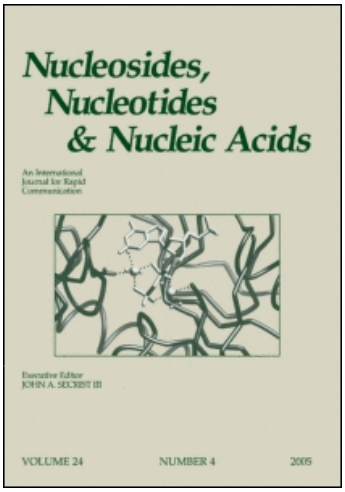

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Nucleosides 137. Synthetic Modifications at the 2'Position of Pyrrolo[3,2-D]Pyrimidine and Thieno[3,2-D]Pyrimidine C-Nucleosides, Synthesis of "2'-Deoxy-9-Deazzadenosine" and of "9-Deaza ARA-A"

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NUCLEOSIDES 137. SYNTHETIC MODIFICATIONS AT THE 2'-POSITION OF PYRROLO[3,2-d]PYRIMIDINE AND THIENO[3,2-d]PYRIMIDINE C-NUCLEOSIDES, SYNTHESIS OF "2'-DEOXY-9-DEAZAADENOSINE" AND OF "9-DEAZA ARA-A."[1a,b]

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Abstract: The syntheses and preliminary biological evaluation of several novel pyrrolo[3,2-d]pyrimidine and thieno[3,2-d]pyrimidine C-nucleosides incorporating the arabinofuranosyl or 2'-deoxyribofuranosyl sugar moiety are described. The 2'-deoxy thieno[3,2-d]pyrimidine C-nucleosides (**15** and **16**) were obtained from 7-(β-D-ribofuranosyl)-4-oxo-3H-thieno[3,2-d]pyrimidine (**3**) and its 4-SMe derivative **8**. "2'-Deoxy-9-deazaadenosine" (**31**), "9-Deaza ara-A" (**38**) and the 2'-substituted arabinosyl pyrrolo[3,2-d]pyrimidine C-nucleosides (**42** - **44**) were synthesized from 4-amino-7-(2,3-O-isopropylidene-5-O-trityl-β-D-ribofuranosyl)-5H-pyrrolo[3,2-d]pyrimidine (**21**)

We recently reported the syntheses and biological activity of several pyrrolo[3,2-d]pyrimidine[2-4] and thieno[3,2-d]pyrimidine[5] C-nucleosides as potential anticancer,[6-8] antileishmanial[9] and anti-trypanosomal[9] agents. Some of the most interesting biologically active compounds in these two series are: 9-deazaadenosine [**1**, 4-amino-7-(β-D-ribofuranosyl)-5H-pyrrolo[3,2-d]pyrimidine], which exhibits pronounced growth inhibitory activity against several cell lines of mouse and human leukemias;[6-8,10] 9-deazainosine [2,7-(β-D-ribofuranosyl)-4-oxo-3H,5H-pyrrolo[3,2-d]pyrimidine] and 7-(β-D-ribofuranosyl)-4-oxo-3H-thieno[3,2-d]pyrimidine (**3**) both of which show promising antileishmanial[9] and anti-trypanosomal[9,11] activity with relatively low toxicity to normal cells.

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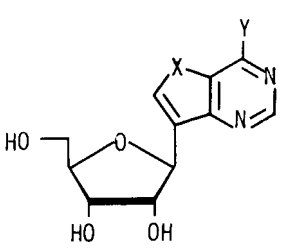
Compounds **1-3** are representative of purine-nucleoside analogs structurally modified at the purine moiety level. Several purine nucleoside analogs incorporating modification of the sugar moiety have also shown useful biomedical activity. One of the best known is perhaps ara-A [**4**, vidarabine, VIRA-A, 9-(β-D-arabinofuranosyl)adenine], an N-nucleoside which has shown antiviral activity[12] against certain DNA viruses such as herpes varicella and cytomegalovirus. Ara-A also demonstrated clinical utility as a topical agent for herpes keratitis of the eye.[13] It was also found to be an effective, relatively nontoxic, systemic agent to treat the usually fatal herpes encephalitis.[14]

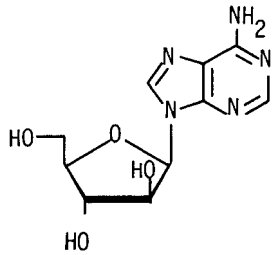
Because of the important biological activities of the compounds (**1-4**) described above, the synthesis and biological evaluation of various 2'-deoxy and 2'-ara substituted derivatives of several thieno[3,2-d]-pyrimidine and pyrrolo[3,2-d]pyrimidine C-nucleosides of type **5** (R = OH, SCH_3; X = H, OH, Cl, Br, I; Y = NH, S) has been undertaken as part of our ongoing research program in the area of C-nucleosides.

This report includes the synthesis and preliminary biological evaluation of 7-(2-deoxy-β-D-ribofuranosyl)-4-oxo-3H-thieno[3,2-d]-pyrimidine (**15**), 7-(2-deoxy-β-D-ribofuranosyl)-4-(methylthio)-thieno[3,2-d]pyrimidine (**16**) (Scheme I), 2'-deoxy-9-deazaadenosine hydrochloride [**31**, 4-amino-7-(2-deoxy-β-D-ribofuranosyl)-5H-pyrrolo[3,2-d]pyrimidine hydrochloride], 9-deaza ara-A [**38**, 4-amino-7-(β-D-arabinofuranosyl)-5H-pyrrolo[3,2-d]pyrimidine] (Scheme IV) and 4-amino-7-(2-deoxy-2-chloro, bromo and iodo-β-D-arabinofuranosyl)-5H-pyrrolo[3,2-d]pyrimidines (**42 - 44**) (Scheme IV).

Thienopyrimidine C-nucleoside **3**[5] was used as a precursor for the synthesis of 2'-deoxy thieno[3,2-d]pyrimidine C-nucleosides **15** and **16**. Acetylation of **3** with Ac_2O in pyridine at 0°C gave 7-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)-4-oxo-3H-thieno[3,2-d]pyrimidine (**6**) in 74% yield (Scheme I). Reaction of **6** with phosphorus pentasulfide in dioxane afforded the corresponding 4-thio derivative **7** in 84% yield. This compound was S-methylated and deacetylated simultaneously by treatment with MeI/NaOH/aq. MeOH to give the corresponding S-methyl ribofuranosyl nucleoside **8** in 99% yield. The ^1H NMR spectrum of **8** showed a singlet at δ 2.75 for the SCH_3 group. Treatment of **3** and **8** with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (TIPDS-Cl_2) in pyridine at 25°C resulted in the formation of the corresponding 3',5'- cyclic disiloxanyl deriva-



1, X=NH, Y=NH_2
2, X=NH, Y=OH
3, X=S, Y=OH



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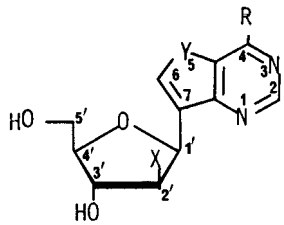

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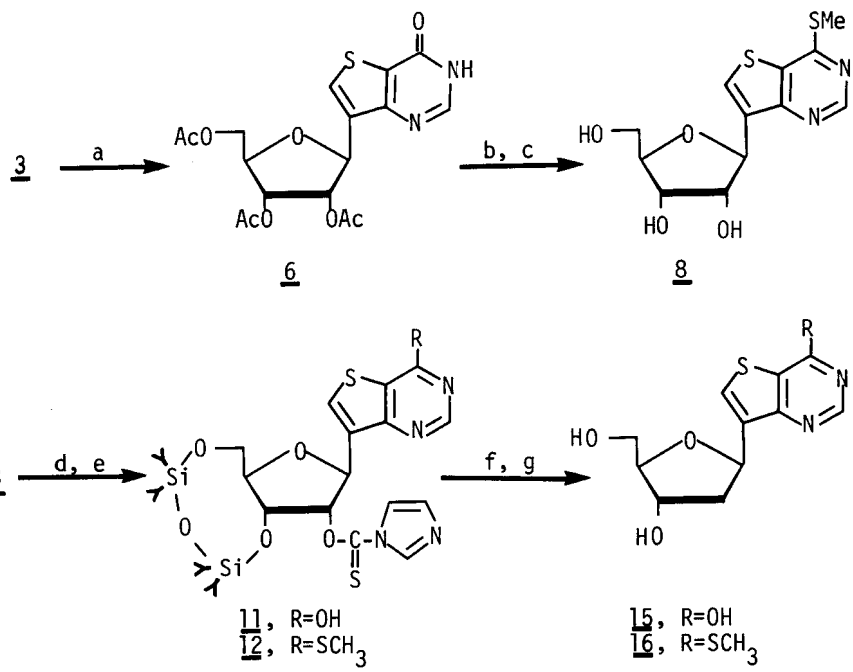
Scheme I

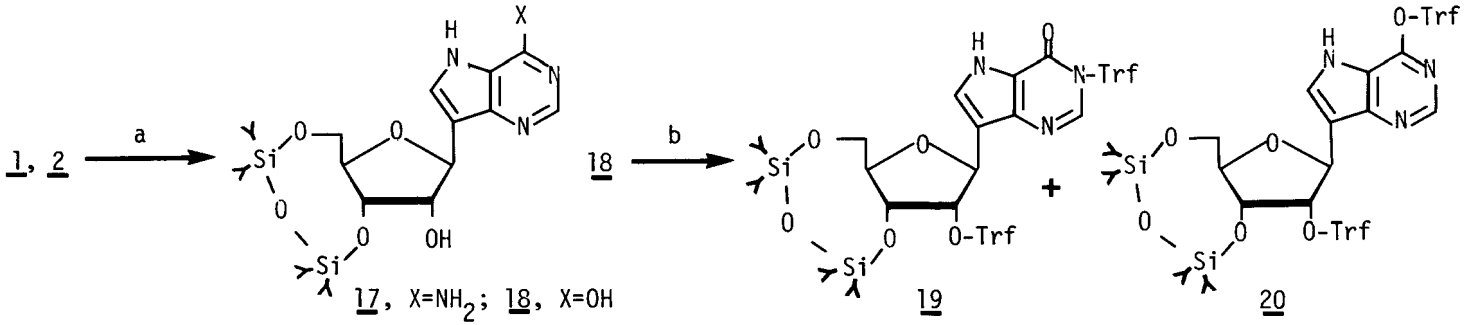


a=Ac_2O, Pyr/25°C; b=P_4S_{10}, Dioxane/refl.; c=CH_3I, NaOH, MeOH/25°C; d=TIPDS-Cl_2, Pyr/25°C; e=TCDI, DMF/85°C; f=(n-But)$_3$SnH, AIBN, Toluene/refl.; g=(n-But)$_4$NF, THF, 25°C.

tives **9** and **10** in 75% and 82% yields, respectively.[15] Reaction of **9** and **10** with 1,1'-thiocarbonyldiimidazole (TCDI) in dry DMF afforded the expected 2'-O-thiocarbonylimidazolide derivatives **11** (82%) and **12** (95%), respectively. Reduction of **11 and 12** with tri-n-butyltin hydride in the presence of α,α'-azobisisobutyronitrile, (AIBN) in refluxing toluene[15f,16] resulted in the formation of 2'-deoxy compounds **13** and **14**, in 94% and 92% yields, respectively. Final deprotection of compounds **13** and **14** with tetra-n-butylammonium fluoride (TBAF) in dry THF[15,17] at 25°C for 5 min gave the desired 2'-deoxy thieno[3,2-d]pyrimidine C-nucleosides **15** and **16** in 81% and 50% yields, respectively.

Since **15** and **16** could be obtained in good overall yields from the corresponding ribofuranosyl nucleosides **3** and **8**, we decided to follow a similar route for the synthesis of 2'-deoxy pyrrolo[3,2-d]pyrimidine C-nucleosides. Of particular interest was the 2'-deoxyadenosine analog, **31**. Thus, 3'- and 5'-OH groups of **1** were protected by reaction with TIPDS-Cl_2 in dry pyridine at 25°C to give 3',5'-cyclic disiloxanyl derivative **17** in 76% yield (Scheme II). Treatment of **17** with TCDI in dry DMF[15f] at 25°C or in refluxing 1,2-dichloroethane[18] did not give the expected 2'-O-thiocarbonylimidazolide derivative, but resulted in the formation of an intractable mixture. The attempted phenoxythiocarbonylation[15e] of the 2'-OH group of **17** with phenyl chlorothionocarbonate in the presence of 4-dimethylaminopyridine (DMAP) in dry CH_3CN was also unsuccessful, due to degradation of **17**. Failure to obtain the desired thionoesters may be due to the reactivity of the unprotected NH_2 and/or pyrrolo NH functions toward the reagents. A promising alternate approach was the utilization of 2'-O-triflate derivatives as an access to the 2'-modified derivatives of pyrrolo[3,2-d]pyrimidine C-nucleosides. Initial studies were conducted with the corresponding inosine analog **2**. Thus, the reaction of **2** with TIPDS-Cl_2 in pyridine at 25°C yielded 86% of the 3',5'-cyclic disiloxanyl derivative **18** (Scheme II). Triflation of **18** with trifluoromethanesulfonic anhydride in CH_2Cl_2 and pyridine gave a mixture of two ditriflated products: 2',3-ditriflate derivative **19** and 2',4-di-O-triflate derivative **20**. These were separated by flash column chromatography on silica gel using pet. ether:EtOAC (90:10) (for **19**) and pet. ether:EtOAC (85:15) (for **20**) as successive eluents. The ^1H NMR spectrum of **19** showed a downfield shift for the H-2' signal, (δ 4.17-4.69 for **18** and δ 5.53 for **19**). The ^1H NMR spectrum of **20** was similar to that of **19** except for a considerable

Scheme II

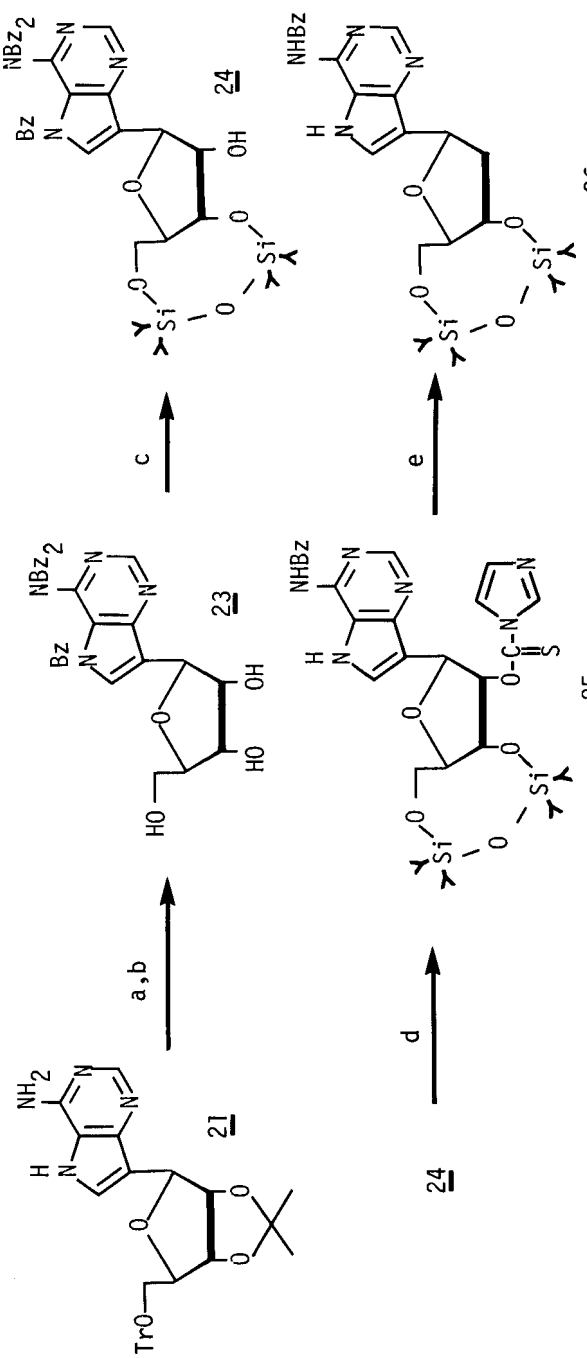


a=TIPDS-Cl_2, Pyr./25°; b=$(CF_3SO_2)_2O$, Pyr., CH_2Cl_2

downfield shift for the H-2 and H-6 signals (δ H-2 = 8.22 and δ H-6 = 7.51 for **19** and δ H-2 = 8.71 and δ H-6 = 7.80 for **20**). The structural assignments of **19** and **20** were also based on the presence of the pyrrole N-H signals in the ^{1}H NMR spectrum and on elemental analyses. The pyrrole NH's of **19** and **20** appeared at δ 10.04 and δ 9.26, respectively as broad singlets. Upon treatment with D_2O, these disappeared while the doublets corresponding to H-6 collapsed into sharp singlets. In an attempt at triflate substitution, **19** and **20** were separately treated with anhydrous CH_3COONa in dry hexamethylphosphoramide (HMPA) at 25°C but the expected 2'-O-acetyl ara compounds were not formed as the reaction resulted in the degradation of starting materials.

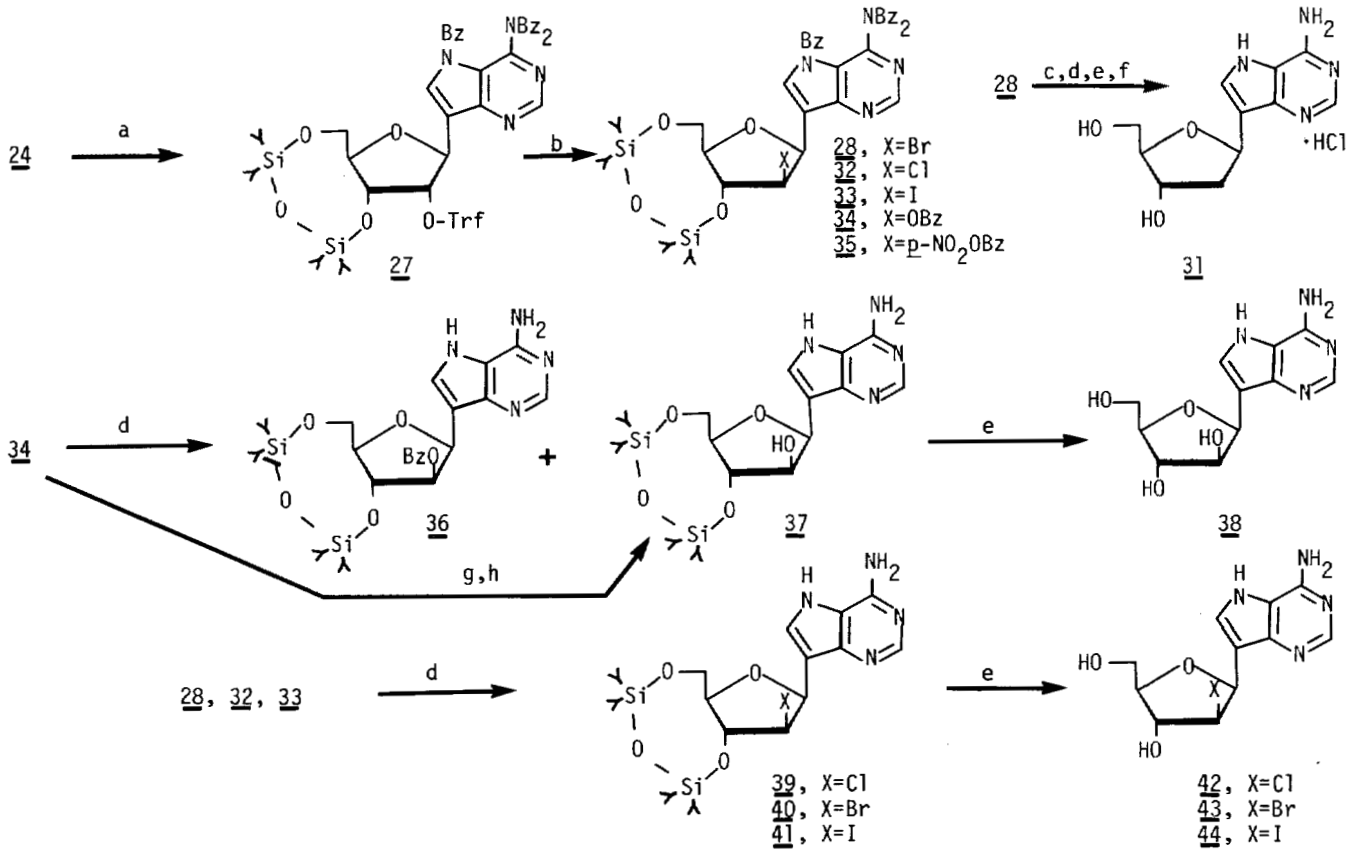
The results described above suggested that it might be necessary in some instances to protect the base moiety in addition to the 3',5'-OH groups of the ribose before conducting any modifications at the 2'-position. 4-Amino-7-(2,3-O-isopropylidene-5-O-trityl-β-D-ribofuranosyl)-5H-pyrrolo[3,2-d]pyrimidine[3] (**21**) was utilized as the starting material for subsequent reactions. Perbenzoylation of **21** with benzoyl chloride in dry pyridine afforded a 97% yield of the tri-N-benzoyl derivative **22**. The ^{1}H NMR spectrum of **22** indicated a downfield shift for the H-2 signal as compared to that of the starting material **21** (δ 8.67 for **22** and δ 7.70 for **21**). The sugar moiety of **22** was selectively deprotected with 6% HCl/MeOH at 25°C to give the tri-N-benzoyl derivative of **1** (**23**) in 75% yield. This was then protected at the 3',5'-positions with TIPDS-Cl_2 in pyridine at 25°C to give a 67% yield of the 3',5'-cyclic disiloxanyl derivative **24**. Compound **24** was then treated with TCDI in dry DMF at 85°C to afford the 2'-O-thiocarbonylimidazolide derivative **25** in only 34% yield. The conversion was accompanied by the loss of two benzoyl groups.[19] Loss of the pyrrolo N-benzoyl group was deduced from the ^{1}H NMR spectrum of **25**, which showed signals at δ 11.13 (broad singlet, 1H, pyrrolo NH, exchanged in D_2O) and at δ 7.69 (broad singlet, 1H, H-6). The H-6 signal sharpened to a narrow singlet after the addition of D_2O. 2'-O-Thiocarbonylimidazolide **25** was then subjected to homolytic deoxygenation at 2' by treatment with tri-n-butyltin hydride with AIBN as initiator in boiling toluene to give a 91% yield of the 2'-deoxy derivative (**26**). Since this approach afforded **26** only in relatively poor overall yield, an alternate route was sought for the synthesis of compound **31** and 2'- substituted ara nucleosides (Scheme IV).

Scheme III



a=BzCl, Pyr./0-25°C; b=6% HCl-MeOH/25°C; c=TIPDS-Cl_2, Pyr./25°C; d=TCDI, DMF/85°C; e=($\underline{n}$-But)$_3$SnH, AIBN, Toluene/Refl.

Scheme IV



a=CF_3SO_2Cl, Et_3N, DMAP, CH_2Cl_2/0-25°C; b=LiBr(or LiCl or KI or NaOBz or NaO-p-NO_2Bz), HMPA/25°C; c=$(n\text{-But})_3SnH$, AIBN, Benzene/Refl.; d=NH_3/MeOH/25°C; e=$(n\text{-But})_4NF$, THF/25°C; f=6% HCl/MeOH; g=0.1M NaOMe/MeOH/90°C; h=Amberlite IRC-50(H^+).

Triflation of the 2'-OH group of **24** with trifluoromethanesulfonyl chloride in the presence of triethylamine and DMAP in dry CH_2Cl_2 gave 2'-triflate (**27**) in 78% yield. Nucleophilic displacement of 2'-triflate by bromide ion using LiBr in dry HMPA at 25°C resulted in the formation of 2'-deoxy-2'-bromo ara derivative **28** in 57% yield. As was expected, the ^1H NMR spectrum of **28** showed an upfield shift of H-2' (δ 4.81) and a downfield shift of H-1' (δ 5.51) as compared to the corresponding signals of **27**. It was also noted that the H-2' peak of **28** appeared as a doublet of doublets ($J_{1',2'}$ = 4.3 Hz, $J_{2',3'}$ = 2.1 Hz) characteristically different from H-2' of **24** ($J_{1',2'}$ = 3.1 Hz, $J_{2',3'}$ = 5.8 Hz). Reductive debromination of **28** with tri-n-butyltin hydride[20] and AIBN in refluxing benzene gave the 2'-deoxy derivative **29** in 80% yield. Selective deprotection of the base moiety was achieved by treating **29** with saturated NH_3/CH_3OH at 25°C for 16 h in a closed, pressure-resistant vessel to give **30** in 77% yield. Deprotection of the 3' and 5'-hydroxyl groups was carried out by treating **30** with TBAF in dry THF at 25°C for 3/4 h to give 2'-deoxy-9-deazaadenosine, isolated as its crystalline hydrochloride salt **31**. The combined yield of these last two steps was 92%. Attempts to deprotect the sugar moiety of **29** prior to debenzoylation of the base moiety was unsuccessful. Thus, treatment of **29** with TBAF in dry THF resulted in an intractable mixture of products possibly due to concurrent, partial debenzoylation. Because of its convenience and general overall efficiency, the synthetic route outlined in Scheme IV has been adopted as the method of choice for the preparation of 2'-deoxy-9-deazaadenosine (**31**).

Reaction of **27** with LiCl in HMPA at 25°C for 1 h gave 2'- chloro ara derivative **32** in 45% yield. In a similar manner, **27** reacted with KI to give the 2'- iodo ara derivative **33** in 46% yield but this reaction was completed only after 24 h, reflecting the more severe steric restrictions placed on nucleophilic displacement by the bulkier I^- ion from the β-face of **27**. Attempts to displace the triflate group by N_3^-, CCl_3COO^- or CH_3COO^- by treatment of **27** with their sodium salts in dry HMPA at 25°C were unsuccessful, resulting in the degradation of the starting materials to intractable mixtures. Reaction of **27** with sodium benzoate in dry HMPA for 1 h, on the other hand, afforded 2'-ara O-benzoyl derivative **34** in 60% yield. Treatment of **34** with saturated NH_3/CH_3OH at 25°C for 30 h gave two major products: a 2'-ara O-benzoyl

derivative **36** (42%) and the fully debenzoylated product **37** (27%). The chromatographic mobilities of **36** and **37** were similar but they could be separated by preparative TLC (silica gel) upon multiple development with CH_2Cl_2:MeOH (10:1). Heating a solution of **36** in saturated NH_3/CH_3OH at 70°C gave more of **37**, but the reaction was still incomplete even after several days, as was indicated by TLC. Since the 2'-ara-O-benzoyl group appeared fairly resistant to ammonolytic cleavage, a much stronger base such as $NaOCH_3$ was tried. Thus, heating **34** in 0.1 M $NaOCH_3$/MeOH at 80°C, followed by neutralization with Amberlite IRC-50 (H^+) resin and chromatographic purification readily afforded **37**. Even though the reaction was complete after 2 h, the yield recovered was only 26%. Improved yields of **37** could be obtained by introducing the more labile p-NO_2 benzoate ester function at the 2'- position. Treatment of **27** with sodium p-nitrobenzoate in dry HMPA at 25°C for 1 h gave the 2'-O-p-nitrobenzoate derivative **35** in 46% yield. Ammonolysis of **35** with saturated NH_3/CH_3OH at 25° C for 36 h afforded the fully deesterified ara derivative **37** in 73% yield. The latter was then desilylated with TBAF in dry THF at 25°C to give 9-deaza ara-A (**38**) in 81% yield.

The fully protected 2'-deoxy-2'-ara chloro (**32**), bromo (**28**) and iodo (**33**) derivatives were readily debenzoylated with saturated NH_3/MeOH at 25°C for 24 h to give **39** (64%), **40** (65%) and **41** (57%) respectively. Intermediates **39** - **41** were fully deprotected by desilylation with TBAF in THF to yield the corresponding 2'-deoxy-2'-ara halo nucleosides (**42** - **44**) in 96, 95 and 38% yields, respectively.

All final C-Nucleosides (**15**, **16**, **31**, **38** and **42** - **44**) were screened in vitro for tumor growth inhibitory activity against mouse leukemia cell lines according to the technique of Fisher[21] with some modifications.[22] The results summarized in Table 1 indicate that 9-Deaza ara-A (**38**) was the most active of all the compounds reported here but was much less active than 9-Deazaadenosine (**1**) itself. Studies of some of these C-nucleosides in other biological systems are in progress.

EXPERIMENTAL SECTION

Melting points were determined on a Thomas-Hoover capillary apparatus and are uncorrected. The ^1H NMR spectra were recorded on a JEOL PFT-100 spectrometer or JEOL FX-90Q spectrometer and chemical shifts are reported as δ values with Me_4Si as the internal standard. Microanalyses

TABLE 1. Comparison of the *in vitro* tumor growth-inhibitory activity of 2'-deoxy and 2'-*ara* substituted derivatives of pyrrolo[3,2-*d*]pyrimidine and thieno[3,2-*d*]pyrimidine C-nucleosides in murine leukemic cell lines.

	ID_{50} (μg/mL)	
Compound	L-1210/0	P-815/0
1	<<0.01	<<0.01
15	33.00	39.00
16	4.12	0.58
31	4.88	48.00
38	0.47	0.09
42	>100	>100
43	4.60	4.17
44	55.50	6.36

were performed by M.H.W. Laboratories, Phoenix, AZ. Thin layer chromatography was performed on 250 μM silica gel GH plates (Analtech, Inc.), and the substances were visualized with a short-wave (254 nm) UV mineral light and/or by spraying with 10% ethanolic sulfuric acid and charring. Preparative TLC was performed on 1,000 μm, 20 x 20 cm silica gel plates (Uniplates by Analtech, Inc.), and the products visualized by short-wave UV light. Preparative column chromatography was performed by standard techniques on Merck Silica gel 60 (70-230 mesh ASTM) or by flash chromatographic techniques[23] on Merck silica gel 60 (230-400 mesh ASTM). Light petroleum ether (bp 30-60°C) was used whenever this solvent was required. 1,3-Dichloro-1,1,3,3-tetraisopropyldisiloxane (TIPDS-Cl_2, 90% pure) was purchased from Aldrich Chemical Company.

7-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-4-oxo-3*H*-thieno[3,2-*d*]pyrimidine (6). A mixture of 7-(β-D-ribofuranosyl)-4-oxo-3*H*-thieno[3,2-*d*]pyrimidine[5] (**3**, 1.5 g, 5.28 mmol), acetic anhydride

5.41 g, 52.99 mmol) and dry pyridine (5 mL) was stirred at 0°C for 1 h. The mixture was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was washed with water, dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography using $CHCl_3$-MeOH (40:1) as the eluent to give **6** (1.61 g, 74%) as a syrup. ^1H NMR ($CDCl_3$): δ 2.12 (s, 9H, $3COCH_3$), 4.38 (m, 3H, H-4', H-5', H-5''), 5.36-5.46 (m, 2H, H-1', H-3'), 5.62 (pseudo t, 1H, H-2'), 7.93 (s, 1H, H-6), 8.16 (s, 1H, H-2, sharp. with D_2O).

Anal. Calcd for $C_{17}H_{18}O_8N_2S$: C, 49.77; H, 4.42; N, 6.82; S, 7.81. Found: C, 49.62; H, 4.41; N, 6.78; S, 7.88.

7-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-4-thio-3H-thieno[3,2-d]pyrimidine (7). Phosphorus pentasulfide (3.0 g, 6.75 mmol) was added in small portions (~ 0.2 g each) to a refluxing mixture of **6** (3.0 g, 7.31 mmol) in dry dioxane (40 mL) for $1^1/_2$ h. Heating was continued until complete reaction was indicated by TLC (~ 3h). After cooling, the suspension was filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography using $CHCl_3$:MeOH (20:1) as the eluent to give **7** as a light yellow foam, yield 2.52 g (84%). ^1H NMR ($CDCl_3$): δ 2.11 (s, 9H, $3COCH_3$), 4.25-4.51 (m, 3H, H-4', H-5', H-5''), 5.32-5.46 (m, 2H, H-1', H-3'), 5.65 (pseudo t, 1H, H-2'), 8.00 (s, 1H, H-6), 8.18 (br s, 1H, H-2, sharp. with D_2O).

Anal. Calcd for $C_{17}H_{18}N_2O_7S_2$: C, 47.88; H, 4.25; N, 6.56; S, 15.04. Found: C, 47.83; H, 4.26; N, 6.36; S, 15.20.

7-(β-D-Ribofuranosyl)-4-(methylthio)thieno[3,2-d]pyrimidine (8). A mixture of **7** (0.35 g, 0.82 mmol) and iodomethane (6.84 g, 48.19 mmol) in CH_3OH (3 mL) and 0.1 N-NaOH (10 mL) was stirred at 25°C for 1 h. The white crystalline precipitate formed was separated by filtration, washed with CH_3OH and then $CHCl_3$ and dried to give **8** as white needles, yield 0.255 g (99%). An analytical sample was obtained by recrystallization from boiling C_2H_5OH; mp 226-228°C. ^1H NMR (DMSO-d_6): δ 2.75 (s, 3H, SCH_3), 3.38-4.33 (m, 5H, H-2', H-3', H-4', H-5', H-5''), 4.91 (d, 1H, OH, exch. with D_2O), 5.13 (m, 3H, H-1' and 2OH's which exch. with D_2O, $J_{1',2'}$ = 5.2 Hz), 8.36 (s, 1H, H-6), 9.00 (s, 1H, H-2).

Anal. Calcd for $C_{12}H_{14}N_2O_4S_2$: C, 45.87; H, 4.49; N, 8.90; S, 20.39. Found: C, 45.89; H, 4.51; N, 8.80; S, 20.25.

7-[3,5-O-(1,1,3,3-Tetraisopropyldisiloxanyl)-β-D-ribofuranosyl]-4-oxo-3H-thieno[3,2-d]pyrimidine (9). A mixture of **3** (1.00 g, 3.52 mmol) and TIPDS-Cl_2 (1.00 g, 3.17 mmol) in dry pyridine (10 ml) was stirred at 25°C for 4 h. The reaction mixture was concentrated in high vacuum and the residue dissolved in CH_2Cl_2. The organic layer was washed with brine (twice), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography using CH_2Cl_2 followed by CH_2Cl_2:MeOH (98:2) as eluents to give **9** as a white solid (1.40 g, 75% yield, mp 180-182°C). ^1H NMR ($CDCl_3$): δ 1.01 - 1.09 (m, 28H, 4 CH_3-CH-CH_3), 3.09 (br s, 1H, OH, exch. with D_2O), 3.98-4.18 (m, 3H, H-4', H-5', H-5''), 4.27 (dd, 1H, H-2', $J_{1',2'}$ = 2.1 Hz, $J_{2',3'}$ = 5.5 Hz), 4.45-4.52 (m, 1H, H-3'), 5.27 (m, 1H, H-1'), 7.95 (d, 1H, H-6, $J_{6,1'}$ = <1 Hz), 8.18 (s, 1H, H-2), 11.26 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{23}H_{38}N_2O_6SSi_2$: C, 52.44; H, 7.27; N, 5.32; S, 6.09. Found: C, 52.52; H, 7.43; N, 5.13; S, 5.99.

7-[3,5-O-(1,1,3,3-Tetraisopropyldisiloxanyl)-β-D-ribofuranosyl]-4-(methylthio)thieno[3,2-d]pyrimidine (10). By a procedure similar to that which gave **9**, deblocked C-nucleoside **8** (1.0 g, 3.18 mmol) was treated with TIPDS-Cl_2 (1.00 g, 3.17 mmol) in dry pyridine (10 mL) to afford, after similar workup, **10** as a colorless syrup (1.46 g, 82%). ^1H NMR ($CDCl_3$): δ 0.99 - 1.09 (m, 28H, 4 CH_3-CH-CH_3), 2.75 (s, 3H, SCH_3), 3.24 (br s, 1H, OH, exch. with D_2O), 4.00 - 4.16 (m, 3H, H-4', H-5', H-5''), 4.31 (dd, 1H, H-2', $J_{1',2'}$ = 2.1 Hz, $J_{2',3'}$ = 5.2 Hz), 4.49 - 4.56 (m, 1H, H-3'), 5.36 (m, 1H, H-1'), 7.93 (d, 1H, H-6, $J_{6,1'}$ = 0.9 Hz), 8.99 (s, 1H, H-2).

Anal. Calcd for $C_{24}H_{40}N_2O_5S_2Si_2$: C, 51.76; H, 7.24; N, 5.03; S, 11.52. Found: C, 51.43; H, 7.12; N, 5.09; S, 11.49.

7-[2-O-[(Imidazol-1-yl)thiocarbonyl]-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-ribofuranosyl]-4-oxo-3H-thieno[3,2-d]pyrimidine (11). A mixture of **9** (1.20 g, 2.28 mmol) and 1,1'-thiocarbonyldiimidazole (TCDI, 0.60 g, 3.37 mmol) in dry DMF (40 mL) was heated at 60°C for 18 h. The mixture was then evaporated *in vacuo* and the crude product was purified by column chromatography using CH_2Cl_2 followed by CH_2Cl_2:MeOH (95:5) as the eluents to give **11** as a white solid (1.19 g, 82%, mp 138-140°C). ^1H NMR ($CDCl_3$): δ 0.92 - 1.09 (m, 28H, 4CH_3-CH-

CH_3), 4.01 - 4.20 (m, 3H, H-4', H-5', H-5''), 4.91 (dd, 1H, H-3', $J_{2',3'}$ = 5.2 Hz, $J_{3',4'}$ = 8.2 Hz), 5.50 (br s, 1H, H-1'), 6.29 (dd, 1H, H-2', $J_{1',2'}$ = <1Hz, $J_{2',3'}$ = 5.2 Hz), 7.08 (s, 1H, H-4 of imidazole), 7.71 (s, 1H, H-5 of imidazole), 8.02 (s, 1H, H-6), 8.12 (s, 1H, H-2, sharp. with D_2O), 8.43 (s, 1H, H-2 of imidazole), 12.02 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{27}H_{40}N_4O_6S_2Si_2$: C, 51.40; H, 6.33; N, 8.80; S, 10.06. Found: C, 51.56; H, 6.56; N, 8.68; S, 10.09.

7-[2-O-[(Imidazol-1-yl)thiocarbonyl]-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-ribofuranosyl]-4-(methylthio)thieno[3,2-d]pyrimidine (12). A mixture of **10** (1.00 g, 1.79 mmol) and TCDI (0.50 g, 2.80 mmol) in dry DMF (10 mL) was heated at 85°C for 3 h. The mixture was then concentrated in high vacuum and the residue chromatographed on a silica gel column using CH_2Cl_2 as the eluent. Fractions containing pure material were pooled together and concentrated *in vacuo* to give thiocarbonylimidazolide **12** as a colorless syrup (1.14 g, 95%). ^1H NMR ($CDCl_3$): δ 0.92 - 1.09 (m, 28H, $4CH_3$-CH-CH_3), 2.76 (s, 3H, SCH_3), 4.01 - 4.20 (m, 3H, H-4', H-5', H-5''), 5.00 (dd, 1H, H-3', $J_{2',3'}$ = 5.2 Hz, $J_{3',4'}$ = 8.2 Hz), 5.56 (m, 1H, H-1'), 6.33 (dd, 1H, H-2', $J_{2',3'}$ = 5.2 Hz, $J_{1',2'}$ = 1.2 Hz), 7.07 (s, 1H, H-4 of imidazole), 7.71 (s, 1H, H-5 of imidazole), 7.99 (d, 1H, H-6, $J_{6,1'}$ = <1Hz), 8.43 (s, 1H, H-2 of imidazole), 8.91 (s, 1H, H-2).

Anal. Calcd for $C_{28}H_{42}N_4O_5S_3Si_2$: C, 50.42; H, 6.35; H, 8.40; S, 14.42. Found: C, 50.31; H, 6.42; N, 8.24; S, 14.67.

7-[2-Deoxy-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-ribofuranosyl]-4-oxo-3H-thieno[3,2-d]pyrimidine (13). A solution of tri-n-butyltin hydride (2.00 g, 6.87 mmol) and α,α'-azobisisobutyronitrile, (AIBN, 0.25 g, 1.52 mmol) in dry toluene (10 mL) was added dropwise to a stirred solution of **11** (1.10 g, 1.73 mmol) in refluxing dry toluene (20 mL) for 30 min. The reaction mixture was then concentrated *in vacuo* and the residue was chromatographed on a silica gel column using CH_2Cl_2, then CH_2Cl_2:MeOH (8:2) as the eluents. Fractions containing the pure product were pooled and evaporated *in vacuo* to give **13** as a white solid (0.83 g, 94%, mp 68- 70°C). ^1H NMR ($CDCl_3$): δ 1.01 - 1.08 (m, 28H, $4CH_3$-CH-CH_3), 2.10 - 2.50 (m, 2H, H-2', H-2''), 3.81 - 4.12 (m, 3H, H-

4', H-5', H-5''), 4.47 - 4.60 (m, 1H, H-3'), 5.47 (pseudo t, 1H, H-1'), 7.90 (d, 1H, H-6, $J_{6,1'}$ = <1 Hz), 8.17 (s, 1H, H-2, sharp. with D_2O), 11.36 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{23}H_{38}N_2O_5SSi_2$: C, 54.08; H, 7.50; N, 5.48; S, 6.28. Found: C, 53.99; H, 7.43; N, 5.45; S, 6.06.

7-[2-Deoxy-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-ribofuranosyl]-4-(methylthio)thieno[3,2-d]pyrimidine (14). By a procedure similar to that which gave **13**, thiocarbonylimidazolide **12** (1.20 g, 1.80 mmol) was treated with tri-n-butyltin hydride (2.00 g, 6.87 mmol) and AIBN (0.25 g, 1.52 mmol) in refluxing dry toluene to give **14** as a colorless syrup (0.90 g, 92%). ^1H NMR ($CDCl_3$): δ 0.99 - 1.09 (m, 28H, $4CH_3$-CH-CH_3), 2.18 - 2.71 (m, 2H, H-2', H-2''), 2.75 (s, 1H, SCH_3), 3.80 - 4.11 (m, 3H, H-4', H-5', H-5''), 4.49 - 4.63 (m, 1H, H-3'), 5.57 (pseudo t, 1H, H-1'), 7.88 (d, 1H, H-6, $J_{6,1'}$ = <1 Hz), 8.97 (s, 1H, H-2).

Anal. Calcd for $C_{24}H_{40}N_2O_4S_2Si_2$: C, 53.29; H, 7.45; N, 5.18; S, 11.86. Found: C, 53.52; H, 7.24; N, 5.37; S, 11.68.

7-(2-Deoxy-β-D-ribofuranosyl)-4-oxo-3H-thieno[3,2-d]-pyrimidine (15). To a solution of **13** (0.80 g, 1.57 mmol) in dry THF (16 mL), was added dropwise a 1 M solution of tetra-n-butylammonium fluoride (TBAF) in THF (5 mL) at 25°C with stirring for a period of 5 min. The reaction mixture was concentrated *in vacuo* and the residue was chromatographed on a silica gel column using CH_2Cl_2:MeOH (95:5) as the eluent. Fractions containing pure product were mixed and concentrated *in vacuo* to afford **15** as a white solid (0.34 g, 81%, mp 133-135°C). ^1H NMR (DMSO-d_6): δ 1.80 - 2.30 (m, 2H, H-2', H-2''), 3.19 - 3.49 (m, 2H, H-5', H-5''), 3.83 (m, 1H, H-4'), 4.21 (m, 1H, H-3'), 4.89 (m, 1H, CH_2OH, exch. with D_2O), 5.08 (d, 1H, CHOH, exch. with D_2O, $J_{OH,3'}$ = 3 Hz), 5.38 (dd, 1H, H-1', $J_{1',2'}$ = 5.5 Hz, $J_{1',2''}$ = 10.1 Hz), 8.05 (d, 1H, H-6, $J_{6,1'}$ = <1 Hz), 8.17 (s, 1H, H-2, sharp. with D_2O), 11.80 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{11}H_{12}N_2O_4S$: C, 49.24; H, 4.51; N, 10.44; S, 11.95. Found: C, 49.43; H, 4.67; N, 10.32; S, 11.65.

7-(2-Deoxy-β-D-ribofuranosyl)-4-(methylthio)thieno[3,2-d]-pyrimidine (16). By a procedure similar to that which gave **15**, compound

14 (0.90 g, 1.66 mmol) was desilylated to give **16** as a white solid (0.25 g, 50%, mp 157-158°C) after isolation by column chromatography (CH_2Cl_2 followed by CH_2Cl_2:MeOH (98:2) as the eluents). ^1H NMR (DMSO-d_6): δ 1.89 - 2.37 (m, 2H, H-2', H-2''), 2.75 (s, 3H, SCH_3), 3.46 - 3.54 (m, 2H, H-5', H-5''), 3.81 - 3.88 (m, 1H, H-4'), 4.24 - 4.27 (m, 1H, H-3'), 4.91 (t, 1H, CH_2OH, exch. with D_2O, $J_{OH,\,3'}$ = 5.8 Hz), 5.10 (d, 1H, CHOH, exch. with D_2O, $J_{OH,\,5'}$ = 4 Hz), 5.44 (m, 1H, H-1', $J_{1',2'}$ = 6.1 Hz, $J_{1',2''}$ = 9.8 Hz), 8.22 (d, 1H, H-6, $J_{6,1'}$ = <1 Hz), 8.98 (s, 1H, H-2).

Anal. Calcd for $C_{12}H_{14}N_2O_3S_2$: C, 48.30; H, 4.73; N, 9.39; S, 21.49. Found: C, 48.27; H, 4.70; N, 9.29; S, 21.31.

4-Amino-7-[3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-ribofuranosyl]-5H-pyrrolo[3,2-d]pyrimidine (17). A mixture of 9-deazaadenosine hydrochloride[3] (**1**, 1.15 g, 3.78 mmol), TIPDS-Cl_2 (1.20 g, 3.51 mmol) in dry pyridine (11 mL) was stirred under argon at 25°C in a sealed flask for 3 h. The reaction mixture was concentrated *in vacuo* at 25°C and the resulting residue partitioned between CH_2Cl_2 and H_2O. The organic layer was washed with H_2O/brine (twice), then with brine, dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by column chromatography using CH_2Cl_2:CH_3OH (20:1) followed by CH_2Cl_2:CH_3OH (15:1) as eluents. Fractions containing the pure product were pooled and evaporated *in vacuo* to give **17** as a white foam (1.474 g, 76%). ^1H NMR (DMSO-d_6): δ 1.00 (m, 28H, $4CH_3$-CH-CH_3), 3.45 (br s, 1H, OH, exch. with D_2O), 3.92 (m, 3H, H-4', H-5', H-5''), 4.25 (m, 1H, H-2', $J_{1',2'}$ = 2.1 Hz, $J_{2',3'}$ = 4.6 Hz), 4.49 (m, 1H, H-3'), 4.93 (d, 1H, H-1'), 7.40 (br s, 2H, NH_2, exch. with D_2O), 7.54 (br s, 1H, H-6, sharp. with D_2O), 8.18 (s, 1H, H-2), 11.49 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{23}H_{40}N_4O_5Si_2$: C, 54.30; H, 7.92; N, 11.01. Found: C, 54.09; H, 7.95; N, 10.93.

7-[3,5-O-(1,1,3,3-Tetraisopropyldisiloxanyl)-β-D-ribofuranosyl]-4-oxo-3H,5H-pyrrolo[3,2-d]pyrimidine (18). TIPDS-Cl_2 (5.75 g, 18.22 mmol) was added slowly to a stirred solution of **2**[4] (5.34 g, 17.58 mmol) in dry pyridine (100 mL) under argon. The mixture was stirred at 25°C for 16 h, then concentrated *in vacuo* and the resulting residue was partitioned between CH_2Cl_2 and H_2O. The aqueous layer was

extracted again with CH_2Cl_2 twice. The organic layers were combined and then washed with brine-H_2O, brine, dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash chromatography using CH_2Cl_2:MeOH (20:1) as the eluent to give **18** as a white solid (7.73 g, 86%, mp 209-210°C). ^1H NMR ($CDCl_3$): δ 1.06-1.10 (m, 28H, $4CH_3$-CH-CH_3), 3.42 (br s, 1H, CONH, exch. with D_2O), 4.11 (m, 3H, H-4', H-5', H-5''), 4.50 (m, 2H, H-2', H-3'), 5.16 (br s, 1H, H-1', changes to d with D_2O, $J_{1',2'}$ = 2.7 Hz), 7.39 (br s, 1H, H-6, sharp. with D_2O), 8.52 (br s, 1H, H-2, sharp. with D_2O), 11.32 (br s, 1H, pyrrolo NH, exch. with D_2O).

Anal. Calcd for $C_{23}H_{39}N_3O_6Si_2$: C, 54.19; H, 7.71; N, 8.24. Found: C, 54.09; H, 7.94; N, 8.05.

7-[3,5-O-(1,1,3,3-Tetraisopropyldisiloxanyl)-2-O-trifluoromethanesulfonyl-β-D-ribofuranosyl]-3-trifluoromethanesulfonyl-4-oxo-5H-pyrrolo[3,2-d]pyrimidine (19) and **7-[3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-2-O-trifluoromethanesulfonyl-β-D-ribofuranosyl]-4-(trifluoromethanesulfonyloxy)-5H-pyrrolo[3,2-d]-pyrimidine (20).** A solution of trifluoromethanesulfonic anhydride (0.338 g, 1.20 mmol) in dry CH_2Cl_2 (2 mL) was added dropwise at -60°C to a stirred mixture of **18** (0.509 g, 1 mmol) and dry pyridine (0.19 g, 2.40 mmol) in dry CH_2Cl_2 (10 mL). The temperature was slowly raised to 25°C. The flask was then cooled to -30°C and pyridine (0.19 g, 2.40 mmol) and trifluoromethanesulfonic anhydride (0.085 g, 0.30 mmol) in CH_2Cl_2 (2 mL) were added successively. The temperature was then slowly raised to 25°C. The mixture was again cooled to -30°C and the last portions of pyridine (0.245 g, 3.10 mmol) and trifluoromethanesulfonic anhydride (0.085 g, 0.30 mmol) in dry CH_2Cl_2 (2 mL) were finally added. The reaction mixture was slowly brought to 25°C, then diluted with CH_2Cl_2, washed with H_2O twice, dried (Na_2SO_4) and concentrated in vacuo. The residue was subjected to flash column chromatography using pet. ether:EtOAC (90:10) to elute **20** which was obtained as a foam (0.235 g, 30%).

^1H NMR ($CDCl_3$): δ 1.03 - 1.07 (m, 28H, $4CH_3$-CH-CH_3), 4.07 (m, 3H, H-4', H-5', H-5''), 5.10 (dd, 1H, H-3', $J_{2',3'}$ = 4.3 Hz, $J_{3',4'}$ = 9 Hz), 5.43 (s, 1H, H-1'), 5.70 (d, 1H, H-2'), 7.80 (d, 1H, H-6, sharp. to s with D_2O), 8.71 (s, 1H, H-2), 9.26 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{25}H_{37}F_6N_3O_{10}S_2Si_2$: C, 38.80; H, 4.82; N, 5.43; S, 8.29. Found: C, 38.68; H, 5.00; N, 5.32; S, 8.26.

Further elution with pet. ether:EtOAc (85:15) afforded the more polar product **19** as foam (0.240 g, 31%.)

^{1}H NMR ($CDCl_3$): δ 1.07 (m, 28H, $4CH_3$-CH-CH_3), 1.68 (br s, 1H, NH, exch. with D_2O), 3.92 - 4.10 (m, 3H, H-4', H-5', H-5''), 4.85 (dd, 1H, H-3', $J_{2',3'}$ = 4.3 Hz, $J_{3',4'}$ = 8.9 Hz), 5.32 (s, 1H, H-1'), 5.53 (d, 1H, H-2'), 7.51 (d, 1H, H-6, $J_{NH,6}$ = 3.0 Hz, changes to s with D_2O), 8.22 (s, 1H, H-2), 10.04 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{25}H_{37}F_6N_3O_{10}S_2Si_2$: C, 38.80; H, 4.82; N, 5.43; S, 8.29. Found: C, 38.41; H, 5.21; N, 5.09; S. 8.09.

5-Benzoyl-7-(2,3-O-isopropylidene-5-O-trityl-β-D-ribofuranosyl)-4-(dibenzoylamino)pyrrolo[3,2-d]pyrimidine (22). Benzoyl chloride (23.01 g, 163.68 mmol) was added dropwise to a stirred solution of 4-amino-7-(2',3'-O-isopropylidene-5'-O-trityl-β-D-ribofuranosyl)-5H-pyrrolo[3,2-d]pyrimidine[3] (**21**, 15.00 g, 27.34 mmol) in dry pyridine (100 mL) at 0°C. The temperature was then slowly raised to 25°C and stirred overnight. The reaction mixture was concentrated *in vacuo* at 25°C and the residue partitioned between H_2O and CH_2Cl_2. The aqueous layer was further extracted with CH_2Cl_2. The organic layers were combined, washed with cold saturated $NaHCO_3$ solution then with H_2O (twice), dried (Na_2SO_4) and concentrated *in vacuo* to give a foam. The crude product was purified by flash column chromatography using first EtOAc:pet.ether (20:80) and then EtOAc:pet.ether (30:70) as eluents. Fractions containing the pure product were pooled and concentrated *in vacuo* to give **22** as a white foam (21.90 g, 97%). ^{1}H NMR ($CDCl_3$): δ 1.35 (s, 3H, CH_3), 1.60 (s, 3H, CH_3), 3.34 (m, 2H, H-5', H-5''), 4.29 (m, 1H, H-4'), 4.81 (dd, 1H, H-3', $J_{2',3'}$ = 4.3 Hz, $J_{3',4'}$ = 6.2 Hz), 5.12 (d, 1H, H-2', $J_{1',2'}$ = 4.3 Hz), 5.28 (d, 1H, H-1'), 7.10 - 8.03 (m, 31H, trityl, 3 benzoyl, H-6), 8.67 (s, 1H, H-2).

Anal. Calcd for $C_{51}H_{44}N_4O_7$: C, 74.25; H, 5.38; N, 6.79. Found: C, 74.41; H, 5.37; N, 6.56.

5-Benzoyl-4-(dibenzoylamino)-7-β-D-ribofuranosylpyrrolo-[3,2-d]-pyrimidine (23). A solution of **22** (1.58 g, 1.91 mmol) in 6% HCl/CH_3OH was stirred in a sealed flask at 25°C for $2^1/_2$ h. The mixture was then concentrated *in vacuo* to a viscous oil. The oily material was washed several times with anhydrous ether and dried overnight, *in vacuo*, over

P_2O_5 to give **23** as a solid (0.979 g, 83%). An analytical sample (mp 118-120°C) was obtained by preparative TLC using CH_2Cl_2:MeOH (10:1) as the developing agent. ^1H NMR (DMSO-d_6): δ 3.54 (m, 2H, H-5', H-5''), 3.85 (m, 1H, H-4'), 4.04 (pseudo t, 1H, H-3'), 4.36 (pseudo t, 1H, H-2'), 4.74 (br s, 3H, 2'-OH, 3'-OH, 5'-OH, exch. with D_2O), 4.95 (d, 1H, H-1', $J_{1',2'}$ = 5.8 Hz), 7.38 - 8.11 (m, 16 H, 3 benzoyl, H-6), 8.77 (s, 1H, H-2).

Anal. Calcd for $C_{32}H_{26}N_4O_7$: C, 66.43; H, 4.53; N, 9.68. Found: C, 66.04; H, 4.61; N, 9.41.

5-Benzoyl-4-(dibenzoylamino)-7-[3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-ribofuranosyl]pyrrolo[3,2-d]pyrimidine (24). TIPDS-Cl_2 (2.36 g, 6.75 mmol) was added dropwise under N_2 atmosphere to a stirred solution of **23** (3.70 g, 6.01 mmol) in dry pyridine (35 mL) and the mixture was stirred for 4 h at 25°C. The reaction mixture was concentrated in high vacuum and the resulting residue partitioned between CH_2Cl_2-50% aq NaCl. The aqueous layer was further extracted with CH_2Cl_2. The organic layers were combined, washed with H_2O-brine (twice) and then with brine (once), dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography using first pet.ether:EtOAc (85:15), then pet.ether-EtOAc (80:20) as eluents. Fractions containing the pure product were pooled and concentrated in vacuo to give **24** as a white solid (2.90 g, 61%, mp 125-127°C). ^1H NMR ($CDCl_3$): δ 1.06 - 1.07 (m, 28H, $4CH_3$-CH-CH_3), 3.13 (br s, 1H, OH, exch. with D_2O), 4.02 (m, 3H, H-4', H-5', H-5''), 4.50 - 4.53 (m, 1H, H-2', changes to dd with D_2O, $J_{1',2'}$ = 3.1 Hz, $J_{2',3'}$ = 5.8 Hz), 4.75 - 4.80 (m, 1H, H-3'), 5.07 (d, 1H, H-1'), 7.24 - 8.05 (m, 16H, 3 benzoyl and H-6), 8.69 (s, 1H, H-2).

Anal. Calcd for $C_{44}H_{52}N_4O_8Si_2$: C, 66.97; H, 6.64; N, 7.10. Found: C, 66.79; H, 6.75; N, 6.94.

4-(Benzoylamino)-7-[2-O-[(Imidazol-1-yl)thiocarbonyl]-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-ribofuranosyl]pyrrolo[3,2-d]-pyrimidine (25). A mixture of **24** (0.20 g, 0.25 mmol) and TCDI (0.124 g, 0.69 mmol) in dry DMF (4.5 mL) was heated at 120°C for $4^1/_2$ h. The mixture was cooled to 50°C and concentrated in vacuo. The residue was then partitioned between CH_2Cl_2 and H_2O and the organic layers were

combined, dried (Na_2SO_4) and concentrated *in vacuo*. This gave a yellow oil which was subjected to preparative TLC (6 plates, 2 developments) using CH_2Cl_2:MeOH (20:1). Extraction of the appropriate bands afforded **25** as a colorless solid (0.065 g, 34%, mp 83-85°C). ^1H NMR ($CDCl_3$): δ 0.95 - 1.08 (m, 28H, $4CH_3$-CH-CH_3), 4.03 - 4.12 (m, 3H, H-4', H-5', H-5''), 5.25 - 5.39 (m, 1H, H-3'), 5.50 (d, 1H, H-1', $J_{1',2'}$ = 1.8 Hz), 6.42 (dd, 1H, H-2', $J_{2',3'}$ = 5.0 Hz), 7.07 (br s, 2H, H-4 of imidazole and CONH), 7.43 - 7.70 (m, 5H, *m*- and *p*- benzoyl, H-6 and H-5 of imidazole), 7.98 - 8.06 (m, 2H, *o* - benzoyl), 8.43 (s, 1H, H-2 of imidazole), 8.50 (s, 1H, H-2), 11.13 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{34}H_{46}N_6O_6SSi_2$: C, 56.48; H, 6.41; N, 11.62; S, 4.43. Found: C, 56.37; H, 6.60; N, 11.42; S, 4.51.

4-(Benzoylamino)-7-[2-deoxy-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-ribofuranosyl]-5H-pyrrolo[3,2-d]pyrimidine (26). A mixture of tri-*n*-butyltin hydride (0.097 g, 0.33 mmol) and AIBN (0.010 g, 0.06 mmol) in dry toluene (0.5 mL) was added dropwise to a stirred refluxing solution of **25** (0.054 g, 0.07 mmol) in dry toluene (1 mL). Refluxing was continued for 2 h and the mixture was then cooled to 60°C and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 and subjected to preparative TLC (3 plates) using CH_2Cl_2:CH_3OH (20:1) as the developing agent. The desired product was extracted (CH_2Cl_2:MeOH, 10:1) and, after evaporation, obtained as a white solid (0.040 g, 91%, mp 63-65°C). ^1H NMR ($CDCl_3$): δ 1.05 - 1.08 (m, 28H, $4CH_3$-CH-CH_3), 2.50 (pseudo t, 2H, H-2', H-2''), 3.86 - 4.18 (m, 3H, H-4', H-5', H-5''), 4.67 (m, 1H, H-3'), 5.49 - 5.63 (pseudo t, 1H, H-1'), 7.55 - 7.62 (m, 4H, *m* and *p*-benzoyl, H-6), 7.99 - 8.05 (m, 2H, *o*-benzoyl), 8.62 (s, 1H, H-2), 8.93 (br s, 1H, CONH, exch. with D_2O), 10.93 (br s, 1H, pyrrolo NH, exch. with D_2O).

Anal Calcd for $C_{30}H_{44}N_4O_5Si_2$: C, 60.37; H, 7.43; N, 9.39. Found: C, 60.01; H, 7.44; N, 9.03.

5-Benzoyl-4-(dibenzoylamino)-7-[3',5'-O-(1,1,3,3-tetraisopropyldisiloxanyl)-2-O-trifluoromethanesulfonyl-β-D-ribofuranosyl]-pyrrolo[3,2-d]pyrimidine (27). Trifluoromethanesulfonyl chloride (0.37 g, 2.20 mmol) was added dropwise at 0°C under N_2 atmosphere to a stirred mixture of **24** (1.45 g, 1.84 mmol), 4-dimethylaminopyridine

(0.234 g, 1.91 mmol) and triethylamine (0.221 g, 2.18 mmol) in dry CH_2Cl_2 (25 mL). The temperature was slowly raised to 25°C and the mixture was stirred for 1 h. The reaction mixture was then diluted with CH_2Cl_2 and poured over crushed ice. The aqueous layer was extracted with CH_2Cl_2 (twice). The organic layers were combined, washed with H_2O (twice), dried (Na_2SO_4) and concentrated in vacuo at 25°C. The residue was dissolved in a minimum quantity of CH_2Cl_2 and purified by flash column chromatography using pet.ether:EtOAc (85:15) as the eluent. Fractions containing the pure product were pooled and concentrated in vacuo to give **27** as a colorless solid, (1.50 g, 86%, mp 104-106°C). ^1H NMR ($CDCl_3$): δ 1.06 - 1.12 (m, 28H, 4-CH_3-CH-CH_3), 3.92 - 4.03 (m, 3H, H-4', H-5', H-5''), 5.13 - 5.29 (m, 2H, H-1', H-3'), 5.86 (d, 1H, H-2', $J_{1',2'}$ = 0 Hz, $J_{2',3'}$ = 4.9 Hz), 7.33 - 7.68 (m, 10H, m and p-benzoyl and H-6), 7.81 - 8.03 (m, 6H, o-benzoyl), 8.62 (s, 1H, H-2).

Anal. Calcd for $C_{45}H_{51}F_3N_4O_{10}SSi_2$: C, 56.71; H, 5.39; N, 5.88; S, 3.36. Found: C, 56.52; H, 5.51; N, 5.82; S, 3.19.

5-Benzoyl-4-(dibenzoylamino)-7-[3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-2-deoxy-2-bromo-β-D-arabinofuranosyl]pyrrolo[3,2-d]pyrimidine (28). A mixture of **27** (1.50 g, 1.57 mmol) and lithium bromide (0.284 g, 3.27 mmol) in dry hexamethylphosphoramide (HMPA, 16 mL) was stirred for 4 h in a sealed vessel under an argon atmosphere. The mixture was poured over ice-water (~ 100 g). The precipitate formed was separated by filtration, washed thoroughly with H_2O and dried in vacuo at 60°C over P_2O_5 for 4 h. The crude product (2.04 g) was purified by flash column chromatography using CH_2Cl_2:MeOH (200:1) as the eluent to give **28** as a white solid (1.16 g, 57%, mp 135-136°C). ^1H NMR ($CDCl_3$): δ 1.06 - 1.09 (m, 28H, 4CH_3-CH-CH_3), 3.92 - 4.20 (m, 3H, H-4', H-5', H-5''), 4.81 (dd, 1H, H-2', $J_{1',2'}$ = 4.3 Hz, $J_{2',3'}$ = 2.1 Hz), 4.92 (m, 1H, H-3'), 5.51 (d, 1H, H-1'), 7.26 - 7.70 (m, 10H, m- and p-benzoyl and H-6), 7.84 - 8.05 (m, 6H, o-benzoyl), 8.72 (s, 1H, H-2).

Anal. Calcd for $C_{44}H_{51}BrN_4O_7Si_2$: C, 59.78; H, 5.81; Br, 9.04; N, 6.34. Found: C, 59.84; H, 5.86; Br, 9.22; N, 6.26.

5-Benzoyl-4-(dibenzoylamino)-7-[2-deoxy-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-ribofuranosyl]pyrrolo[3,2-d]-pyrimidine (29). Tri-n-butyltin hydride (1.76 g, 6.06 mmol) was added quickly under argon

to a solution of **28** (1.78 g, 2.02 mmol) in dry benzene. The mixture was refluxed under an argon atmosphere for 2 min. A solution of AIBN (20 mg) in dry benzene was then added quickly to the reaction mixture and heating was continued for 3 h. The mixture was then cooled to 35°C and concentrated *in vacuo*. The crude product was purified by flash column chromatography using first CH_2Cl_2:MeOH (150:1) then CH_2Cl_2:MeOH (80:1) as eluents. After evaporation of appropriate fractions, **29** was obtained as a white solid (1.30 g, 80%, mp 93-95°C). ^{1}H NMR ($CDCl_3$): δ 1.04 (m, 28H, $4CH_3$-CH-CH_3), 2.50 (pseudo t, 2H, H-2', H-2''), 3.80 - 4.10 (m, 3H, H-4', H-5', H-5''), 4.62 - 4.72 (m, 1H, H-3'), 5.40 (pseudo t, 1H, H-1'), 7.26 - 7.61 (m, 10H, *m* and *p*-benzoyl and H-6), 7.82 - 8.06 (m, 6H, *o*-benzoyl), 8.71 (s, 1H, H-2).

Anal. Calcd for $C_{44}H_{52}N_4O_7Si_2$: C, 65.64; H, 6.51; N, 6.96. Found: C, 65.26; H, 6.70; N, 6.60.

4-Amino-7-[3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-2-deoxy-β-D-ribofuranosyl]-5H-pyrrolo[3,2-d]pyrimidine (30). A solution of **29** (0.30 g, 0.37 mmol) in saturated methanolic ammonia (60 mL) was stirred in a closed pressure-resistant vessel for 16 h at ambient temperature. The mixture was concentrated *in vacuo* and the residue purified by preparative TLC (4 plates) using CH_2Cl_2:MeOH (10:1) as the developing agent. The desired product was extracted with CH_2Cl_2:MeOH (10:1), filtered and the filtrate concentrated *in vacuo* to give **30** as a white solid (0.138 g, 77%, mp 220-222°C). ^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 1.04 - 1.07 (m, 28H, $4CH_3$-CH-CH_3), 2.36 - 2.59 (m, 2H, H-2', H-2''). 3.50 - 4.13 (m, 3H, H-4', H-5', H-5''), 4.58 - 4.73 (m, 1H, H-3'), 5.44 (pseudo t, 1H, H-1'), 6.25 (br s, 2H, NH_2, exch. with D_2O), 7.34 (s, 1H, H-6, sharp. with D_2O), 8.29 (s, 1H, H-2), 10.78 - 10.87 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{23}H_{40}N_4O_4Si_2$: C, 56.06; H, 8.18; N, 11.37. Found: C, 55.84; H, 8.12; N, 11.21.

4-Amino-7-(2-deoxy-β-D-ribofuranosyl)-5H-pyrrolo[3,2-d]pyrimidine hydrochloride (31). TBAF (dried overnight *in vacuo* over P_2O_5 before use; 0.121 g, 0.46 mmol) was added quickly, under argon, to a suspension of **30** (0.107 g, 0.22 mmol) in dry THF (2.5 mL). The reaction mixture was stirred in a sealed vessel for 45 min. The mixture was then concen-

trated *in vacuo* and the residue dissolved in CH_2Cl_2–CH_3OH and purified by preparative TLC (4 plates, 2 developments) using $CHCl_3$:MeOH (4:1) as the developing agent. The desired product was extracted with warm $CHCl_3$:MeOH (3:1), filtered and the filtrate concentrated *in vacuo* to give the free base of **31** as a hygroscopic solid. This material was converted to the hydrochloride salt by the addition of 6% HCl/CH_3OH 2 mL), followed by evaporation *in vacuo*. The resulting product was washed thoroughly with anhydrous ether and dried *in vacuo* over P_2O_5 to give **31** as its crystalline hydrochloride salt (0.050 g, 92%, mp > 300°C). ^1H NMR (DMSO-d_6): δ 2.00 – 2.13 (m, 2H, H-2', H-2''), 3.56 – 4.00 (m, 2H, H-5', H-5''), 3.71 – 3.85 (m, 1H, H-4'), 4.29 (m, 1H, H-3'), 5.29 (pseudo t, 1H, H-1'), 7.70 (br s, 2H, 2OH's exch. with D_2O), 7.87 (d, 1H, H-6, $J_{NH,6}$ = 3.5 Hz, changes to s with D_2O), 8.50 (s, 1H, H-2), 9.15 (br s, 2H, NH_2, exch. with D_2O), 11.13 (s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{11}H_{14}N_4O_3$.HCl: C, 46.08; H, 5.27; Cl, 12.36; N, 19.54. Found: C, 46.01; H, 5.30; Cl, 12.28; N, 19.36.

5-Benzoyl-4-(dibenzoylamino)-7-[3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-2-deoxy-2-chloro-β-D-arabinofuranosyl]pyrrolo[3,2-*d*]pyrimidine (32). A mixture of **27** (1.31 g, 1.38 mmol) and lithium chloride (1.50 mmol) in dry HMPA (10 mL) was stirred under argon in a sealed vessel at 25°C for 1 h. The mixture was poured over ice-water. The light yellow precipitate formed was separated by filtration, washed thoroughly with H_2O and dried over P_2O_5 *in vacuo* to give a crude product, which was purified by preparative TLC (5 plates) using CH_2Cl_2:MeOH (100:1) as the developing agent. The plates were developed twice. The desired product was extracted with CH_2Cl_2:MeOH (100:2), filtered and the filtrate concentrated *in vacuo* to give **32** as a white solid (0.525 g, 45%, mp 124–126°C). ^1H NMR ($CDCl_3$): δ 1.04 – 1.10 (m, 28H, 4CH_3–C*H*–CH_3), 3.85 – 4.00 (m, 3H, H-4', H-5', H-5''), 4.71 – 4.75 (m, 2H, H-2', H-3'), 5.62 (dd, 1H, H-1', $J_{1',2'}$ = 4.3 Hz, $J_{6,1'}$ = <1 Hz), 7.32 – 7.70 (m, 10H, *m* and *p*-benzoyl and H-6), 7.82 – 8.11 (m, 6H, *o*-benzoyl), 8.72 (s, 1H, H-2).

Anal. Calcd for $C_{44}H_{51}ClN_4O_7Si_2$: C, 62.95; H, 6.12; Cl, 4.22; N, 6.67. Found: C, 62.72; H, 6.25; Cl, 4.07; N, 6.48.

5-Benzoyl-4-(dibenzoylamino)-7-[3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-2-deoxy-2-iodo-β-D-arabinofuranosyl]pyrrolo[3,2-*d*]-

pyrimidine (33). A mixture of **27** (2.85 g, 2.99 mmol) and potassium iodide (0.496 g, 2.99 mmol) in dry HMPA (30 mL) under argon in a sealed vessel, was sonicated for 10 min and then magnetically stirred at 25°C for 24 h. The mixture was then poured over crushed ice and the resulting precipitate filtered, washed thoroughly with H_2O and dissolved in CH_2Cl_2. The CH_2Cl_2 solution was washed with H_2O, dried (Na_2SO_4) and evaporated *in vacuo*. The resulting residue was subjected to flash column chromatography using CH_2Cl_2:MeOH (300:1) as the eluent. Fractions containing the pure product were pooled and concentrated *in vacuo* to give **33** as a white solid (1.30 g, 46%, 124-126°C). ^1H NMR ($CDCl_3$): δ 1.03 - 1.09 (m, 28H, $4CH_3$-CH-CH_3), 4.02 (m, 3H, H-4', H-5', H-5''), 4.82 - 5.08 (m, 3H, H-1', H-2', H-3', $J_{1',2'}$ = 4.6 Hz), 7.22 - 7.66 (m, 10H, *m* and *p*-benzoyl and H-6), 7.84 - 8.00 (m, 6H, *o*-benzoyl), 8.72 (s, 1H, H-2).

Anal. Calcd for $C_{44}H_{51}IN_4O_7Si_2$: C, 56.76; H, 5.52; I, 13.63; N, 6.02. Found: C, 57.00; H, 5.63; I, 13.76; N, 5.98.

5-Benzoyl-4-(dibenzoylamino)-7-[2'-O-benzoyl-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-arabinofuranosyl]pyrrolo[3,2-*d*]-pyrimidine (34). A mixture of **27** (0.95 g, 1.00 mmol) and sodium benzoate (0.15 g, 1.04 mmol) in dry HMPA (10 mL) was stirred under argon atmosphere for 1 h. The mixture was then poured in ice-water and the resulting precipitate filtered and dried *in vacuo* over P_2O_5 to give the crude product. Purification by flash column chromatography using CH_2Cl_2:CH_3OH (200:1) as the eluent afforded **34** as a white solid (0.55 g, 60%, mp 118-120°C. ^1H NMR ($CDCl_3$): δ 1.03 - 1.06 (m, 28H, $4CH_3$-$4CH$-CH_3), 3.92 - 4.18 (m, 3H, H-4', H-5', H-5''), 4.84 (m, 1H, H-3'), 5.70 - 5.83 (m, 2H, H-1', H-2'), 6.22 - 7.93 (m, 21H, 4 benzoyls and H-6), 8.68 (s, 1H, H-2).

Anal. Calcd for $C_{51}H_{56}N_4O_9Si_2$: C, 66.21; H, 6.10; N, 6.05. Found: C, 66.10; H, 6.15; N, 5.99.

5-Benzoyl-4-(dibenzoylamino)-7-[2-O-*p*-nitrobenzoyl-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-arabinofuranosyl]pyrrolo[3,2-*d*]pyrimidine (35). A mixture of **27** (5.887 g, 6.18 mmol), sodium *p*-nitrobenzoate (1.18 g, 6.22 mmol) in dry HMPA (62 mL) was stirred at 25°C under an argon atmosphere in a sealed vessel for 1 h. The mixture was then poured over crushed ice. The precipitate formed was filtered,

washed thoroughly with H_2O, dried in vacuo over P_2O_5 and the crude product purified by flash column chromatography using CH_2Cl_2:MeOH (200:1) as the eluent. Fractions containing the pure product were pooled and concentrated in vacuo to give **35** as a white solid, (yield 2.777 g, 46%, mp 126-127°C). ^1H NMR ($CDCl_3$): δ 0.99 - 1.07 (m, 28H, $4CH_3$-CH-CH_3), 4.04 (m, 3H, H-4', H-5', H-5''), 4.91 (m, 1H, H-3'), 5.65 - 5.90 (m, 2H, H-1', H-2'), 7.18 - 8.19 (m, 20H, o, m and p-benzoyl, H-6), 8.61 (s, 1H, H-2).

Anal. Calcd for $C_{51}H_{55}N_5O_{11}Si_2$: C, 63.14; H, 5.71; N, 7.22. Found: C, 63.19; H, 5.61; N, 7.12.

4-Amino-7-[2-O-Benzoyl-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-arabinofuranosyl]-5H-pyrrolo[3,2-d]pyrimidine (36) and **4-Amino-7-[3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-arabinofuranosyl]-5H-pyrrolo[3,2-d]pyrimidine (37).**

METHOD A: A solution of **34** in saturated methanolic ammonia was stirred at 25°C in a pressure-resistant vessel for 30 h. The mixture was then concentrated in vacuo and the residue subjected to preparative TLC using CH_2Cl_2:MeOH (10:1) as developing agent. Plates were developed twice. Two major bands were observed under UV light. Each was extracted with CH_2Cl_2:CH_3OH (10:1). Filtration and evaporation to dryness afforded **36** and **37** as white solids.

The less polar compound was identified as **36** (0.069 g, 42%, mp 260-261°C). ^1H NMR ($CDCl_3$ + DMSO-d_6): δ 1.03 - 1.13 (m, 28H, CH_3-CH-CH_3), 3.95 - 4.90 (m, 3H, H-4', H-5', H-5''), 4.90 (m, 1H, H-3'), 5.67 (m, 2H, H-1', H-2'), 6.18 (s, 2H, NH_2, exch. with D_2O), 7.32 - 7.53 (m, 4H, m and p-benzoyl, H-6), 7.71 - 7.78 (m, 2H, o-benzoyl), 8.21 (s, 1H, H-2), 10.71 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{30}H_{44}N_4O_6Si_2$: C, 58.79; H, 7.24; N, 8.49. Found: C, 58.81; H, 7.36; N, 8.18.

The more polar product was identified as **37** (0.037 g, 27%, mp 145-146°C). ^1H NMR (DMSO-d_6): δ 1.03 - 1.06 (m, 28H, CH_3-CH-CH_3), 3.72 - 3.95 (m, 3H, H-4', H-5', H-5''), 4.13 (m, 1H, H-2'), 4.36 (m, 1H, H-3'), 5.10 (d, 1H, H-1', $J_{1',2'}$ = 4.0 Hz), 6.83 (s, 2H, NH_2, exch. with D_2O), 7.54 (d, 1H, H-6, $J_{NH,6}$ = <1 Hz, changes to s with D_2O), 8.07 (s, 1H, H-2), 10.99 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{23}H_{40}N_4O_5Si_2$: C, 54.30; H, 7.92; N, 11.01. Found: C, 54.13; H, 7.92; N, 10.99.

METHOD B: A solution of **34** (0.55 g, 0.59 mmol) in 0.01 M $NaOCH_3$ in CH_3OH (44 mL) was heated to reflux for 2 h. The mixture was then cooled, neutralized with Amberlite IRC-50 (H^+) (~ 12 mL), filtered, and the filtrate concentrated *in vacuo*. The crude product was purified by preparative TLC (4 plates) using CH_2Cl_2:MeOH (8:1) as the developing agent. The plates were developed twice. The desired product was extracted with CH_2Cl_2:MeOH (8:1), filtered and the filtrate evaporated *in vacuo* to give **37** as a white solid (0.08 g, 26%, mp 144-146°C), which was identical to the product obtained by Method A.

METHOD C: A solution of **35** (0.25 g, 0.13 mmol) in saturated methanolic ammonia was stirred at 25°C in a closed pressure-resistant vessel for 36 h. The mixture was then concentrated *in vacuo* and the residue purified by preparative TLC (2 plates) using $CHCl_2$:MeOH (10:1) as the developing agent. Plates were developed twice. The desired product was extracted with warm CH_2Cl_2:MeOH (10:1), filtered and the filtrate evaporated *in vacuo* to give **37** as a white solid, (0.096 g, 73%, mp 146 147°C), which was identical to the product obtained by Methods A and B.

4-Amino-7-(β-D-arabinofuranosyl)-5H-pyrrolo[3,2-d]pyrimidine ("9-DEAZA ARA-A") (38). A mixture of **37** (1.24 g, 2.44 mmol) and TBAF (1.354 g, 5.18 mmol) in dry THF (35 mL) was stirred at 25°C under an argon atmosphere in a sealed vessel for $^1/_2$ h. The mixture was concentrated *in vacuo* and the residue was purified by flash column chromatography using first CH_2Cl_2:MeOH (4:1) and then CH_2Cl_2:MeOH (3:1) as eluents. Fractions containing the pure product were combined, evaporated to dryness *in vacuo* and the residue crystallized from CH_3OH to give **38** as a white crystalline, analytically pure solid (0.52 g, 81%, mp 225-226°C). ^1H NMR (DMSO-d_6): δ 3.57 (m, 2H, H-5', H-5''), 3.66 (m, 1H, H-4'), 3.89 - 4.10 (m, 2H, H-2', H-3'), 5.16 - 5.25 (m, 3H, H-1', changes to d with D_2O, $J_{1',2'}$ = 3.1 Hz, 2 OH's exch. with D_2O), 5.72 (br m, 1H, OH, exch. with D_2O), 6.76 (s, 2H, NH_2, exch. with D_2O), 7.54 (d, 1H, H-6, $J_{NH,6}$ = 2.8 Hz, changes to s with D_2O), 8.06 (s, 1H, H-2), 10.88 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{11}H_{14}N_4O_4$: C, 49.62; H, 5.30; N, 21.04. Found: C, 49.71; H, 5.47; N, 20.88.

4-Amino-7-[2-deoxy-2-chloro-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-arabinofuranosyl]-5H-pyrrolo[3,2-d]pyrimidine (39). A solution of **32** (0.25 g, 0.30 mmol) in saturated methanolic ammonia (50 mL) was stirred at 25°C in a sealed pressure-resistant vessel for 24 h. The mixture was then concentrated in vacuo and the residue purified by preparative TLC (2 plates, developed twice) using CH_2Cl_2:MeOH (10:1) as the developing agent to give **39** as a white solid (0.10 g, 64%, mp 215-216°C). ^1H NMR (DMSO-d_6): δ 1.03 - 1.11 (m, 28H, $4CH_3$-CH-CH_3), 3.80 - 4.05 (m, 3H, H-4', H-5', H-5''), 4.67 (pseudo t, 1H, H-2'), 4.90 (pseudo t, 1H, H-3'), 5.48 (d, 1H, H-1', $J_{1',2'}$ = 5.2 Hz), 6.73 (s, 2H, NH_2, exch. with D_2O), 7.46 (d, 1H, H-6, $J_{6,NH}$ = 2.4 Hz, changes to s with D_2O), 8.06 (s, 1H, H-2), 10.93 (d, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{23}H_{39}ClN_4O_4Si_2$: C, 52.40; H, 7.46; Cl, 6.72; N, 10.63. Found: C, 52.16; H, 7.60; Cl, 6.86; N, 10.53.

4-Amino-7-[2-deoxy-2-bromo-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-arabinofuranosyl]-5H-pyrrolo[3,2-d]pyrimidine (40). A mixture of **28** (0.395 g, 0.45 mmol) in saturated methanolic ammonia was stirred at 25°C in a sealed pressure-resistant vessel for 24 h. The reaction mixture was concentrated in vacuo. The crude product was dissolved in CH_2Cl_2-CH_3OH and subjected to preparative TLC (2 plates, developed twice) using CH_2Cl_2-CH_3OH (8:1) as the developing agent. The desired product was extracted with CH_2Cl_2:MeOH (10:2), filtered and the filtrate was evaporated in vacuo to give **40** as a white solid (0.165 g, 65%, mp 189-190°C). ^1H NMR (DMSO-d_6): δ 1.03 - 1.08 (m, 28H, $4CH_3$-CH-CH_3), 3.80 - 4.08 (m, 3H, H-4', H-5', H-5''), 4.74 (pseudo t, 1H, H-2'), 5.06 (pseudo t, 1H, H-3'), 5.36 (d, 1H, H-1', $J_{1',2'}$ = 5.2 Hz), 6.77 (br s, 2H, NH_2, exch. with D_2O), 7.46 (br s, 1H, H-6, sharp. with D_2O), 8.06 (s, 1H, H-2), 10.94 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{23}H_{39}BrN_4O_4Si_2$: C, 48.32; H, 6.88; Br, 13.98; N, 9.80. Found: C, 48.33; H, 6.88; Br, 13.88; N, 9.65.

4-Amino-7-[2-deoxy-2-iodo-3,5-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-arabinofuranosyl]-5H-pyrrolo[3,2-d]pyrimidine (41). By a procedure identical to that which gave **39**, the tri-N-benzoyl derivative **33** (0.35 g, 0.23 mmol) was treated with saturated NH_3/CH_3OH (70 mL) to give **41** as a white solid (0.133 g, 57%, mp 174-175°C). ^1H NMR (DMSO-d_6): δ 1.05 - 1.12 (m, 28H, $4CH_3$-CH-CH_3), 3.72 - 4.14 (m, 3H,

H-4', H-5', H-5''), 4.71 - 4.82 (m, 1H, H-2'), 4.94 (d, 1H, H-1', $J_{1',2'}$ = 5.8 Hz), 5.23 (pseudo t, 1H, H-3'), 6.81 (s, 2H, NH_2, exch. with D_2O), 7.45 (d, 1H, H-6, $J_{NH,6}$ = <1 Hz, changes to s with D_2O), 8.09 (s, 1H, H-2), 10.95 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{23}H_{39}IN_4O_4Si_2$: C, 44.65; H, 6.35; I, 20.51; N, 9.06. Found: C, 45.02; H, 6.68; I, 20.91; N, 9.19.

4-Amino-7-(2-Deoxy-2-halo-β-D-arabinofuranosyl)-5H-pyrrolo[3,2-d]pyrimidines (general procedure) (42-44). A mixture of each of the 4-Amino-7-[(2'-deoxy-2'-halo-3',5'-O-(1,1,3,3-tetraisopropyldisiloxanyl)-β-D-arabinofuranosyl]-5H-pyrrolo[3,2-d]pyrimidines **39** - **41** (0.68 mmol) and TBAF (1.45 mmol) in dry THF (9mL) was stirred at 25°C under an argon atmosphere in a closed vessel for 1 h. Each of the reaction mixtures was then concentrated in vacuo and the residues dissolved in CH_2Cl_2-CH_3OH and subjected to preparative TLC (3 plates, developed twice) using CH_2Cl_2:MeOH (3:1 or 4:1) as the developing agent. The desired products were extracted with warm CH_2Cl_2:MeOH (3:1), filtered and the filtrates concentrated in vacuo to give **42** - **44** as white solids, which were recrystallized from CH_2Cl_2-CH_3OH.

i) **4-Amino-7-(2-deoxy-2-chloro-β-D-arabinofuranosyl)-5H-pyrrolo[3,2-d]pyrimidine (42).** Yield: 96%, mp 225-227°C. ^1H NMR (DMSO-d_6): δ 3.64 (m, 3H, H-4', H-5', H-5''), 4.30 (m, 1H, H-3'), 4.47 (dd, 1H, H-2'), 5.01 (br s, 1H, CH_2OH, exch. with D_2O), 5.52 (d, 1H, H-1', $J_{1',2'}$ = 3.3 Hz), 5.73 (d, 1H, CHOH, exch. with D_2O, $J_{OH,3'}$ = 4.3 Hz), 6.72 (s, 2H, NH_2, exch. with D_2O), 7.48 (d, 1H, H-6, $J_{NH,6}$ = 2.1 Hz, changes to s with D_2O), 8.07 (s, 1H, H-2), 10.90 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{11}H_{13}ClN_4O_3$: C, 46.41; H, 4.60; Cl, 12.45; N, 19.68. Found: C, 46.46; H, 4.73; Cl, 12.56; N, 19.46.

ii) **4-Amino-7-(2-deoxy-2-bromo-β-D-arabinofuranosyl)-5H-pyrrolo[3,2-d]pyrimidine (43).** Yield: 95%, mp 200-202°C. ^1H NMR (DMSO-d_6): δ 3.71 (m, 3H, H-4', H-5', H-5''), 4.45 (m, 1H, H-3'), 4.57 (dd, 1H, H-2', $J_{1',2'}$ = 3.7 Hz, $J_{2',3'}$ = < 1Hz), 5.02 (m, 1H, CH_2OH, exch. with D_2O), 5.36 (d, 1H, H-1'), 5.94 (d, 1H, CHOH, $J_{OH,3'}$ = 4.3 Hz, exch. with D_2O), 6.72 (s, 2H, NH_2, exch. with D_2O), 7.47 (d, 1H, H-6,

changes to s with D_2O), 8.07 (s, 1H, H-2), 10.87 (br s, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{11}H_{13}BrN_4O_3$: C, 40.14; H, 3.98; Br, 24.28; N, 17.02. Found: C, 40.30; H, 4.07; Br, 24.39; N, 16.66.

iii) **4-Amino-7-(2-deoxy-2-iodo-β-D-arabinofuranosyl)-5H-pyrrolo[3,2-d]pyrimidine (44).** Yield: 38%, mp 127-129°C. ^1H NMR (DMSO-d_6): δ 3.72 (s, 3H, H-4', H-5', H-5''), 4.64 (m, 2H, H-2', H-3'), 4.79 (d, 1H, H-1', $J_{1',2'}$ = 4.1 Hz), 5.21 (m, 1H, CH_2OH, exch. with D_2O), 5.93 (d, 1H, CHOH, $J_{OH,3'}$ = 4.4 Hz, exch. with D_2O), 6.73 (s, 2H, NH_2, exch. with D_2O), 7.43 (d, 1H, H-6, changes to s with D_2O), 8.05 (s, 1H, H-2), 10.87 - 10.91 (m, 1H, NH, exch. with D_2O).

Anal. Calcd for $C_{11}H_{13}IN_4O_3$: C, 35.12; H, 3.38; I, 33.74; N, 14.90. Found: C, 34.90; H, 3.63; I, 33.61; N, 14.72.

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