A New Synthetic Route to β-2′-Deoxyribosyl-5-substituted Pyrrolo[2,3-*d*]pyrimidines. Synthesis of 2′-Deoxycadeguomycin

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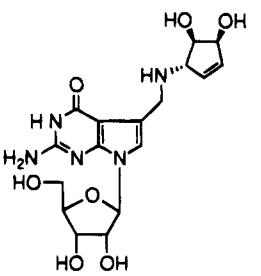
A new and flexible synthetic route to β-2′-deoxyribosyl-5-substituted pyrrolo[2,3-*d*]pyrimidines has been developed. Formation of the pyrrole ring is effected by combining sodium *N*-(4-nitrophenethyl)-glycinate with a differently protected 6-chlorouracil derivative generating a substitution adduct. Heating of this material in acetic anhydride affords the 5-(acetyloxy)pyrrolo[2,3-*d*]pyrimidine **9** in high yield. Base-mediated removal of the pyrrole protecting group gives free pyrrole **10** which is then glycosylated with 1-chloro-2-deoxy-3,5-ditoluoyl-α-D-*erythro*-pentofuranose (**11**) using the sodium salt method. The resulting glycosides **15a,b** (α:β, 1:4) are readily separated following hydrolysis of the C-5 acetyloxy group. The subsequently derived pure β-5-(trifluoromethanesulfonyl) derivative **14** undergoes four types of palladium-catalyzed carbon–carbon bond-forming reactions and results in C-5 substituted compounds **15**–**18**. An efficient synthetic route to the pyrrolo[2,3-*d*]pyrimidine nucleotide analogue, 2′-deoxycadeguomycin (**27**), is presented. The key transformation involves the conversion of the differentially protected pyrrolo[2,3-*d*]pyrimidine-2,4-dione base portion in **15** into a protected 2-aminopyrrolo[2,3-*d*]pyrimidin-4-one **24**. An alternative route to **27** was developed which involved prior conversion of the pyrrole-protected precursor **9** into its C-5 triflate derivative **20** followed by palladium-catalyzed carboxylation leading to ester **21**. Removal of the pyrrole protecting group and then sodium salt-promoted glycosidation afforded the same β-2′-deoxyribosyl intermediate **15** as prepared earlier. The stereochemistry of glycosidation was found to be dependent upon the electronic effect of the C-5 substituent on the pyrrole ring.

Introduction

Over the past three decades, pyrrolo[2,3-*d*]pyrimidine (7-deazapurine) nucleoside analogues, both of natural and nonnatural[1] origin, have revealed significant biological profiles, including broad spectrum antitumor, antiviral, and antibacterial activities. The intense interest in this class of compounds was initiated by the discovery of the antibacterial and antitumor agents tubercidin, toyocamycin, and sangivamycin.[2] A major subset of pyrrolo[2,3-*d*]pyrimidine nucleosides has the common structural feature of a C-5 substituent which can be derived from a carboxylate residue and a 7-deazaquanine-type base portion. A prominent example is the hypermodified nucleoside Q (queuosine) **1** which is located at the first position of the anticodon of various tRNA's.[3] The related nucleoside component, cadeguomycin (**2a**), was isolated from a strain of the actinomycete culture filtrate *Streptomyces hygroscopicus* IM7912T and has exhibited antitumor activity against transplantable animal tumors.[4] More recently, the structurally intriguing nucleoside, archaeosine (**2b**), was identified as a phylogenetically distinct residue in tRNA of the Achaea domain and represents one of the most conserved sites throughout numerous tRNA sequences known from archaeal kindoms.[5] It is speculated that the unusual formamidine side chain is involved in the stabilization of tertiary interactions. The echiquanines A, **2c**, and B, **2d**, were isolated from the culture broth of *Streptomyces* strain M1698-50F1, lack a carbohydrate portion connected to the pyrrole nitrogen, and have amide substituents at the C-5 position.[6] These simplified pyrrolo[2,3-*d*]pyrimidines were found to be potent inhibitors of phosphatidylinositol kinase.



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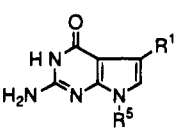

2a, $R^1 = CO_2H$, R^5 = α-D-ribosyl
b, $R^1 = C{=}NHNH_2$, R^5 = α-D-ribosyl
c, $R^1 = CONH(CH_2)_2C{=}NHNH_2$, $R^5 = H$
d, $R^1 = CONH(CH_2)_3NH_2$, $R^5 = H$

Over this period considerable effort has been directed toward the synthesis of the variously substituted pyrrolo[2,3-*d*]pyrimidine base subunits[7] and their nucleoside derivatives resulting in many milestone discoveries.[8] In most cases, the synthetic source of the pyrrolo[2,3-*d*]-pyrimidine portion comes from the pioneering work of Davoll[9a] or Robins and Noell.[9b] The more recent development of the sodium salt glycosidation method[8a] has greatly improved the access to key pyrrolo[2,3-*d*]pyrimi-

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(1) For recent examples of non-natural pyrrolo[2,3-*d*]pyrimidine nucleoside analogues, see ref 8. Serafinowski, P.; Dorland, E.; Harrap, K. R.; Balzarini, J.; De Clercq, E. *J. Med. Chem.* **1992**, *35*, 4576. Quijano, M. L.; Nogueras, M.; Melguizo, M.; Alverez de Cienfuegos, G.; Melgarejo, M.; Sanchez, A. *Nucleosides Nucleotides* **1989**, *8*, 1519. Prober, J. M.; Trainor, G. L.; Dam, R. J.; Hobbs, F. W.; Robertson, C. W.; Zagursky, R. J.; Cocuzza, A. J. *Science* **1987**, *238*, 336.

(2) Anzai, K.; Nakamura, G.; Suzuki, S. *J. Antibiot. (Tokyo)* **1957**, *10A*, 201. Nishimura, H.; Katagiri, K. K.; Sato, K.; Mayama, M.; Shimaoka, N. *J. Antibiot. (Tokyo)* **1956**, *9A*, 60. Rao, K. V.; Renn, D. W. *Antimicrob. Agents Chemother.* **1963**, 77.

(3) Kasai, H.; Ohashi, Z.; Harada, F.; Nishimura, S.; Oppenheimer, N. J.; Crain, P. F.; Liehr, J. C.; von Minden, D. L.; McCloskey, J. A. *Biochemistry* **1975**, *14*, 4198.

(4) Tanaka, N.; Wu, R. T.; Okabe, T.; Yamashita, H.; Shimazu, A.; Nishimura, T. *J. Antibiotics*, **1982**, *35*, 272.

(5) Gregson, J. M.; Crain, P. F.; Edmonds, C. G.; Gupta, R.; Hashizume, T.; Phillipson, D. W.; McCloskey, J. A. *J. Biol. Chem.* **1993**, *268*, 10076.

(6) Nishioka, H.; Sawa, T.; Nakamura, H.; Iinuma, H.; Ikeda, D.; Sawa, R.; Naganawa, H.; Hayashi, C.; Hamada, M.; Takeuchi, T.; Iitaka, Y.; Umezawa, K. *J. Nat. Prod.* **1991**, *54*, 1321.

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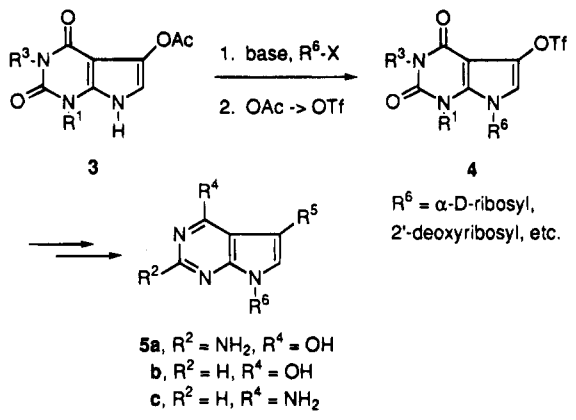
Scheme 1



dine nucleoside analogues. However, some difficulties still remain regarding the limited solubility and manipulation of key intermediates. Additionally, the desired substitution pattern on the base portion can require many steps to introduce different types of functional groups. A number of new methods for the synthesis of pyrrolo[2,3-*d*]pyrimidines has appeared in recent years which are applicable to specific ring substitution patterns.[10]

We are interested in the development of a new approach for the elaboration of pyrrolo[2,3-*d*]pyrimidines and their nucleoside analogues using a cyclodehydrative pyrrole annulation reaction developed earlier in our laboratory.[11] This strategy has the distinct advantage of using a common synthetic intermediate **4** which incorporates a differentially protected pyrimidine-2,4-dione ring portion and a C-5 triflate functional handle (Scheme 1). In this way, a variety of C-5 substituents can be introduced via palladium-catalyzed carbon–carbon bond-forming reactions.[12] In addition, any number of cyclic and acyclic carbohydrate portions can be attached by alkylation of the free pyrrole intermediate **3**. By using a differentially protected pyrimidine-2,4-dione ring portion, **4**, in the form of a 7-deazaxanthine, conversion into 2-amino-4-oxo-, 4-oxo-, and 4-aminopyrrolo[2,3-*d*]pyrimidine nucleoside analogues **5a-c** (7-deazaguanosines, 7-deazainosines, and 7-deazaadenosines, respectively) can be realized.

Our initial goal was to prepare 2′-deoxyribosyl-substituted pyrrolo[2,3-*d*]pyrimidine nucleosides which would serve as the basis for the elaboration of other analogues having variously modified carbohydrate portions. Focusing on the base portion, a number of key issues needed to be addressed, such as the choice of the appropriate protecting groups for the *N*-1, *N*-3, and *N*-7 nitrogens, at which stage to introduce the C-5 substituent, and when to modify the pyrimidine-2,4-dione ring portion. In considering protecting groups, the following requirements had to be met; differential protection at *N*-1 and *N*-3 which allowed for selective deprotection at either position later on, an alkyl protecting group for the pyrrole nitrogen which was compatible with the pyrrole annulation step, and the need for removal of these groups under mild reaction conditions. Another issue is the stage when the carbohydrate portion is introduced. We chose the sodium salt glycosidation method of Robins and co-workers,[8a] which involves alkylation of a pyrrolo[2,3-*d*]pyrimidine-based anion with a protected 2′-deoxyribosyl chloride. The stereochemical outcome for this step is dependent upon the reactivity of the pyrrole anion which, in turn, was expected to be influenced by the electronic effect of the C-5 substituent. It was also anticipated that the steric size of the *N*-1 protecting group would have an influence on the glycosidation stereochemistry and further dictate when the pyrimidine-2,4-dione ring portion was modified.

Our first efforts in developing a general new route for the synthesis of 2′deoxyribosyl-5-substituted pyrrolo[2,3-*d*]pyrimidine nucleosides are described below.[13] We highlight the utility of this approach by demonstrating the conversion of a 2′-deoxyribosylpyrrolo[2,3-*d*]pyrimidine-2,4-dione into a protected 2-aminopyrrolo[2,3-*d*]-pyrimidin-4-one which, in turn, leads to the synthesis of 2′-deoxycadeguomycin, an analogue of cadeguomycin (**2a**).[14]

Results and Discussion

A methoxymethyl (MOM) protecting group at *N*-3 was chosen based on its successful use in the total synthesis of nucleoside Q.[15] Our previous experience with the total synthesis of the pyrrolo[2,3-*d*]pyrimidine-2,4-dione alkaloid, rigidin,[11] suggested benzyloxymethyl (BOM) protection for the *N*-1 position and a 2,4-dimethoxybenzyl (DMB) group for the pyrrole nitrogen due to their ease of removal using TMSI and/or TFA for the latter. However, the DMB group proved unworkable in the current scheme[16] and was abandoned. In its place we elected to try a new protecting group which could be

(7) For a review of the methods available for the synthesis of pyrrolo-[2,3-*d*]pyrimidine aglycones prior to 1974, see: Amarnath, V. Madhav, R. *Synthesis* **1974**, 837. Several papers have appeared since this time which are either extensions or variations of earlier methods; e.g., see: (a) Wamoff, H.; Wehling, B. *Chem. Ber.* **1976**, *109*, 2983. (b) Seela, F.; Richter, R. *Chem. Ber.* **1978**, *111*, 2925. (c) Secrist, J. A.; Lui, S. P. *J. Org. Chem.* **1978**, *43*, 20. (d) Taylor, E. C.; Kuhnt, D.; Shih, C.; Rinzel, S. M.; Grindey, G. B.; Barredo, J.; Jannatipour, M.; Moran, R. G. *J. Med. Chem.* **1992**, *35*, 4450. (e) Shih, C.; Gossett, L. S. *Heterocycles*, **1993**, *35*, 825. (f) Shih, C.; Hu, Y. *Tetrahedron Lett.* **1994**, *35*, 4677.

(8) For a comprehensive review discussing the synthesis of various pyrrolo[2,3-*d*]pyrimidine nucleoside derivatives prior to 1990, see: (a) Revankar, G. R.; Robins, R. K. In *Chemistry of Nucleosides and Nucleotides*; Townsend, L. B., Ed.; Plenum Press: New York, 1991; Chapter 4. Since this time, see: (b) Seela, F.; Soulimane, T.; Mersmann, K.; Jürgens, T. *Helv. Chim. Acta* **1990**, *73*, 1879. (c) Pudlo, J. S.; Nassiri, M. R.; Kern, E. R.; Wotring, L. L.; Drach, J. C.; Townsend, L. B. *J. Med. Chem.* **1990**, *33*, 1984. (d) Bergstrom, D. E.; Beal, P.; Jenson, J.; Lin, X. *J. Org. Chem.* **1991**, *56*, 5598. (e) Chen, X.; Siddiqi, S. M.; Schneller, S. W. *Tetrahedron Lett.* **1992**, *33*, 2249.

(9) (a) Davoll, J. *J. Chem. Soc.* **1960**, 131. (b) Noell, W. C.; Robins, R. K. *J. Heterocycl. Chem.* **1963**, *1*, 34.

(10) For new approaches to pyrrolo[2,3-*d*]pyrimidines reported since 1974, see: Senda, S.; Hirota, K. *Chem. Pharm. Bull.* **1974**, *22*, 1459. Itoh, T.: Melik-Ohanjanian, R. G.; Ishikawa, I.; Kawahara, N.; Mizuno, Y.; Honma, Y.; Hozumi, M.; Ogura, H. *Chem. Pharm. Bull.* **1989**, *37*, 3184. Edstrom, E. D.; Wei, Y. *Tetrahedron Lett.* **1991**, *32*, 323. Sakamoto, T.; Satoh, C.; Kondo, Y.; Yamanaka, H. *Chem. Pharm. Bull.* **1993**, *41*, 81. Miwa, T.; Hitaka, T.; Akimoto, H. *J. Org. Chem.* **1993**, *58*, 1696.

(11) (a) Edstrom, E. D.; Wei, Y. *J. Org. Chem.* **1993**, *58*, 403. (b) Edstrom, E. D.; Yu, T. *Tetrahedron Lett.* **1994**, *35*, 6985.

(12) For a review on organotriflates, see: Ritter, K. *Synthesis* **1993**, 735. For recent efforts involving the palladium-catalyzed reactions with 5-iodopyrrolo[2,3-*d*]pyrimidine nucleosides, see ref 7d-f and: Hobbs, F. W. *J. Org. Chem.* **1989**, *54*, 3420. Robins, M. J.; Vinayak, R. S.; Wood, S. G. *Tetrahedron Lett.* **1990**, *31*, 3731.

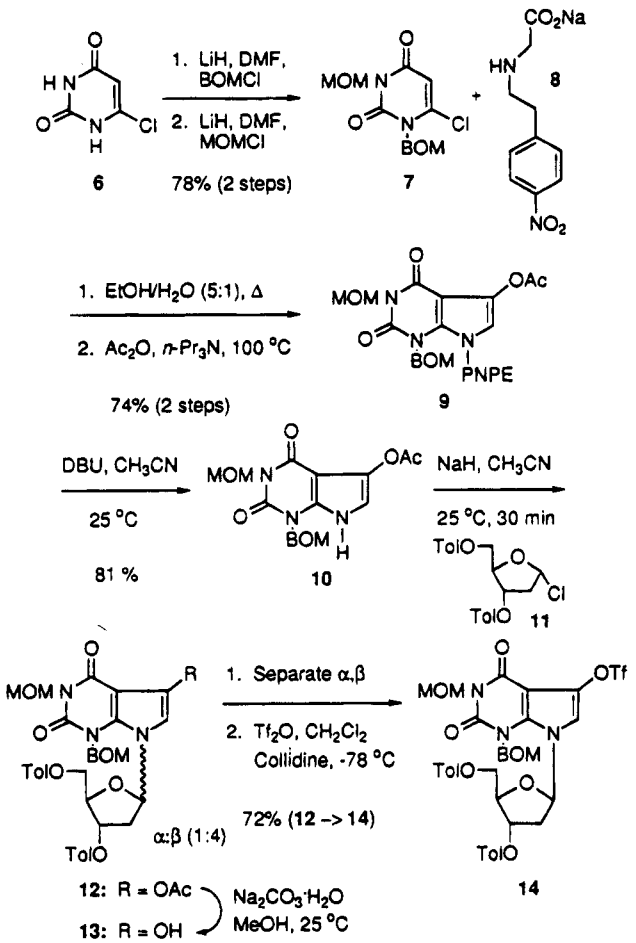
(13) Portions of this work have been submitted in preliminary form. Edstrom, E. D.; Wei, Y. *J. Org. Chem.* **1994**, *59*, 6902. Edstrom, E. D.; Wei, Y. *Tetrahedron Lett.* **1994**, *35*, 8989.

(14) For the first synthesis of 2′-deoxycadeguomycin, see: Ramasamy, K.; Joshi, R. V.; Robins, R. K.; Revankar, G. R. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2375.

(15) Ohgi, T.; Goto, T. *Chem. Lett.* **1979**, 1283. Kondo, T.; Nakatsuka, S.; Goto, T. *Chem. Lett.* **1980**, 559.

(16) The DMB group proved inefficient in our current scheme since it could not be cleanly removed from intermediates analogous to compounds **9**, **20**, and **21** using a variety of reaction conditions, i.e., DDQ, PhH, reflux; $Ce(NH_3)_2(NO_3)_6$, MeCN; TFA, rt; TMSI, MeCN, reflux. Under acidic conditions the MOM group at *N*-3 was prematurely cleaved, whereas under oxidative conditions, low yields were obtained resulting from destruction of the product, most likely due to over oxidation at the pyrrole ring.

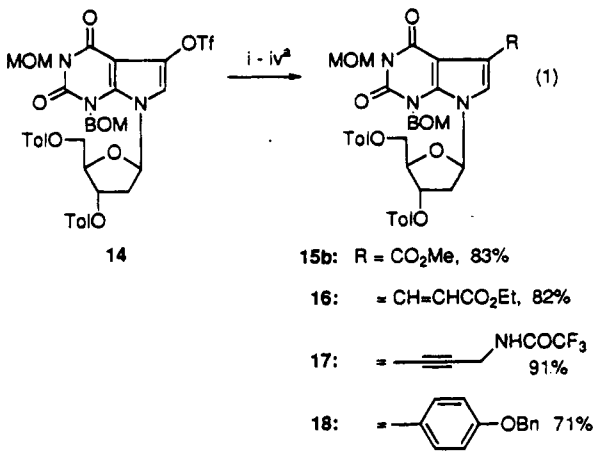
Scheme 2



cleaved under mild base conditions in analogy with previous work involving the protection of the O-6 position in quanosine nucleosides.[17] The choice narrowed down to the *p*-nitrophenethyl (PNPE) group due to its ease of incorporation into our synthetic scheme. This represents the first application of this protecting group for a pyrrole nitrogen.

Our primary target became the key C-5 triflate intermediate **14** having the standard bis-toluoyl ester-protected 2′-deoxyribosyl portion and the other protecting groups mentioned above, attached as shown in Scheme 2. Starting with 6-chlorouracil (**6**), sequential alkylation at *N*-1[18] and then *N*-3 using LiH in DMF with the appropriate alkyl chloride provided the differentially protected uracil derivative **7** in 78% yield. Treatment of **7** with the sodium salt derived from ethyl *N*-(*p*-nitrophenethyl)glycinate (**8**) afforded a substitution adduct which was isolated as its crude acid. Subsequent exposure of this material to acetic anhydride and amine base, with heating, afforded the 5-(acetyloxy)pyrrolo[2,3-*d*]-pyrimidine-2,4-dione **9** in 74% isolated yield for the two steps. It proved advantageous at this stage to remove the *p*-nitrophenethyl blocking group using mild base conditions to afford the free pyrrole **10**. In the next step

Scheme 3



[a] All reactions used 10 mol % palladium catalyst. [b]Metal to ligand ratio (1:3). [c]20 mol % CuI used. [d]Metal to ligand ratio (1:2).

the sodium salt glycosidation reaction[8a] of **10** using 1-chloro-2-deoxy-3,5-ditoluoyl-α-D-*erythro*-pentofuranose (**11**) could be effected with a preference for the β isomer (α:β, 1:4).[19] This result contrasts with the glycosidation stereochemistry observed for a system having an electron-withdrawing group at the C-5 position, as discussed below. The resulting adduct **12** from above was treated with mild base to effect hydrolysis of the 5-acetyloxy group and provide the 5-ketopyrrole **13**. The resulting mixture of α and β isomers revealed the unique advantage of being readily separable by simple column chromatography over silica gel. Attempted separation of the α and β isomers at later stages proved much more tedious (*vide infra*). With the pure β isomer of **13** in hand, conversion to the 5-(trifluoromethanesulfonyl)-pyrrolo[2,3-*d*]pyrimidine-2,4-dione **14** was performed in high yield using standard reaction conditions.[11]

Representative reactions of pyrrolo[2,3-*d*]pyrimidine triflate **14**[20] using four major types of palladium-catalyzed carbon–carbon bond-forming reactions[12] are illustrated in eq 1 (Scheme 3). Methoxycarbonylation of **14** was performed using the standard protocol of Ortar and coworkers[21a] and afforded ester **15b** in good yield. The Heck reaction with an electron-deficient alkene, represented by ethyl acrylate, provided **16** in respectable

(17) For the use of the PNPE group in the protection of O-6 of 2′-deoxyquanosine, see: Gaffney, B. L.; Jones, R. A. *Tetrahedron Lett.* **1982**, *23*, 2257. A related group, 2-pyridylethyl, has been used for the protection of indoles and pyrroles; however, it requires prior activation by reaction with methyl iodide forming a pyridinium salt which then undergoes the β-cleavage process upon base treatment. Katritzky, A. R.; Khan, G. R.; Marson, C. M. *J. Heterocycl. Chem.* **1987**, *24*, 641.

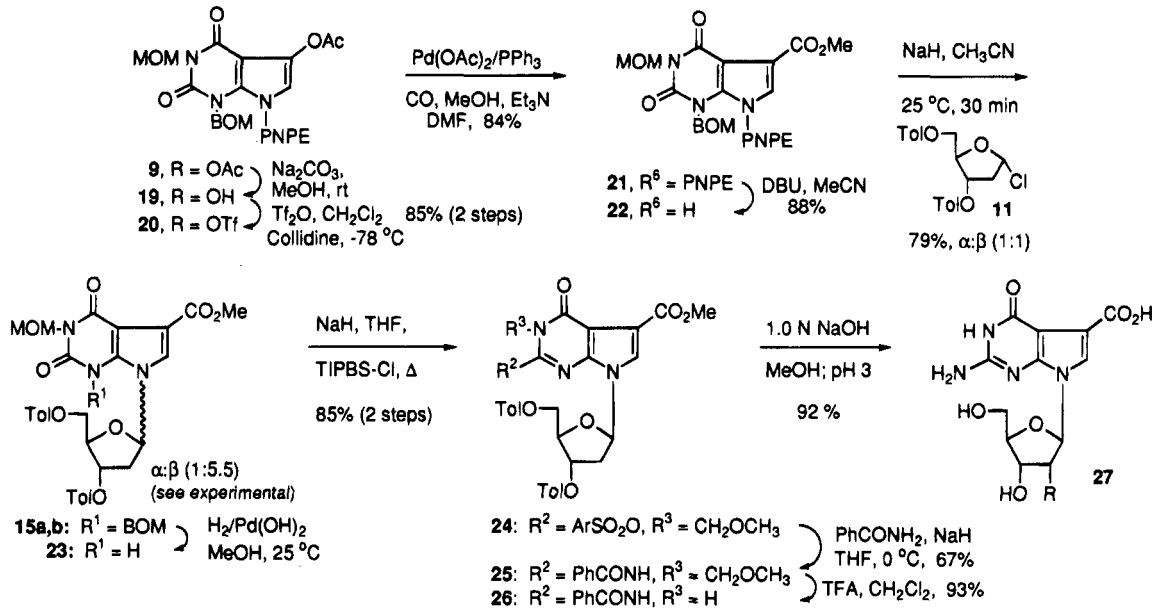
(18) This regiochemistry has been confirmed by X-ray analysis. Ishikawa, I.; Itoh, T.; Melik-Ohanjanian, R. G.; Takayanagi, H.; Mizuno, Y.; Ogura, H. *Heterocycles* **1990**, *31*, 1641.

(19) The ratio of α:β anomers was determined by integration of the respective OAc signals in an ^{1}H NMR spectrum of the crude reaction mixture. The assignment of the β-anomeric configuration for compound **12** was based on comparison of the C-1′ methine hydrogen coupling constants with the adjacent C-2′ protons, i.e., ($CDCl_3$) δ 6.77 (dd, J = 5.9, 7.3 Hz). This compares with the literature values reported for closely related compounds [β-2′-deoxyribosyl-1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione, (d_6-DMSO) δ 6.63 (apparent t, J = 6.0 Hz) and β-2′-deoxyribosyl-2-amino-4-chloropyrrolo[2,3-*d*]pyrimidine, (d_6-DMSO) δ 6.54 (dd, J = 5.8, 8.7 Hz)]. By way of comparison, the α-anomer of **7** had data for H-1′ of ($CDCl_3$) δ 6.84 (dd, J = 2.2, 7.7 Hz) as compared to α-2′-deoxyribosyl-1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione, (d_6-DMSO) δ 6.63 (dd, J_{total} = 10.0 Hz), see refs 8b and: Ramasamy, K.; Imamura, N.; Robins, R. K.; Revankar, G. R. *J. Heterocycl. Chem.* **1988**, *25*, 1893.

(20) For related Heck coupling reactions using an indole-3-triflate, see: Gribble, G. W.; Conway, S. C. *Synth. Commun.* **1992**, *22*, 2129.

(21) (a) Cacchi, S.; Ciattini, P. G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1986**, *27*, 3931. (b) Cabri, W.; Candiani, I.; DeBernardinis, S.; Francalanci, F.; Penco, S. *J. Org. Chem.* **1991**, *56*, 5796. (c) Farina, V.; Baker, S. R.; Benigni, D. A.; Hauck, S. I.; Sapino, C. *J. Org. Chem.* **1990**, *55*, 5833.

Scheme 4



yield.[21b] The copper(I)-promoted coupling with *N*-(trifluoroacetyl)propargylamine, leading to **17**, proceeded in high yield using reaction conditions which proved effective in related 5-iodopyrrolo[2,3-*d*]pyrimidine derivatives.[12] The Stille-type coupling with a more demanding electron rich arylstannane was carried out using the modified reaction conditions developed by Farina and coworkers.[21c] The C-5 aryl-substituted compound **18** was isolated in a reasonable 71% yield.

This reactivity study demonstrates the range of palladium-catalyzed carbon–carbon bond-forming reactions that can be realized for the 5-(trifluoromethanesulfonyl)-pyrrolo[2,3-*d*]pyrimidine-2,4-dione **14**. Since no optimization of reaction conditions was required, i.e., variation of ligand, solvent, catalyst, and additives, it can be expected that **14** will reveal general reactivity toward other coupling partners used in this type of palladium-catalyzed reactions.

At this stage we focused on the conversion of the pyrrolo[2,3-*d*]pyrimidine-2,4-dione ring portion into a 2-amino-4-oxopyrrolo[2,3-*d*]pyrimidine characteristic of 7-deazaguanosines. As an end target of this venture we elected to synthesize 2′-deoxycadeguomycin **27**, a known analogue of cadeguomycin.[14] This exercise would also allow us to determine the correct protecting scheme to eventually unleash a fully unmasked nucleoside. Starting with the 5-(acetyloxy)pyrrolo[2,3-*d*]pyrimidin-2,4-dione **9**, hydrolysis under mild basic conditions afforded the trione **19** which was directly processed to the C-5 triflate derivative **20** in 85% yield for the two steps (Scheme 4). Palladium-catalyzed methoxycarbonylation, as described above, provided an 84% yield of ester **21**. The PNPE group was cleanly removed from the pyrrole nitrogen using DBU in acetonitrile at room temperature. The reaction of the pyrrole anion derived from **22** with ribosyl chloride **11** provided **15a,b** as a 1:1 mixture of α and β isomers. This contrasts with the C-5 acetoxy-substituted system from above and other pyrrolo[2,3-*d*]-pyrimidine anions[8a,b] which show a moderate to exclusive preference for the β isomer, respectively. Thus, the electron-withdrawing ester group in **22** stabilizes the corresponding negative charge on its pyrrole nitrogen, thereby diminishing its reactivity, allowing time for the ribosyl chloride to isomerize under the reaction conditions. Another factor that would inhibit the reactivity of the pyrrole anion derived from **22** would be the steric bias provided by the adjacent *N*-1 BOM protecting group.

The next key transformation involved introduction of the 2-amino substituent on the pyrrolo[2,3-*d*]pyrimidine ring. Differential protection of the *N*-1 and *N*-3 positions allowed us to selectively remove the *N*-1 benzyloxymethyl (BOM) group from **15** using Pearlman's catalyst.[22] The resulting free amide **23** was converted into its 2-*O*-sulfonyl derivative **24** (α:β, 1:1) by treatment with sodium hydride and triisopropylbenzenesulfonyl chloride (TIPBS-Cl). The pure β isomer of **24** was obtained somewhat tediously by sequential recrystallizations from ethyl acetate/hexanes. Attempted separations at later stages proved impossible due to the similar R_f's of the two isomers. The amination at C-2 in compound **24** presented difficulties due to completing side reactions. For example, the reaction with various nitrogen nucleophiles (NH_3, $CH_3CONHNa$) afforded significant amounts of precursor **23** resulting from cleavage of the sulfonyl ester bond.[23] This problem was circumvented by using a sterically larger nucleophile derived from benzamide. As a result, the desired amination product **25** was afforded in 67% yield with the 2-amino group conveniently introduced as its protected benzamide derivative. At this stage, the methoxymethyl group at *N*-3 was removed by treatment with TFA to afford **26** in high yield. The final step involved simple base hydrolysis of the toluoyl esters from the 3′ and 5′ hydroxyl groups, the benzamide group at the 2-amino position, and the methyl ester at C-5. The final product, 2′-deoxycadeguomycin (**27**), was conveniently isolated by precipitation from the reaction solution following acidification to pH 3. The identity of our sample of 2′-deoxycadeguomycin with the literature[14] was confirmed by comparison of ^1H NMR, UV, and mp data.

An improved synthetic route to 2′-deoxycadeguomycin (**27**) was now in place by utilizing the chemistry developed in Scheme 2. The advantage of introducing of the

(22) Hanessian, S. In *Trends in Synthetic Carbohydrate Chemistry*; Horton, D., Hawkins, L. D., McGarvey, G. J., Eds.; ACS Symposium Series No. 386; American Chemical Society: Washington, DC, 1989; p 64.

(23) Vorbrüggen, H. In *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Ed.; Academic Press: New York, 1990; Vol. 49, pp 159–62.

C-5 ester group after the glycosidation step became obvious. Since the glycosidation stereochemistry obtained from alkylation of the 5-(acetyloxy)pyrrolo[2,3-*d*]-pyrimidine **10** gave a preference for the β isomer, and the ready separation of the minor α isomer was easily accomplished by simple silica gel chromatography of the subsequently derived pyrrolo[2,3-*d*]pyrimidine-2,4,5-trione **13**, an overall higher chemical throughput to the pure β ester **15b** was provided. This compound was then processed into **27** using the same route shown in Scheme 4.

Conclusions

The utility of a new approach for the synthesis of 7-deazapurine nucleosides as revealed by the synthesis of 2-deoxycadeguomycin, a 7-deazaguanosine derivative, has been demonstrated. A key feature is illustrated by the conversion of differentially protected 2′-deoxyribosylpyrrolo[2,3-*d*]pyrimidine-2,4-dione into a protected 2-aminopyrrolo[2,3-*d*]pyrimidin-4-one. Work in progress is aimed at the conversion of key intermediates related to compounds **15a-d** into 4-amino- and 4-oxopyrrolo[2,3-*d*]pyrimidine nucleotide analogues (7-deazaadenosines and 7-deazainosines, respectively). Aspects of this methodology which need further improvement are the glycosidation stereoselectivity and the incorporation of protected ribose units. In order to address these issues, removal of the steric bias imposed by the *N*-1 protecting group and conversion into the 2-unsubstituted or 2-aminopyrrolo[2,3-*d*]pyrimidines will be essential.

Experimental Section

The following solvents and reagents were distilled from calcium hydride under a nitrogen atmosphere: dichloromethane, 2,4,6-collidine, 1-methyl-2-pyrrolidinone (NMP), and acetonitrile. DMF (0.034% of water) was purchased from EM Industries, Inc., and used without further purification. Melting points were recorded on a Thomas-Hoover apparatus and are uncorrected. IR spectra were determined with a FT-IR instrument. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ or d_6-DMSO. Elemental analyses were performed by Atlantic Microlab, Inc. Analytical thin-layer chromatography (TLC) was performed on glass E. Merck precoated TLC plates (silica gel 60 F-254, layer thickness 0.2 mm). Flash column chromatography was performed with silica gel (E. Merck 60 Å, 230–400 mesh ASTM). The final product solutions were dried over Na_2SO_4 and concentrated on a rotary evaporator.

1-[(Benzyloxy)methyl]-6-chlorouracil. A mixture of 6-chlorouracil (**6**) (4.00 g, 27.2 mmol) and LiH (0.33 g, 40.8 mmol) in DMF (100 mL) was stirred at 0 °C for 5 min under an atmosphere of N_2, and then (benzyloxy)methyl chloride (5.12 g, 32.6 mmol) was added. The mixture was stirred for 0.5 h and then treated with 2% NaOH solution (200 mL) and extracted with benzene (100 mL). The aqueous layer was acidified with concentrated HCl to pH 3, filtered, and washed with water to give 5.67 g (78%) of product as a colorless powder. An analytical sample was obtained by recrystallization from 95% ethanol as a colorless solid: mp 154–155 °C; IR (KBr) 3153, 1733, 1713, 1599, 1500 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 8.80 (1 H, br s), 7.36–7.26 (5 H, m), 5.88 (1 H, s), 5.55 (2 H, s), 4.69 (2 H, s); ^{13}C NMR ($CDCl_3$) δ 160.6, 150.2, 147.3, 136.8, 128.5, 128.1, 127.6, 103.6, 74.4, 72.1. Anal. Calcd for $C_{12}H_{11}ClN_2O_3$: C, 54.05; H, 4.16; N, 10.50. Found: C, 53.91; H, 4.18; N, 10.43.

1-[(Benzyloxy)methyl]-6-chloro-3-(methoxy)methyluracil (7). A mixture of 1-[(benzyloxy)methyl]-6-chlorouracil (3.00 g, 11.2 mmol) and LiH (135 mg, 16.9 mmol) in DMF (70 mL) was stirred at 0 °C for 10 min under an atmosphere of N_2, and then methoxymethyl chloride (1.36 g, 16.8 mmol) was added. The mixture was stirred for 0.5 h and then treated with 200 mL of water and extracted with CH_2Cl_2 (150 mL). The organic layer was washed with water (2 × 100 mL) and brine (100 mL), dried, filtered, and concentrated under reduced pressure to provide 3.71 g (99%) of **7** as a colorless solid (this material was used in the next step without further purification): IR (KBr) 1719, 1674, 1615, 1500 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.35–7.26 (5 H, m), 5.92 (1 H, s), 5.58 (2 H, s), 5.30 (2 H, s), 4.71 (2 H, s), 3.42 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 160.3, 151.3, 146.0, 137.0, 128.4, 128.0, 127.6, 103.1, 75.2, 72.5, 72.2, 58.0.

Ethyl *N*-(*p*-Nitrophenethyl)glycinate (8). To a solution of 9.18 g of *p*-nitrophenethylamine hydrochloride[24] in 75 mL of water was added 30% NaOH until pH 12. The mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried, concentrated, and dried in vacuo to give 8.22 g (49.2 mmol) of free base. This material was dissolved in 400 mL of ether under nitrogen, vigorous overhead stirring was commenced, and then ethyl bromoacetate (4.15 g, 24.8 mmol) was added dropwise via an addition funnel over a period of 15 min. After continued stirring for 80 h, the amine salt was removed by filtration and recovered for reuse. The organic layer was washed with water (3 × 75 mL). After concentration of the organic layer, the resultant crude product mixture, which contained a mixture of mono- and dialkylated materials, was purified by column chromatography over silica gel using ethyl acetate/hexanes (1:1) as the eluant. The top eluting band afforded 2.00 g of dialkylated material, whereas the second eluting band contained 3.11 g (50%, based on 0.5 equiv of total amine used) of compound **8**. For **8** as an orange oil: ^{1}H NMR ($CDCl_3$, 270 MHz) δ 8.06 (2 H, d, J = 8.5 Hz), 7.31, (2 H, d, J = 8.5 Hz), 4.10 (2 H, q, J = 7.3 Hz), 3.34 (2 H, m), 2.85 (3 H, m), 1.18 (3 H, t, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 172.1, 147.6, 146.3, 129.3, 123.4, 60.6, 50.5, 49.7, 36.1, 14.0.

1-[(Benzyloxy)methyl]-6-[*N*-(carboxymethyl)-*N*-(*p*-nitrophenethyl)amino]-3-(methoxymethyl)uracil. To a solution of NaOH (2.12 g, 53.0 mmol) in 80 mL of 80% ethanol was added ethyl *N*-(*p*-nitrophenethyl)glycinate (13.37 g, 53.0 mmol). The mixture was stirred at room temperature for 0.5 h. Compound **7** (11.0 g, 35.4 mmol), prepared as described above, was then added. The mixture was refluxed for 1 h, and 1.5 g of $NaHCO_3$ was added. After the mixture was refluxed for an additional 1 h, an additional 1.5 g of $NaHCO_3$ was added. The mixture was refluxed for 4 h and concentrated under reduced pressure. The residue was treated with 200 mL of 1% NaOH and extracted with benzene (150 mL). The aqueous layer was acidified with concentrated HCl to pH 3 and extracted with ethyl acetate (2 × 200 mL). The combined organic layers were washed with brine (100 mL), dried, and concentrated to provide 16.45 g of product as a yellow foam (this material was used in the next step without further purification): IR (KBr) 3116, 1713, 1661, 1606, 1519 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 8.00 (2 H, d, J = 8.9 Hz), 7.37–7.27 (5 H, m), 7.18 (2 H, d, J = 8.9 Hz), 5.53 (1 H, s), 5.35 (2 H, s), 5.30 (2 H, s), 4.81 (2 H, s), 3.55 (2 H, t, J = 7.7 Hz), 3.46 (3 H, s), 2.95 (2 H, t, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$) δ 171.2, 163.9, 158.9, 153.3, 146.8, 145.4, 137.0, 129.5, 128.5, 128.2, 128.1, 123.7, 90.7, 75.9, 73.2, 72.3, 58.0, 53.4, 52.9, 33.3.

5-Acetoxy-1-[(benzyloxy)methyl]-3-(methoxymethyl)-7-(*p*-nitrophenethyl)pyrrolo[2,3-*d*]pyrimidine-2,4-dione (9). A mixture of crude acid (16.45 g, prepared as described above) and tripropylamine (20.27 g, 141.5 mmol) in 200 mL of acetic anhydride was refluxed for 45 min under an atmosphere of N_2. The solvent was evaporated under vacuum to provide a brown syrup which was purified by flash chromatography using ethyl acetate/hexanes (1:4) as the eluant. Afforded was 13.67 g (74% for two steps) of **9** as a light yellow solid. An analytical sample of **9** was obtained by recrystallization from ethyl acetate/hexanes as a light yellow crystalline solid: mp 145–146 °C; IR (KBr) 1772, 1709, 1662, 1599, 1586, 1542, 1513 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 8.05 (2 H, d, J = 8.6 Hz), 7.35–7.26 (5 H, m), 7.12 (2 H, d, J = 8.6 Hz), 6.51 (1 H, s), 5.54 (2 H, br s), 5.42 (2 H, s), 4.79 (2 H, s), 4.42 (2 H, t, J = 7.4 Hz), 3.45 (3 H, s), 3.12 (2 H, t, J = 7.4 Hz), 2.35 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 168.8, 157.1, 152.4, 147.1, 144.1, 136.6, 134.5, 133.3, 129.6, 128.6, 128.4, 128.2, 123.9, 111.1, 94.7, 74.3, 72.5, 72.2, 57.7, 49.0, 37.6, 20.7. Anal. Calcd for

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$C_{26}H_{26}N_4O_8$: C, 59.77; H, 5.13; N, 10.72. Found: C, 59.59; H, 5.02; N, 10.65.

5-Acetoxy-1-[(benzyloxy)methyl]-3-(methoxymethyl)-pyrrolo[2,3-*d*]pyrimidine-2,4-dione (10). A mixture of **9** (4.00 g, 7.7 mmol) and DBU (6.00 g, 39.5 mmol) in 200 mL of anhydrous acetonitrile was stirred at room temperature for 4 h. The reaction was quenched by adding 3.0 g of acetic acid. The solvent was removed under reduced pressure and gave a syrup which was treated with 200 mL of water and extracted with CH_2Cl_2 (2 × 150 mL). The combined organic layers were dried, filtered, and concentrated. The residue was purified by flash chromatography using ethyl acetate/hexanes (1:1) as the eluant to provide 2.30 g (80.5%) of **10** as a light yellow foam. An analytical sample of **10** was obtained by recrystallization from ethyl acetate/hexanes as a colorless crystalline solid: mp 101−102 °C; IR (KBr) 3216, 1765, 1698, 1646, 1606, 1562 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 8.67 (1 H, br s), 7.34−7.26 (5 H, m), 6.64 (1 H, s), 5.56 (2 H, s), 5.40 (2 H, s) 4.63 (2 H, s), 3.44 (3 H, s), 2.32 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 169.0, 157.6, 151.0, 136.2, 135.1, 133.1, 128.4, 128.2, 128.0, 106.3, 93.0, 73.3, 72.0, 71.6, 57.5, 20.6. Anal. Calcd for $C_{18}H_{19}N_3O_6$: C, 57.91; H, 5.13; N, 11.25. Found: C, 57.82; H, 5.19; N, 11.09.

5-Acetoxy-1-[(benzyloxy)methyl]-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-α-D-*erythro*-pentofuranosyl]-3-(methoxymethyl)pyrrolo[2,3-*d*]pyrimidine-2,4-dione (12a) and 5-Acetoxy-1-[(benzyloxy)methyl]-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-3-(methoxy)-methylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (12b). To a solution of **10** (2.30 g, 6.2 mmol) in anhydrous acetonitrile (220 mL) was added sodium hydride (60% in oil, 0.30 g, 7.4 mmol), and the mixture was stirred under an atmosphere of N_2 at room temperature for 30 min. The β-chloro-2′-deoxyribose derivative **11** (3.59 g, 9.2 mmol) was added, and stirring was continued for 30 min. The reaction was quenched by adding 0.5 g of acetic acid. After evaporation to dryness, the residue was dissolved in ethyl acetate (200 mL) and filtered. The filtrate was concentrated, and the residue was purified by flash chromatography using ethyl acetate/hexanes (3:7 then 7:3) as the eluants. The first band that eluted afforded 3.32 g (74%) of **12a** and **12b** as a colorless foam while a second band contained 0.21 g of starting material, **10**. The ratio of to **12a** to **12b** was determined to be α:β 1:4 by integration of the appropriate OAc signals in a ^1H NMR spectrum of the mixture.[19] Pure **12b** was obtained by two recrystallizations from ethyl acetate/hexanes as a light yellow crystalline solid: mp 140−141 °C; IR (KBr) 1758, 1713, 1666, 1611, 1577, 1539 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.89 (2 H, d, J = 7.6 Hz), 7.85 (2 H, d, J = 7.6), 7.33−7.17 (9 H, m), 6.77 (2 H, m), 5.84−5.62 (3 H, m), 5.42 (2 H, s), 4.81 (2 H, s), 4.69−4.88 (3 H, m), 3.49 (3 H, s), 2.87−2.64 (2 H, m), 2.42 (6 H, s), 2.31 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 168.7, 166.1, 165.8, 157.2, 152.5, 144.5, 137.0, 135.6, 133.6, 129.7, 129.6, 129.3, 128.4, 128.0, 127.7, 126.6, 126.2, 106.4, 95.3, 85.0, 82.0, 74.2, 74.1, 72.2, 72.0, 63.6, 57.7, 37.9, 21.7, 20.6. Anal. Calcd for $C_{39}H_{39}N_3O_{11}$: C, 64.53; H, 5.42; N, 5.79. Found: C, 64.29; H, 5.43; N, 5.68.

1-[(Benzyloxy)methyl]-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-α-D-*erythro*-pentofuranosyl]-3-(methoxy)methylpyrrolo-[2,3-*d*]pyrimidine-2,4,5-trione (13a) and 1-[(Benzyloxy)-methyl]-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-3-(methoxy)methylpyrrolo[2,3-*d*]-pyrimidine-2,4,5-trione (13b). To a solution of the mixture of **12a** and **12b** (1:4) (500 mg, 0.69 mmol) in 15 mL of THF was added 35 mL of MeOH and 2.5 g of $NaHCO_3$. The mixture was stirred at room temperature for 50 min and then treated with 200 mL of CH_2Cl_2. The organic phase was washed with 70 mL of cooled brine, dried for 20 min, and concentrated under reduced pressure at room temperature. The residue was purified by flash chromatography using ethyl acetate/CH_2Cl_2/hexanes (7:1:2) and then ethyl acetate/CH_2Cl_2 (9:1) as the eluants to furnish 283 mg of **13b** (75%, based on **12b**), 57 mg of **13a**, and 40 mg of **12**. For **13a** as a colorless foam: ^1H NMR ($CDCl_3$, 270 MHz) δ 7.88 (4 H, d, J = 7.9 Hz), 7.30 (7 H, m), 7.17 (2 H, d, J = 7.9 Hz), 6.62 (1 H, q, J = 4.0 Hz), 5.70−5.55 (3 H, m), 5.34 (3 H, s), 4.78 (1 H, d, J = 11.9 Hz), 4.74 (1 H, d, J = 11.9 Hz) 4.73−4.48 (3 H, m), 4.31 (1 H, d, J = 18.5 Hz), 4.02 (1 H, d, J = 18.5 Hz), 3.42 (3 H, s), 2.97 (2 H, m), 2.43 (3 H, s), 2.39 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 187.4, 166.2, 166.1, 166.0, 155.9, 151.9, 144.8, 144.2, 136.4, 129.6, 129.6, 129.5, 129.2, 128.5, 128.2, 127.8, 126.5, 125.9, 94.9, 86.2, 83.2, 74.9, 74.3, 72.5, 72.0, 64.3, 58.0, 55.1, 36.5, 21.7, 21.6. An analytical sample of **13b** was obtained by recrystallization from ethyl acetate/hexanes as a colorless crystalline solid: mp 148−149 °C; IR (KBr) 1739, 1717, 1702, 1659, 1611, 1559, 1537 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.88 (2 H, d, J = 7.9 Hz), 7.84 (2 H, d, J = 8.6 Hz), 7.31−7.20 (7 H, m), 7.15 (2 H, d, J = 7.9 Hz), 6.58 (1 H, t, J = 6.9 Hz), 5.68−5.56 (3 H, m), 5.35 (2 H, s), 4.90 (1 H, d, J = 17.4 Hz), 4.86 (1 H, d, J = 17.4 Hz), 4.58−4.35 (3 H, m), 4.15 (1 H, d, J =17.8 Hz), 3.87 (1 H, d, J = 17.8 Hz), 3.42 (3 H, s), 2.50−2.46 (2 H, m), 2.42 (3 H, s), 2.40 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 186.6, 166.7, 166.1, 165.7, 155.7, 152.1, 144.5, 144.4, 136.7, 129.7, 129.5, 129.4, 129.3, 128.5, 128.1, 127.6, 126.4, 126.2, 95.0, 84.9, 81.5, 74.5, 74.2, 72.7, 72.0, 63.6, 58.0, 54.4, 35.9, 21.7. Anal. Calcd for $C_{37}H_{37}N_3O_{10}$: C, 65.00; H, 5.45; N, 6.15. Found: C, 64.84; H, 5.54; N, 6.06.

1-[(Benzyloxy)methyl]-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-3-(methoxymethyl)-5-(trifluoromethanesulfonyl)pyrrolo[2,3-*d*]pyrimidine-2,4-dione (14). A mixture of **13b** (446 mg, 0.65 mmol) and 2,4,6-collidine (87 mg, 0.72 mmol) in 10 mL of CH_2Cl_2 at −78 °C was treated with triflic anhydride (203 mg, 0.72 mmol). The mixture was stirred at −78 °C for 15 min and diluted with CH_2Cl_2 (100 mL). The solution was washed with water (50 mL) and brine (50 mL), dried, and concentrated. The residue was purified by flash chromatography using ethyl acetate/hexanes (2:3) as the eluant to give 507 mg (95.3%) of **14** as a colorless foam: IR (KBr) 1719, 1681, 1613, 1579, 1542 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.89 (2 H, d, J = 2 Hz), 7.86 (2 H, d, J = 2 Hz), 7.31−7.19 (9 H, m), 6.78 (2 H, m), 5.82−5.65 (3 H, m), 5.43 (2 H, s), 4.82 (2 H, s), 4.71−4.51 (3 H, m), 3.45 (3 H, s), 2.71−2.66 (2 H, m), 2.43 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 166.0, 165.8, 156.3, 152.1, 144.6, 144.5, 136.8, 135.7, 131.6, 129.7, 129.6, 129.4, 129.4, 129.3, 128.4, 128.1, 127.7, 126.4, 126.1, 118.6 (q, J = 321.7 Hz), 107.7, 95.3, 85.4, 82.5, 74.4, 74.1, 72.2, 72.1, 63.4, 57.8, 38.3, 21.7, 21.6. Anal. Calcd for $C_{38}H_{36}F_3N_3O_{12}S$: C, 55.95; H, 4.45; N, 5.15. Found: C, 55.86; H, 4.47; N, 5.10.

1-[(Benzyloxy)methyl]-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-5-(methoxycarbonyl)-3-(methoxymethyl)pyrrolo[2,3-*d*]pyrimidine-2,4-dione (15b). Triethylamine (68.0 μL) was added to a solution of **14** (100 mg, 0.12 mmol) in DMF (5 mL) and MeOH (0.3 mL) followed by $Pd(OAc)_2$ (2.7 mg, 0.012 mmol) and PPh_3 (9.6 mg, 0.036 mmol). A stream of CO was passed into the solution for 5 min. The resulting mixture was stirred at 70 °C for 2 h under a CO balloon and then evaporated to dryness under reduced pressure. The residue was purified by flash chromatography using ethyl acetate/hexanes (3:2) as the eluant to provide 74 mg (83%) of **15b**. An analytical sample of **15b** was obtained by recrystallization from ethyl acetate/hexanes as a colorless powder: mp 112−113 °C; IR (KBr) 1747, 1730, 1714, 1667, 1611, 1553, 1515 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.90 (2 H, d, J = 2 Hz), 7.86 (2 H, d, J = 2 Hz), 7.52 (1 H, s), 7.31−7.18 (9 H, m), 6.82 (1 H, t, J = 6.6 Hz), 5.72 (1 H, m), 5.47 (2 H, s), 4.83 (2 H, s), 4.62−4.53 (3 H, m), 3.75 (3 H, s), 3.47 (3 H, s), 2.89−2.62 (2 H, m), 2.42 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 166.0, 165.8, 162.3, 156.7, 152.3, 144.5, 144.2, 139.3, 136.9, 129.9, 129.7, 129.6, 129.3, 128.4, 128.0, 127.8, 127.7, 126.4, 126.1, 123.4, 114.1, 100.0, 85.3, 82.4, 74.5, 74.1, 72.8, 72.0, 63.5, 57.9, 51.7, 38.3, 21.7, 21.6. Anal. Calcd for $C_{39}H_{39}N_3O_{11}$: C, 64.54; H, 5.42; N, 5.79. Found: C, 64.45; H, 5.41; N, 5.75.

1-[(Benzyloxy)methyl]-5-(2′-carbethoxyethenyl)-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-3-(methoxymethyl)pyrrolo[2,3-*d*]pyrimidine-2,4-dione (16). To a stirred solution of **14** (100 mg, 0.12 mmol) in 5 mL of DMF were sequentially added 0.6 mL of triethylamine, ethyl acrylate (124 mg, 1.24 mmol), and $Pd(PPh_3)_2Cl_2$ (8.6 mg, 0.012 mmol). The solution was degassed with N_2 and then stirred at 85 °C overnight. The DMF and excess ethyl acrylate were removed under vacuum. The residue was purified by flash chromatography using ethyl acetate/hexanes (1:1) as the eluant to afford 81 mg (86%) of **16** as a light yellow powder. An analytical sample of **16** was obtained by recrystallization from ethyl acetate/hexanes as a light yellow crystalline solid: mp 121−122 °C; IR (KBr) 1707, 1668, 1639, 1610, 1557, 1547

cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.90–7.85 (4 H, m), 7.71 (1 H, d, J = 16.1 Hz), 7.31–7.19 (9 H, m), 7.04 (1 H, s), 6.78 (1 H, t, J = 6.6 Hz), 6.67 (1 H, d, J = 16.1 Hz), 5.72 (3 H, m), 5.46 (2 H, s), 4.82 (2 H, s), 4.74–4.50 (3 H, m), 4.23 (2 H, q, J = 7.3 Hz), 3.46 (3 H, s), 2.68 (2 H, m), 2.42 (3 H, s), 1.32 (3 H, t, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 167.2, 166.0, 165.9, 158.4, 152.4, 144.6, 139.3, 137.0, 134.7, 129.7, 129.6, 129.5, 129.4, 129.3, 128.4, 128.0, 127.7, 126.4, 126.1, 119.6, 118.8, 118.2, 100.0, 85.0, 82.4, 74.4, 74.1, 72.6, 72.0, 63.2, 60.1, 57.7, 38.0, 21.7, 21.6, 14.4. Anal. Calcd for $C_{42}H_{43}N_3O_{11}$: C, 65.87; H, 5.66; N, 5.47. Found: C, 65.68; H, 5.64; N, 5.38.

1-[(Benzyloxy)methyl]-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-3-(methoxymethyl)-5-[3′-(trifluoroacetamido)propyn-1-yl]pyrrolo[2,3-*d*]pyrimidine-2,4-dione (17). A mixture of **14** (100 mg, 0.12 mmol), $Pd(PPh_3)_4$ (14 mg, 0.012 mmol), triethylamine (0.068 mL), and propargyltrifluoroacetamide (56 mg, 0.37 mmol) in 5 mL of DMF was degassed with N_2. Then CuI (4.7 mg, 0.025 mmol) was added, and the mixture was stirred under N_2 at room temperature for 50 min. The solution was evaporated to dryness under reduced pressure. The residue was purified by flash chromatography using ethyl acetate/hexanes (1:1) as the eluant to provide 93 mg (91%) of **17** as a light yellow foam: IR (thin film) 3310, 2244, 1718, 1672, 1612, 1572, 1557, 1515 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.88 (2 H, d, J = 3.3 Hz), 7.85 (2 H, d, J = 3.3 Hz), 7.42 (1 H, br s), 7.30–7.19 (9 H, m), 7.04 (1 H, s), 6.72 (1 H, t, J = 6.3 Hz), 5.85–5.65 (3 H, m), 5.42 (2 H, s), 4.79, 2 H, s), 4.64–4.50 (3 H, m), 4.36 (2 H, d, J = 5.3 Hz), 3.44 (3 H, s), 2.81–2.62 (2 H, m), 2.42 (3 H, s), 2.41 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 166.0, 165.8, 157.9, 156.8 (q, J = 37.4 Hz), 152.3, 144.5, 144.3, 137.6, 136.8, 129.7, 129.6, 129.3, 129.3, 128.4, 128.0, 127.7, 126.4, 126.1, 121.6, 115.7 (q, J = 287.6 Hz), 102.0, 101.8, 85.2, 85.1, 82.2, 74.2, 74.0, 72.5, 72.0, 63.4, 57.7, 38.0, 30.9, 21.7, 21.6. Anal. Calcd for $C_{42}H_{39}F_3N_4O_{10}$: C, 61.76; H, 4.81; N, 6.86. Found: C, 61.41; H, 4.86; N, 6.87.

1-[(Benzyloxy)methyl]-5-[4-(benzyloxy)phenyl]-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-3-(methoxymethyl)pyrrolo[2,3-*d*]pyrimidine-2,4-dione (18). A solution of **14** (100 mg, 0.12 mmol) in 5 mL of NMP was degassed with N_2. Zinc chloride (33.4 mg, 0.24 mmol) and tris-2-furylphosphine (6.2 mg, 0.03 mmol) were added. The mixture was stirred at room temperature for 5 min, and then Pd_2dba_3 (5.9 mg, 0.012 mmol) was added. After 10 min [*p*-(benzyloxy)phenyl]tri-*n*-butyltin (121 mg, 0.17 mmol) was added. The reaction mixture was stirred at 55 °C for 24 h, diluted with ethyl acetate (100 mL), washed with water (3 × 50 mL) and brine (50 mL), and dried. Concentration of the organic phase gave a residue which was redissolved in acetonitrile (100 mL) and washed with pentane (2 × 50 mL). Evaporation of the polar phase and flash chromatography of the residue using ethyl acetate/hexanes (3:7) as the eluant provided 74 mg (71%) of **18**. An analytical sample of **18** was obtained by recrystallization from ethyl acetate/hexanes as a colorless solid: mp 154–155 °C; IR (KBr) 1725, 1709, 1670, 1613, 1551, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.90–7.85 (4 H, m), 7.47–7.23 (12 H, m), 7.18 (2 H, d, J = 7.9 Hz), 7.10 (2 H, d, J = 7.9 Hz), 6.91 (2 H, d, J = 8.6 Hz), 6.86 (1 H, t, J = 6.9 Hz), 6.78 (1 H, s), 5.89–5.70 (3 H, m), 5.46 (2 H, s), 5.08 (2 H, s), 5.86 (2 H, s), 4.71–4.51 (3 H, m), 3.44 (3 H, s), 2.90–2.61 (2 H, m), 2.42 (3 H, s), 2.35 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 166.0, 165.9, 158.5, 158.2, 152.6, 144.5, 144.2, 138.6, 137.2, 137.1, 130.0, 129.7, 129.6, 129.5, 129.3, 128.6, 128.4, 127.9, 127.7, 127.4, 126.6, 126.2, 125.1, 123.9, 114.3, 99.5, 84.9, 82.1, 74.6, 74.5, 72.5, 71.9, 70.0, 63.6, 57.7, 38.0, 21.7, 21.6. Anal. Calcd for $C_{50}H_{47}N_3O_{10}$: C, 70.66; H, 5.57; N, 4.97. Found: C, 70.46; H, 5.64; N, 5.01.

1-[(Benzyloxy)methyl]-3-(methoxymethyl)-7-(*p*-nitrophenethyl)pyrrolo[2,3-*d*]pyrimidine-2,4,5-trione (19). A mixture of finely powdered **9** (1.00 g, 1.92 mmol) and $Na_2CO_3 \cdot H_2O$ (4.0 g) in 60 mL of methanol was stirred vigorously and immersed in a 90 °C oil bath for 3 min. The reaction mixture was cooled with an ice–water bath to 10 °C and then treated with 100 mL of cooled water and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with brine (50 mL), dried, filtered, and concentrated to give 0.90 g of crude **19** as light yellow foam (this material was used in the next step of the reaction without further purification). Recrystallization of **19** from ethyl acetate/hexanes afforded light yellow crystals: mp 144–145 °C; IR (KBr) 1728, 1697, 1642, 1568, 1528, 1512 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 8.07 (2 H, d, J = 9.2 Hz), 7.40–7.27 (5 H, m), 7.24 (2 H, d, J = 9.2 Hz), 5.47 (2 H, br s), 5.34 (2 H, s), 4.88 (2 H, s), 4.11 (2 H, t, J = 7.3 Hz), 3.97 (2 H, s), 3.44 (3 H, s), 3.08 (2 H, t, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 187.3, 166.3, 155.,6, 152.1, 147.1, 144.0, 136.3, 129.6, 128.7, 128.6, 128.3, 124.0, 94.2, 74.5, 73.4, 71.9, 60.9, 58.0, 50.1, 35.0.

1-[(Benzyloxy)methyl]-3-(methoxymethyl)-7-(*p*-nitrophenethyl)-5-(trifluomethanesulfonyl)pyrrolo[2,3-*d*]pyrimidine-2,4-dione (20). A mixture of crude **19** (0.90 g, 1.88 mmol) and 2,4,6-collidine (0.30 g, 2.49 mmol) in 10 mL of CH_2Cl_2 at −78 °C was treated with triflic anhydride (0.70 g, 2.49 mmol). The mixture was stirred at −78 °C for 15 min and diluted with CH_2Cl_2 (100 mL). The solution was washed with brine (50 mL), dried, and concentrated. The residue was purified by flash chromatography using ethyl acetate/hexanes (2:5) as eluant to give 1.00 g (85%) of **20** as light yellow semisolid. An analytical sample of **20** was obtained by recrystallization from ethyl acetate/hexanes as a colorless microcrystalline solid: mp 122–23 °C; IR (KBr) 1718, 1676, 1603, 1575, 1550, 1521 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 8.07 (2 H, d, J = 8.7 Hz), 7.36–7.26 (5 H, m), 7.13 (2 H, d, J = 8.7 Hz), 6.42 (1 H, s), 5.58 (2 H, br s), 5.42 (2 H, s), 4.80 (2 H, s), 4.48 (2 H, t, J = 7.5 Hz), 3.46 (3 H, s), 3.12 (2 H, t, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 156.2, 152.0, 147.2, 143.5, 136.4, 134.7, 131.0, 129.6, 128.6, 128.5, 128.2, 124.0, 121.0, 116.3, 112.4, 95.2, 74.3, 72.71, 72.6, 72.3, 57.9, 49.6, 37.5, 37.4. Anal. Calcd for $C_{25}H_{23}F_3N_4O_9S$: C, 49.02; H, 3.78; N, 9.15. Found: C, 48.98; H, 3.90; N, 9.25.

1-[(Benzyloxy)methyl]-5-(methoxycarboxyl)-3-(methoxymethyl)-7-(*p*-nitrophenethyl)pyrrolo[2,3-*d*]pyrimidine-2,4-dione (21). Triethylamine (1.0 mL) was added to a solution of **20** (1.00 g, 1.63 mmol) in DMF (7.6 mL) and MeOH (3.4 mL) followed by $Pd(OAc)_2$ (26.7 mg, 0.12 mmol) and PPh_3 (76.2 mg, 0.29 mmol). A stream of CO was passed into the solution for 5 min. The resulting mixture was stirred at 70–72 °C for 4 h under a CO balloon and was then evaporated to dryness under reduced pressure. The residue was purified by flash chromatography using ethyl acetate/hexanes (7:3) as eluant to provide 715 mg (84%) of **21** as a light yellow foam. An analytical sample of **21** was obtained by recrystallization from ethyl acetate/hexanes as a light yellow crystalline solid: mp 140–142 °C; IR (KBr) 1742, 1706, 1669, 1601, 1558, 1518 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 8.06 (2 H, d, J = 8.6 Hz), 7.35–7.26 (5 H, m), 7.14 (1 H, s), 7.13 (2 H, d, J = 8.6 Hz), 5.60 (2 H, br s), 5.47 (2 H, s), 4.80 (2 H, s), 4.51 (2 H, t, J = 7.8 Hz), 3.87 (3 H, s), 3.50 (3 H, s), 3.13 (2 H, t, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 162.7, 156.7, 152.3, 147.2, 143.6, 138.5, 136.5, 129.5, 128.6, 128.5, 128.2, 124.0, 113.6, 99.9, 74.4, 72.8, 72.7, 58.0, 51.9, 49.6, 37.6. Anal. Calcd for $C_{26}H_{26}N_4O_8$: C, 59.71; H, 5.02; N, 10.72. Found: C, 59.48; H, 5.01; N, 10.63.

1-[(Benzyloxy)methyl]-5-(methoxycarbonyl)-3-(methoxymethyl)pyrrolo[2,3-*d*]pyrimidine-2,4-dione (22). A mixture of **21** (0.95 g, 1.82 mmol) and DBU (1.00 g, 6.58 mmol) in 20 mL of anhydrous acetonitrile was stirred at room temperature overnight. The reaction was quenched by adding 0.5 g of acetic acid. The mixture was evaporated under reduced pressure to a syrup which was treated with 100 mL of water and then extracted with $CHCl_3$ (2 × 100 mL). The combined organic layers were dried, filtered, and concentrated. The residue was purified by flash chromatography using ethyl acetate/dichloromethane (4:1) as the eluant to provide 0.60 g (80.5%) of **22** as a white solid. An analytical sample of **22** was obtained by recrystallization from ethyl acetate/hexanes as a colorless crystalline solid: mp 205–206 °C; IR (thin film) 3279, 1711, 1665, 1603, 1552, 1518 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 9.35 (1 H, br s), 7.36 (1 H, s), 7.32–7.23 (5 H, m), 5.62 (2 H, s), 5.46 (2 H, s), 4.63 (2 H, s), 3.87 (3 H, s), 3.46 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 163.2, 157.2, 150.8, 139.2, 136.0, 128.8, 128.6, 128.5, 124.1, 113.8, 97.7, 73.9, 72.6, 71.9, 57.8, 51.8. Anal. Calcd for $C_{18}H_{19}N_3O_6$: C, 57.91; H, 5.13; N, 11.25. Found: C, 57.67; H, 5.10; N, 11.15.

1-[(Benzyloxy)methyl]-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-α-D-*erythro*-pentofuranosyl]-5-(methoxycarbonyl)-3-(methoxymethyl)pyrrolo[2,3-*d*]pyrimidine-2,4-dione (15a) and 1-[(benzyloxy)methyl]-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-5-(methoxycarbonyl)-3-(methoxymethyl)pyrrolo[2,3-*d*]pyrimidine-2,4-dione (15b). To a solution of **22** (300 mg, 0.80 mmol) in anhydrous acetonitrile (60 mL) was added sodium hydride (50% in oil, 46 mg, 0.96 mmol) and the mixture stirred under an atmosphere of N_2 at 45 °C for 30 min. Then the ribosyl chloride **11** (524 mg, 1.35 mmol) was added, and stirring was continued for 1.5 h. The reaction was quenched by adding several drops of acetic acid. After evaporation to dryness the residue was dissolved in ethyl acetate (100 mL) and filtered. The filtrate was concentrated, and the residue was purified by flash chromatography, first using ethyl acetate/hexanes (3:7) and then ethyl acetate/hexanes (7:3) as the eluants to yield 462 mg (79%) of a mixture of **15a** and **15b** as a colorless foam. The ratio of to **15a** to **15b** was determined to be 1:1 by integration of the appropriate OAc signals in a ^{1}H NMR spectrum of the mixture. Pure **15a** was obtained from this mixture by recrystallization from ethyl acetate/hexanes (mother liquid contains **15a** and **15b** in the ratio of 1.0:5.5). For **15a** as a colorless powder: mp 153–154 °C; IR (KBr) 1738, 1712, 1674, 1612, 1558, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.95 (2 H, d, J = 7.6 Hz), 7.91 (2 H, d, J = 7.9 Hz), 7.84 (1 H, s), 7.29–7.18 (9 H, m), 6.88 (1 H, d, J = 6.6 Hz), 5.82–5.70 (3 H, m), 5.47 (2 H, s), 4.79–4.57 (3 H, m), 3.81 (3 H, s), 3.47 (3 H, s), 3.12–2.71 (2 H, m), 2.44 (3 H, s), 2.41 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 166.0, 165.9, 162.7, 156.9, 152.3, 144.8, 144.2, 138.9, 136.8, 129.9, 129.6, 129.4, 129.3, 128.5, 128.1, 127.8, 126.6, 125.9, 125.4, 113.0, 100.1, 87.0, 84.5, 74.8, 74.0, 72.8, 72.0, 64.0, 57.9, 51.7, 38.5, 21.7, 21.6.

7-[2′-Deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-5-(methoxycarbonyl)-3-(methoxymethyl)-2-(2,4,6-triisopropylbenzenesulfonyl)pyrrolo[2,3-*d*]pyrimidin-4-one (24). A mixture of **15a** and **15b** (1:5.5), (220 mg, 0.30 mmol) and 220 mg of 20% $Pd(OH)_2$ on carbon in 40 mL of methanol was stirred at room temperature for 2 days under a H_2 balloon. The progress of the reaction was monitored by TLC (ethyl acetate) until the starting material had been consumed. The catalyst was filtered, and filtrate was evaporated to dryness. The residue containing **23** was dissolved in 10 mL of THF. Triisopropylbenzenesulfonyl chloride (230 mg, 0.76 mmol) and NaH (60% in oil, 15.2 mg, 0.38 mmol) were added. The mixture was refluxed for 8 h and then cooled to room temperature. Several drops of acetic acid were added, and then the solvent was removed under reduced pressure. The residue was purified by flash chromatography using ethyl acetate/hexanes (1:4) as the eluant to provide 190 mg (85% based on **15b**) of **24** as light yellow foam: IR (thin film) 1746, 1723, 1611, 1593, 1526 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.00 (2 H, d, J = 8.2 Hz), 7.92 (2 H, d, J = 8.2 Hz), 7.72 (1 H, s), 7.33 (2 H, d, J = 8.2 Hz), 7.24 (2 H, d, J = 8.2 Hz), 7.22 (2 H, s), 6.15 (1 H, t, J = 6.7 Hz), 5.62 (1 H, m), 5.58 (1 H, d, J = 10.1 Hz), 5.56 (1 H, d, J = 10.1 Hz), 4.67–4.51 (3 H, m), 4.14 (3 H, m), 3.76 (3 H, s), 3.45 (3 H, s), 2.86–2.55 (2 H, m), 2.49 (3 H, s), 2.43 (3 H, s), 1.29–1.22 (18 H, m); ^{13}C NMR ($CDCl_3$) δ 166.1, 165.9, 162.6, 156.7, 155.0, 150.7, 148.3, 145.4, 144.6, 144.1, 131.0, 130.0, 129.6, 129.5, 129.3, 129.2, 126.5, 126.4, 126.1, 123.8, 112.8, 103.3, 84.0, 82.6, 74.5, 73.0, 63.9, 57.6, 51.5, 39.1, 34.2, 30.1, 24.6, 24.5, 23.5, 23.4, 21.7, 21.6.

Alternatively, compound **24** was prepared from **15b** (pure β isomer obtained from the route shown in Scheme 2 and eq 1, Scheme 3) using the same procedure described above with the following quantities of materials: 360 mg (0.497 mmol) of **15b**, 360 mg of $Pd(OH)_2$ in 25 mL of MeOH, 376 mg (1.24 mmol) of triisopropylbenzenesulfonyl chloride, and 25 mg (0.621 mmol) of NaH (60% in oil) in 15 mL of THF. Following purification by column chromatography, 396 mg (92%) of **24** was obtained.

2-(Benzoylamino)-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-5-(methoxycarbonyl)-3-(methoxymethyl)pyrrolo[2,3-*d*]pyrimidin-4-one (25). A mixture of benzamide (115 mg, 0.95 mmol) and NaH (60% in oil, 40 mg, 1.00 mmol) in 7 mL of THF was refluxed for 5 min and was then cooled to −10 °C. A solution of **24** (330 mg, 0.38 mmol) in 8 mL of THF was added. The mixture was stirred at -10 °C for 15 min and then at 0 °C for 75 min. The reaction was monitored by TLC (ethyl acetate/hexanes (1:4)) until the starting material was consumed. The reaction was quenched by adding several drops of acetic acid, and then the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography using ethyl acetate/hexanes (1:1) and then ethyl acetate as the eluants to provide 180 mg (67%) of **25** as light yellow solid. An analytical sample of **25** was obtained by recrystallization from ethyl acetate/hexanes as a colorless solid: mp 206–207 °C; IR (thin film) 3357, 1723, 1612, 1581, 1530, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 9.44 (1 H, br s), 7.99–7.83 (6 H, m) 7.73 (1 H, s), 7.66–7.20 (7 H, m), 6.53 (1 H, t, J = 6.9 Hz), 5.76–5.64 (3 H, m), 4.69–4.58 (3 H, m), 3.77 (3 H, s), 3.56 (3 H, s), 2.94–2.67 (2 H, m), 2.44 (3 H, s), 2.40 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 166.1, 165.9, 164.3, 162.8, 157.1, 147.2, 145.7, 144.3, 143.9, 133.2, 132.8, 129.8, 129.6, 129.2, 129.1, 128.9, 127.4, 126.9, 126.7, 126.4, 112.2, 102.9, 85.0, 82.6, 74.8, 73.7, 64.0, 57.3, 51.5, 38.2, 21.7, 21.7, 21.6. Anal. Calcd for $C_{38}H_{36}N_4O_{10}$: C, 64.40; H, 5.12; N, 7.91. Found: C, 64.14; H, 5.15; H, 7.81.

2-(Benzoylamino)-7-[2′-deoxy-3′,5′-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-5-(methoxycarbonyl)pyrrolo-[2,3-*d*]pyrimidin-4(3*H*)-one (26). To a solution of **25** (234 mg, 0.33 mmol) in 10 mL of CH_2Cl_2 was added 1.5 mL of TFA. The mixture was stirred at room temperature for 15 min. The volatiles were removed under reduced pressure. The resulting residue was purified by flash chromatography using ethyl acetate/CH_2Cl_2/methanol (7.0:2.5:0.5) as eluant to afford 204 mg (93%) of **26**. An analytical sample of **26** was obtained by recrystallization from methanol as a colorless crystalline solid: mp 128–130 °C; IR (KBr) 1718, 1671, 1612, 1543, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 11.92 (1 H, br s), 9.44 (1 H, br s), 8.05 (2 H, d, J = 7.5 Hz), 7.94 (2 H, d, J = 8 Hz), 7.81 (2 H, d, J = 8 Hz), 7.65 −7.14 (8 H, m), 6.34 (1 H, t, J = 6.4 Hz), 3.07 (1 H, m), 2.67 (1 H, m), 2.43 (3 H, s), 2.38 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 167.6, 166.5, 166.1, 163.2, 156.0, 148.2, 147.1, 144.4, 144.3, 133.5, 131.6, 129.7, 129.5, 129.4, 129.2, 129.2, 128.8, 127.9, 127.5, 126.4, 111.9, 103.9, 85.9, 82.0, 74.4, 63.1, 51.6, 37.1, 21.7, 21.6.

2-Amino-7-(2′-deoxy-β-D-*erythro*-pentofuranosyl)-4(3*H*)-oxopyrrolo[2,3-*d*]pyrimidine-5-carboxylic Acid (2′-Deoxycadeguomycin) (27). A suspension of **26** (100 mg, 0.15 mmol) in 8 mL of 1 N NaOH and 3 mL of methanol was stirred at room temperature for 4 days. The mixture was concentrated into 5 mL under reduced pressure, cooled to 5 °C, stirred, and carefully acidified to pH 3 using concentrated HCl. After the mixture was stirred for 1 h, the precipitate was collected by filtration, washed with a small amount of water, and dried in vacuo. The solid was suspended in 10 mL of $CHCl_3$, stirred vigorously at room temperature for 2 h, and then collected by filtration and washed with $CHCl_3$ to provide 43 mg (92%) of **27** as a colorless powder: mp >300 °C; IR (KBr) 3399, 3328, 1646, 1615, 1566, 1523 cm^{-1}; ^{1}H NMR (DMSO, 400 MHz) δ 14.09 (1 H, br s), 11.56 (1 H, br s), 7.78 (1 H, s), 6.74 (2 H, br s), 6.30 (1 H, dd, J = 7.9, 5.9 Hz), 5.23 (1 H, d, J = 3.8 Hz), 4.94 (1 H, t, J = 5.2 Hz), 4.31 (1 H, m), 3.81 (1 H, m), 3.53 (2 H, m), 2.37 (1 H, m), 2.15 (1 H, m); ^{13}C NMR (DMSO) δ 162.6, 161.3, 153.2, 151.4, 125.4, 110.8, 96.3, 87.5, 82.8, 70.8, 61.6, 39.5. The IR and ^{1}H NMR spectra for our sample of **27** were indentical in comparison with the material reported by Ramasamy and co-workers.[14]

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compounds **7**, **24**, **26**, and **27** (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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