyrrolo[2,3-*d*]pyrimidine (82).** Procedure as per **75**. Compound **74** (53.1 mg, 0.2148 mmol), aqueous ammonium hydroxide (3 mL, 28% yield), and aqueous hydrogen peroxide (0.5 mL, 30% yield) gave 45.7 mg of **82** (0.1722 mmol, 79% yield): mp 235–238 °C; $R_f$ = 0.13 [TLC, silica, 4:1 $CH_2Cl_2$–MeOH] $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 8.06 (s, 1 H, H-2 or H-6), 7.98 (s, 1 H, H-2 or H-6), 7.87 (s, b, 1 H, –CONH–), 7.24 (s, b, 1 H, –CONH–), 4.98 (d, $J$ = 5.1 Hz, 1 H, OH), 4.39 (t, $J$ = 5.1 Hz, 1 H, OH), 4.20–3.86 (m, 3 H), 3.50 (m, 2 H), 1.46 (m, 2 H, –$CH_2$–). The 4-amino group appeared as a low broad signal from 8.8–7.0 ppm. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 166.6, 158.0, 152.6, 150.6, 129.2, 109.3, 100.7, 66.3, 57.5, 50.6, 37.6. MS [high-resolution EI] $m/z$: meas. 265.1168, calcd for $C_{11}H_{15}N_5O_3$, 265.1175. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [280 (10300), 238 (12500)], pH = 7 [284 (11800), 250 (7900)*, 236 (9400)], pH = 13 [284 (11900), 250 (7800), 236 (9150)]. The λ and $A$ values for the shoulder peak* were determined by extrapolation.

**4-Amino-5-(aminocarbonyl)-6-(methylsulfinyl)-7-[(2-hydroxyethoxy)methyl]pyrrolo[2,3-*d*]pyrimidine (83).** Aqueous hydrogen peroxide (3.5 mL, 30%) was added to a mixture of **68** (330.6 mg, 1.184 mmol) in aqueous ammonium hydroxide (18 mL, 28%) and the solution was stirred at room temperature until the reaction was judged to be complete by TLC (45 min). The mixture was evaporated to dryness under reduced pressure at $T$ = 40 °C. Flash chromatography using dry loading techniques gave 245.6 mg of what first appeared to be homogeneous material by TLC [$R_f$ = 0.32, 4:1 EtOAc–MeOH]. $^1H$ NMR showed this to be a mixture of 2 or more compounds which appear to be the result of reaction of the methylthio group in addition to the nitrile group. Preparative TLC (multiple elutions with 5:1 EtOAc–MeOH) allowed separation of a small amount of **83** for characterization. The isolated product was then recrystallized from ethanol: mp 215–219 °C; $R_f$ = 0.31 [TLC, silica, 4:1 EtOAc–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 9.13 (b, 1 H, –CONH–), 8.35–8.00 [m, 4 H; contains a singlet at 8.20 (H-2) and broad NH signals (–CONH–, $-NH_2$)], 5.895 (d, $J$ = 10.8 Hz, 1 H –NCH*HO*–), 5.738 (d, $J$ = 10.8 Hz, 1 H, –NC*H*HO–), 4.62 (m, 1 H, OH), 3.42 (m, 4 "H"; $-CH_2CH_2-$ + $H_2O$ peak), 3.20 (s, 3 H, $CH_3$). Upon $D_2O$ exchange the signal at 4.62 disappears, and the multiplet at 8.35–8.00 is reduced in intensity. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ 165.6, 158.7, 154.8, 150.5, 136.2, 115.1, 101.3, 71.3, 70.5, 59.7, 38.86 (overlap with m from DMSO). MS [high-resolution CI, $NH_3$] $m/z$: meas. 314.092 27, calcd for M ($C_{11}H_{15}N_5O_4S$) + $H^+$, 314.092 301 0. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [290 (7520), 237 (8600)*], pH = 7 [300 (6610)], pH = 13 [292 (6660), 220 (11000)]. The λ and $A$ values for the shoulder peak are determined by extrapolation.

**4-Amino-5-(aminocarbonyl)-6-(methylthio)-7-[(2-hydroxyethoxy)methyl]pyrrolo[2,3-*d*]pyrimidine (76).** To a sample of **68** (45.8 mg, 0.164 mmol) was added aqueous ammonium hydroxide (4 mL, 28%) and aqueous hydrogen peroxide (0.5 mL, 30% solution). The mixture was stirred at room temperature for 25 min and then freeze-dried. Flash chromatography, using dry loading techniques (3 × 20 cm of silica, eluted with 4:1 EtOAc–MeOH), allowed separation of unreacted starting material **68** (15.7 mg, 34% recovery) from **76** which was contaminated with sulfoxide **83** (20.0 mg, 4:1 mixture of **76**:**83** by $^1H$ NMR). Preparative TLC (multiple elution with 6:1 EtOAc–MeOH) allowed separation of a small portion of pure **76** for characterization. Recrystallization from MeOH–EtOH provided a sample for biological testing: mp 203–205 °C; $R_f$ = 0.39 [TLC, silica, 4:1 EtOAc–MeOH]. $^1H$ NMR [DMSO-$d_6$, 200 MHz]: δ 8.15 (s, 1 H, –CONH–), 8.12 (s, 1 H, H-2), 8.01 (s, 1 H, –CONH–), 5.69 (s, 2 H, –$NCH_2O$–), 4.64 (t, 1 H, OH), 3.46 (m, 4 H, $-CH_2CH_2-$), 2.43 (s, 3 H, $SCH_3$). The 4-amino group appears as a low broad 2 H signal from 7–9 ppm. $^{13}C$ NMR [DMSO-$d_6$, 75.4 MHz]: δ, 166.0, 157.6, 153.8, 151.3, 130.1, 115.7, 101.1, 71.0, 70.5, 59.9, 20.4. MS [high-resolution EI] $m/z$: meas. 298.097 32; calcd for M ($C_{11}H_{15}N_5O_3S)^+$, 298.097 39. UV ($H_2O$) $\lambda_{max}$ (ε): pH = 1 [296 (9800), 236 (9500)], pH = 7 [298 (10100)], pH = 13 [298 (9300), 234 (8100)].

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