Synthesis of Benzyl and Benzyloxycarbonyl Base-Blocked 2'-Deoxyribonucleosides

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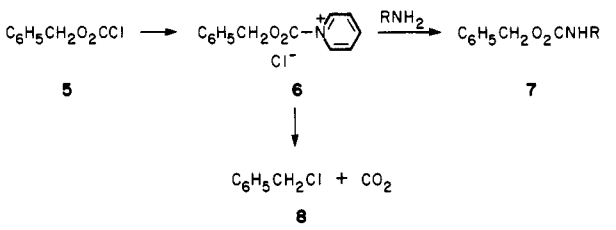
Acylimidazoles have been alkylated with trialkyloxonium tetrafluoroborates to form acylimidazolium salts. These salts, particularly (benzyloxycarbonyl)imidazolium salts, are shown to be effective agents for the direct, mono-N-protection of deoxynucleosides as their acyl derivatives. These acyl nucleosides are also available via thiocarbamate intermediates. Thus 3',5'-bis(*tert*-butyldimethylsilyl)-2'-deoxyguanosine (**4b**), on treatment with phenyl chlorothioformate, gave the 6-thiophenyl-substituted purine **38a**. The thiophenyl group of **38a** can be replaced by hydrogen, amino, and alkoxy groups to give a variety of substituted purine deoxyribonucleosides.

In our synthetic efforts directed toward oligonucleotides,[1] natural and unnatural nucleosides, and nucleoside antibiotics, we have sought to develop more versatile methods for blocking the nucleoside bases. The *exo*-amino groups of cytidine, adenosine, and guanosine have been almost invariably blocked as amide derivatives,[2] although there are a few examples of carbamates[3-6] and one example of the (dimethylamino)methylene group being used for this purpose.[7] All these blocking groups, with one exception,[6] are removed under alkaline hydrolytic conditions.

We have been exploring the benzyloxycarbonyl (Cbz) group as a blocker for these *exo*-amino functions since it may be removed under neutral, hydrogenolytic conditions. The Cbz group has been of primary importance in peptide chemistry,[8] and we considered that the methodology developed in that area could be applied to nucleoside and oligonucleotide problems. Indeed, we have shown[1] that Cbz base-blocked nucleosides are useful intermediates for oligonucleotide synthesis, being stable to the necessary subsequent reaction conditions and cleanly removed when desired by transfer hydrogenation without reduction of any of the bases.

Other reactive centers, besides the exocyclic amino groups, present on nucleoside bases are the 6-oxygen of guanosine and the 4-oxygens of uridine and thymidine.[2] These positions have been shown[9-11] to react with the reagents used in generating P–O bonds in oligonucleotide synthesis. Thymidine was found to be much less reactive to these reagents than guanosine or uridine. Recently[12] substituted phenyl groups have been introduced to block these positions, and in our previous work[1] we used a benzyl group to block the 6-oxygen of 2'-deoxyguanosine. The detailed methodology developed to synthesize the blocked naturally occurring nucleosides used previously as well as new extensions and methodology to synthesize Cbz-blocked modified nucleosides are described here.

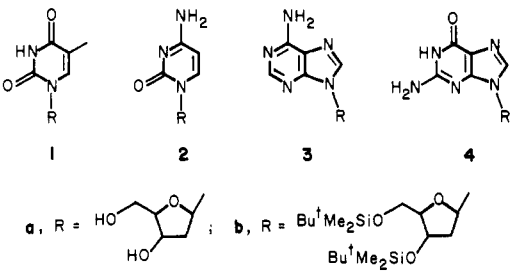
Scheme I



Results and Discussion

Acylation with Benzyl Chloroformate. The Cbz group is most commonly introduced by using benzyl chloroformate (**5**) under aqueous alkaline conditions. This procedure is not applicable to acylation of nucleosides because of their tendancy to undergo ring-opening reactions[13] under these conditions and because of their poor nucleophilicity. Therefore new methods had to be developed.

Benzyl chloroformate fails to react with the four deoxyribonucleotides **1a–4a** in tetrahydrofuran (THF) in the



presence of K_2CO_3. Under these conditions chloride ion is not a sufficiently good leaving group to allow acylation of the weakly nucleophilic centers of the nucleosides. In pyridine at −20 °C benzyl chloroformate will react with nucleosides **1a**, **3a**, and **4a** to give moderate yields of ribose-*O*-acylated nucleosides. With the 2'-deoxynucleosides which are blocked as their *tert*-butyldimethylsilyl (TBDMS) ethers **3b** or **4b**, no reaction occurs under these conditions. 2'-Deoxycytidine (**2a**), on the other hand, reacts with benzyl chloroformate in pyridine to give moderate yields of a mixture of the *N*- and *O*-acylcytidines **9a** and **9b**. However, the major product isolated from these reactions is benzyl chloride (**8**).

It appears that acylpyridinium complex **6** is formed, which is an active acylating agent, but the benzylic carbon is also activated toward nucleophilic attack by chloride ion (Scheme I). In the case of 2'-deoxycytidine, the most

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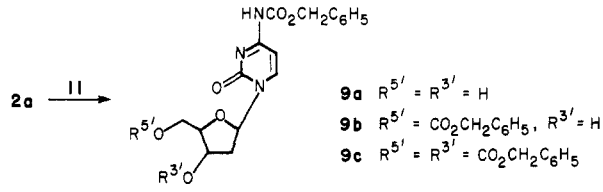
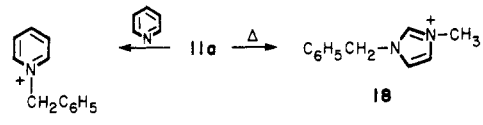
easily acylated nucleoside, acylation is competitive with this destruction of the benzyl chloroformate, whereas in the case of the less nucleophilic 2′-deoxyadenosine and 2′-deoxyguanosines, **3b** and **4b**, benzyl chloride formation occurs to the exclusion of acylation. To test this hypothesis, we allowed benzyl chloroformate to react with **2a** in



the presence of the highly hindered amine 1,2,2,6,6-pentamethylpiperidine which should be sterically incapable of forming an acylammonium complex. Indeed, benzyl chloroformate was found to be stable under these conditions; however acylation of **2a** also does not occur.

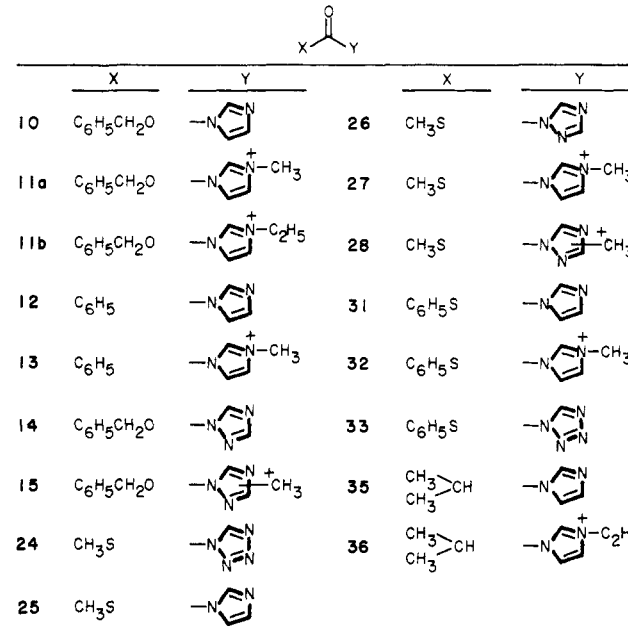
Acylimidazolium Salts. An acylammonium complex was expected to be an effective acylating agent for nucleosides if it could be generated under conditions where the nucleoside is the most nucleophilic species present. Clearly, generating such a species in the absence of chloride ions is a necessity. The imidazolide **10** is readily obtained as a low-melting crystalline solid from benzyl chloroformate and imidazole; however, this imidazolide is a poor acylating agent. Alkylation of **10** with either trimethyl- or triethyloxonium tetrafluoroborate gave the stable acylimidazolium salts **11a,b** which proved to be very potent acylating reagents since the leaving group is now a neutral *N*-alkylimidazole. The ribose-blocked adenosine **3b** reacts with either **11a** or **11b** in CH_2Cl_2 to produce the Cbz-substituted adenosine **16b** in 95% yield. Bis(*tert*-butyldimethylsilyl)-2′-deoxyadenosine **3a** itself reacts with **11a** or **11b** to give the triacyldeoxyadenosine **16a**. Both **16a** and **16b** may be converted to the hydroxy-free acyldeoxyadenosine **16c** under standard conditions;[14,15] however, the conversion of **16a** to **16c** proceeds in only 50% yield due to the large amount of alkali-catalyzed depurination. There appears to be little difference between the methyl and ethyl salts in acylating ability.

The acylimidazolium salts and the others to be discussed below are stable up to 70 °C in nonnucleophilic, nonbasic solvents such as CH_2Cl_2, acetone, and acetonitrile. They react with basic solvents such as pyridine at room temperature to give *N*-benzylpyridinium salts **17** and upon warming lose CO_2 to give benzylalkylimidazolium salts **18**.



Acylimidazolium species have been used as acylating agents previously[16] but not for the preparation of nucleoside intermediates. Another problem associated with nucleoside blocking is over acylation,[17] and this is also overcome with the imidazolium reagents. Thus the benzyloxycarbonyl and benzoylimidazolium salts **11** and **13** (from **12**) react with bis(*tert*-butyldimethylsilyl)deoxyadenosine to give only the monoacylated deoxynucleosides **16** and **19**, respectively, with no detectable bis-acylation.

Chart I. Some Activated Carbonyl Reagents



2′-Deoxycytidine (**2a**) also reacts with **11a** or **11b** to give a mixture of acylcytidines **9a–c** as described previously.[1] This is an improvement over the benzyl chloroformate–pyridine procedure in that the yields are higher and are not dependent on the scale of the reaction. The bis(*tert*-butyldimethylsilyl)guanosine **4b** fails to react with either **11a** or **11b** at room temperature. In refluxing CH_2Cl_2, a benzyl, (benzyloxycarbonyl)guanine of unknown structure was isolated from which the deoxy sugar had been lost.

Acyltrizolium salts have also been used as acylating agents.[18] (Benzyloxycarbonyl)triazole (**14**), easily prepared from benzyl chloroformate and triazole, was alkylated to give a mixture of the two possible regioisomers **15** (Chart I). These reacted with the bis(*tert*-butyldimethylsilyl)-deoxyadenosine **3b** and the bis(*tert*-butyldimethylsilyl)-deoxyguanosine (**4b**) to give only polar alkylated materials. It would appear that **15** is a better alkylating agent than it is an acylating agent.

Neither the bis(*tert*-butyldimethylsilyl)deoxyguanosine **4b** nor any of the 2-aminopurines subsequently described reacted with any of the acylimidazolium or triazolium salts or ac tetrazoles to give acyl nucleosides; only educt or polar, alkylated products were observed. The 2,6-diaminopurine **40b** reacts with the (benzyloxycarbonyl)-imidazolium salt **11b** to yield the monocarbamate **40c**.

Doubly Activated Carbonyl Route. Since the acylimidazolium salts were ineffective for the acylation of deoxyguanosine, a process based on chlorothioformates was investigated (Scheme II). The nucleoside thiocarbamate **21** should be readily available from the ribose-blocked nucleoside and a chlorothioformate, **20**. We expected that **20** would be stable to activation with amines such as pyridine if the R group was selected so that it would not be susceptable to nucleophilic displacement as in the benzyloxy series.

This approach was first investigated with 2′-deoxyadenosine derivatives (Scheme III). The bis(*tert*-butyldimethylsilyl)deoxyadenosine **3b** was treated with methyl chlorothioformate or phenyl chlorothioformate and gave the diacyladenosines **22a,b** in high yield. The bis(methylthiocarbamate) **22a** can be selectively hydrolyzed un-

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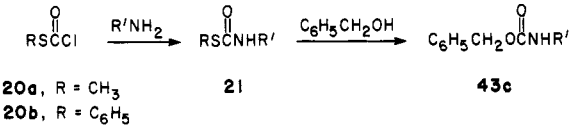
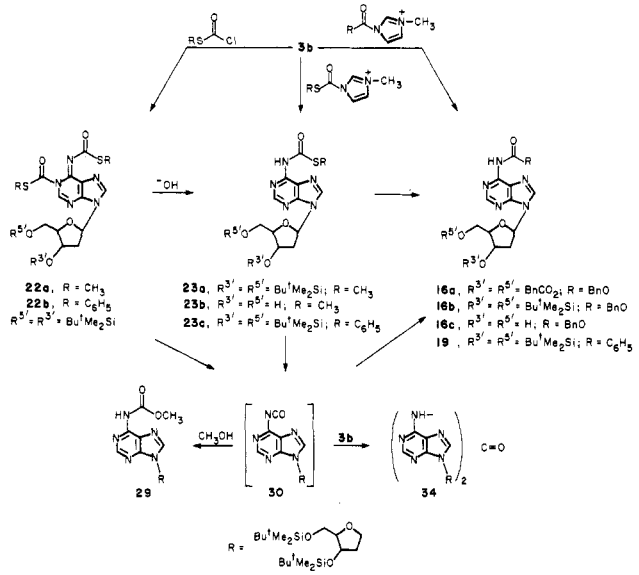
Scheme II. Carbamates from Chlorothioformates



Scheme III. Reactions of Deoxyadenosine Thiocarbamates



der alkaline conditions to the monothiocarbamate **23a** which can be desilylated under standard conditions[14] to yield the monothiocarbamate **23b**. Alternatively, **23b** can be prepared directly from 2′-deoxyadenosine **3a** by treatment with methyl chlorothioformate followed by selective hydrolysis of the thiocarbamate residues.

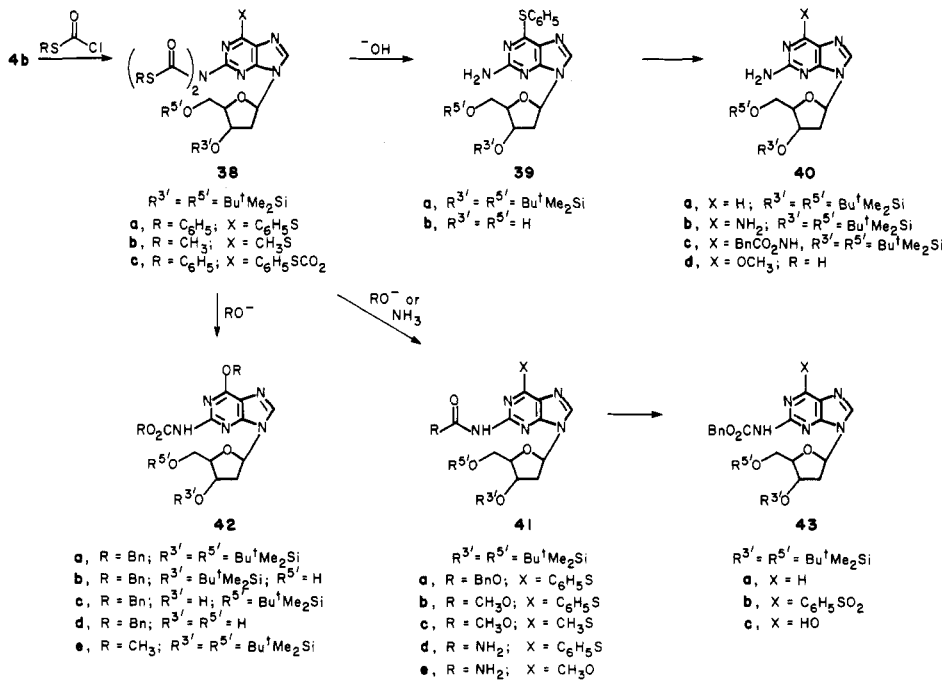
In order to prepare the monothiocarbamate **23a** without proceeding through the bis(thiocarbamate) **22a**, reagents other than chlorothioformates were utilized. Since acyltetrazoles[5] have been used to selectively acylate adenosine derivatives, 5-[(methylthio)carbonyl]tetrazole (**24**) was prepared from the chloroformate and did react with the adenosine **3b** in refluxing THF to give the monothiocarbamate **23a**. However, the monothiocarbamate **23a** is more conveniently prepared in 60% yield by treating bis(*tert*-butyldimethylsilyl)deoxyadenosine **3b** with acylimidazolium salt **27** (from imidazole **25**) in CH_2Cl_2. The acyltriazolium salt **28** reacted with **2b** to give only polar products with no **23** being observed. Presumably **28** is acting as an alkylating agent under these conditions, as we observed previously.

Attempts to prepare monothiocarbamate **23c** failed. Unlike monothiocarbamate **23a**, when bis(thiocarbamate) **22b** is treated with aqueous sodium hydroxide, it is reconverted to the silyladenosine **3b**, and when **22b** is treated with sodium hydroxide in aqueous methanol, methyl carbamate **29** is the major product. The monothiocarbamate **23c** does not appear to be a stable species and rapidly eliminates thiophenol to give the isocyanate **30**[4b] which is trapped by the most reactive nucleophile present to give the observed products **3b**, **29**, and **34**. Adenosine **3b** reacts with the acylimidazolium salt **32** to give only polar products; however, **3b** reacts with the acyltetrazole **33** to give the urea **34**.[4b] In this case the phenyl thiocarbamate **23c** is probably initially formed and then rapidly eliminates thiophenol to produce the isocyanate **30**. The most reactive nucleophile present is unreacted adenosine **3b** which can than trap the isocyanate to give the urea **34**. These reactions are summarized in Scheme III.

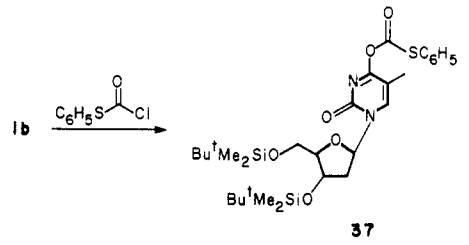
When treated with benzyl alcohol in the presence of $AgNO_3$, monothiocarbamates **23a,b** are converted to the benzyl carbamates **16b,c** in 47% and 50% yields, respectively. These yields could not be raised by varying the reaction conditions, and the remainder of the material balance was accounted for as the adenosines **3a,b**.

Reaction of Phenyl Chlorothioformate with Guanosine. Chlorothioformates did not react with 2′-deoxyguanosine derivatives in a fashion analogous to adenosine. Bis(*tert*-butyldimethylsilyl)deoxyguanosine **4b**, when allowed to react with phenyl chlorothioformate, gave the 6-(phenylthio)guanosine **38a** (Scheme IV). This product was quite unexpected and could arise from intermediate **38c** which upon loss of CO_2 results in the formation of **38a**. The yield is dependent on substrate and reagent concen-

Scheme IV. Blocked Deoxyguanosine Derivatives



tration as well as reaction time since **38a** is not stable to the reaction conditions; however, an 85% yield of **37a** can be obtained when phenyl chlorothioformate is used in large excess. This reaction is not limited to the phenyl series as the bis(*tert*-butyldimethylsilyl)deoxyguanosine **4b** also reacts with methyl chlorothioformate to give the 6-methylthioguanosine **38b**, but seems to be limited to purines as the bis(*tert*-butyldimethylsilyl)thymidine **1b** gives the 6-*O*-acylthymine **37** with phenyl chlorothioformate.



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The 6-phenylthioguanosine **38a** is an intermediate in which the functionality at C-6 and 2-N may be selectively elaborated and provides a useful synthetic route to 6-substituted 2′-deoxyguanosines (Scheme IV). In the ribose series the 6-position of guanosine may be modified by treatment either with $POCl_3$ or P_4S_{10}, and the resulting 6-chloro-[19] or 6-thioguanosine[20] can be elaborated to a large variety of derivatives. This is not the case with 2′-deoxyguanosine due to the increased lability of the glycosidic bond which prohibits direct thiation or chlorination in high yield. 2′-Deoxyguanosines which are substituted at the 6-position are potentially available via the 6-*O*-mesylate[12] and the nitrotriazolide;[9] however, their synthetic scope has not been investigated.

The bis(thiocarbamate) **38a** can be hydrolyzed to the 6-(phenylthio)guanosine **39a**. When treated with Raney nickel, **39a** is cleanly desulfurized to give the 2-aminopurine deoxyribonucleoside **40a**. Similarly, the diaminopurine **40b** can be obtained in 80% yield from **38a** and ethanolic ammonia at 150 °C. With sodium methoxide under a variety of conditions, a number of products are obtained from **39a** resulting from random desilylation. If **39a** is first desilylated to **39b**, the thiophenyl group of **39b** can be cleanly displaced with sodium methoxide to give 2′-deoxy-6-*O*-methylguanosine **40d** in 60% yield.

The thiocarbamate functionality of **38a** may be selectively manipulated in the presence of the 6-thioether, or both may be manipulated simultaneously. Thus the phenyl thioguanosine **38a** can be treated with aqueous sodium benzyloxide or sodium methoxide to give the benzyl or methyl carbamates **41a,b**. Likewise the (methylthio)guanosine **38b** can be treated with aqueous sodium methoxide to give the methyl carbamate **41c**. With **38a** and either anhydrous sodium methoxide or sodium benzyl oxide, the guanosine–benzyl ether–benzyl carbamate **42a** or methyl ether–methyl carbamate **42e** are produced. In each case a large amount of desilylation occurs under the alkaline reaction conditions. The conditions necessary to convert thioether–thiocarbamate **38a** to methyl ether–methylcarbamate **42e** are much milder than those to convert thioether **39b** to methyl ether **40d** due to the presence of the acylated 2-amine. The silyl groups may be readily removed from **42a** to give the 6-O-2-N-blocked guanosine **42d**. This guanosine derivative was effectively incorporated into an oligonucleotide synthetic scheme. Besides blocking the 6-oxygen, this additional modification increased the lipophilic properties of the oligomers.[1]

Most attempts to manipulate the 6-thiophenyl group in the presence of the carbamate functionality in **41a,b** failed. When treated with deactivated Raney nickel, **41a** gives the 2-aminopurine benzyl carbamate **43a**. If active Raney nickel is used, both desulfurization and debenzylation occur to give the isoadenosine **40a**. Attempts to hydrolyze thioethers **39a** or **41a** or ether–carbamates **42a** or **42e** to enter the 6-substituted guanosine series gave complex mixtures. The thioether–carbamate **41a** or the ether–carbamate **42e** react with ammonia to give the ureas **41d** and **41e**. Urea **41d** is also available directly from **38a**.

We anticipated that by oxidizing sulfide **41a** to sulfone **43b**, the 6-position would be manipulable in the presence of the 2-*N*-carbamate. Treating **41b** with *m*-chloroperbenzoic acid presumably gives **43b** as an intermediate; however, only the guanosine benzyl carbamate **43c** was isolated. It appears that sulfone **43b** is not stable to these reaction or isolation conditions and readily hydrolyzes to **43c**. Attempts to generate **43b** in situ and displace the sulfoxide with ammonia or methoxide gave the guanosine carbamate **43c** as the only product.

Experimental Section

Melting points were obtained with a Büchi (capillary) apparatus and are uncorrected. IR spectra were determined as KBr pellets with a Perkin-Elmer 137 spectrophotometer with polystyrene film for calibration (1601.4-cm^{-1} absorption). UV spectra were determined on a Cary 219 spectrophotometer in 95% ethanol. ^1H NMR spectra were determined on a Varian T-60 (60 MHz), Varian E-390 (90 MHz), or UCB-250 (a homemade FT instrument operating at 250.80 MHz) spectrometer and were recorded in $CDCl_3$ unless otherwise noted; they are expressed in parts per million (δ) downfield from Me_4Si with the coupling constants (J) given in hertz. The ^1H NMR spectra reported do not contain the resonances for the 3′-, 4′-, and 5′-position ribose protons as they were of no analytical value. Elemental analyses were performed by the Analytical Laboratory, College of Chemistry, University of California, Berkeley. Field-desorption mass spectra were performed by the Bio-Organic, Biomedical Mass Spectrometer Resource supported by Grant No. RR00719 from the Division of Research Resources, NIH.

High-pressure liquid chromatography (HPLC) was performed on an Altex analytical system consisting of an Altex stainless-steel column (3.2 × 250 mm, 5 mm LiChrosorb C-18). A flow rate of 1.0 mL/min (one column volume equals 1.5 mL) was used, with monitoring at 254 mm. The solvent systems were acetonitrile with varying amounts of water. Column chromatography was performed with 63–200 μm silica gel 60 (EM Reagents). Analytical thin-layer chromatography (TLC) was done with aluminum-backed silica plates (E. Merck) which were developed in $CHCl_3$ with 0–15% ethanol.

Unless otherwise noted, reactions were conducted under a nitrogen atmosphere with magnetic stirring at room temperature (20–26 °C). Organic layers were dried over $MgSO_4$ and evaporated with a Berkeley rotary evaporator with water aspirator or oil pump reduced pressure, followed by static evaporation with an oil pump. All distillations were bulb to bulb (Kugelrohr-type apparatus) unless otherwise noted. Most of the nucleosidic compounds described were obtained as glasses without defined melting points.

The following solvents were freshly distilled as needed: tetrahydrofuran (THF) and toluene from sodium/benzophenone; pyridine from toluenesulfonyl chloride and then from calcium hydride; acetonitrile and CH_2Cl_2 from P_2O_5. Triethylamine was distilled from calcium hydride and stored over 4 Å molecular sieves. Imidazole and 1,2,4-triazole were dried in vacuo over P_2O_5 before use. Tetrabutylammonium fluoride was prepared from an aqueous solution of the hydroxide by neutralization with concentrated aqueous HF and rendered anhydrous by repeated addition and evaporation of pyridine.

The silyl ethers **3b** and **4b**,[14] benzoylimidazole,[21] isopropyl

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Table I. Characterization of New Activated Carbonyl Compounds

compd[a]	yield, %	mp, °C	recryst solv	^{1}H NMR, δ
14	30	49–50	Et_2O	5.48 (s, 2 H), 7.14 (s, 5 H), 8.03 (s, 1 H), 8.78 (s, 1 H)
24	91	47–48	Et_2O	1.69 (s, 3 H), 9.5 (s, 1 H)
25	40	30	Et_2O	2.55 (s, 3 H), 7.0 (s, 1 H), 7.37 (s, 1 H), 8.07 (s, 1 H)
26	50	49–50	petroleum ether	2.55 (s, 3 H), 7.98 (s, 1 H), 8.83 (s, 1 H)
31	38	65–68	hexane	7.03 (s, 1 H), 7.43 (s, 6 H), 8.13 (s, 1 H)
33	90	105–107 dec	CH_2Cl_2/isooctane	7.57 (s, 5 H), 9.17 (s, 1 H)
35	40	<20	isooctane	1.44 (d, 6 H, J = 7 Hz), 3.87 (m, 1 H, J = 7 Hz), 7.07 (s, 1 H), 7.42 (s, 1 H), 8.17 (s, 1 H)

[a] Satisfactory C, H, and N analytical data were obtained for all compounds in this table.

chlorothioformate, phenyl chlorothioformate,[22] and tetrazole[23] were prepared according to published procedures. Methyl chlorothioformate was a gift from the Stauffer Chemical Co.

Preparation of Acyl Azoles. Characterization of the various azoles is summarized in Table I. The acyl imidazoles and triazoles were prepared from the corresponding acid chloride and imidazole or triazole (200 mol %) in toluene. After being stirred overnight, the suspensions were filtered and evaporated, and the residue was crystallized. In two cases (**25** and **35**) the resulting oils were distilled. The tetrazoles were prepared from the acid chlorides, tetrazole (100 mol %), and triethylamine (100 mol %) in THF and isolated as above. The tetrazole **33** was sublimed (90 °C, 20 μmHg).

Preparation and Use of Acylimidazolium and Acyltriazolium Salts. To the appropriate acylimidazole or triazole in CH_2Cl_2 (20 mL/g) at 0 °C was added triethyloxonium[24] or trimethyloxonium[25] tetrafluoroborate (95 mol %). The mixture was stirred at room temperature from 2–12 h to give solutions of the acylimidazolium salts which were characterized by ^{1}H NMR. **11a** (CD_3CN): δ 3.91 (s, 3 H), 5.50 (s, 2 H), 7.45 (s, 6 H), 7.75 (s, 1 H), 9.05 (s, 1 H). **11b** ($CDCl_3$): 1.47 (t, 3 H, J = 7), 4.20 (q, 2 H, J = 7), 5.42 (s, 2 H), 7.3 (m, 6 H), 7.65 (s, 1 H), 8.98 (s, 1 H). **15** (CD_3CN): δ 3.93 (s, $^1/_3$ H), 4.06 (s, $^2/_3$ H), 5.53 (s 2 H, 7.4 (s, 5 H), 8.55 (s, $^1/_3$ H), 8.96 (s, $^2/_3$ H), 9.73 (s, $^2/_3$ H), 9.88 (s, $^1/_3$ H). **27** (CD_3CN): δ 2.51 (s, 3 H), 3.93 (s, 3 H), 7.45 (s, 1 H), 7.78 (s, 1 H), 9.10 (s, 1 H). **28** (CD_3CN): δ 2.63 (s, 3 H), 4.00 (s, 3 H), 8.63 (s, 1 H), 9.86 (s, 1 H). **32** (CD_3CN): δ 3.96 (s, 3 H), 7.5 (s, 6 H), 7.81 (s, 1 H), 9.14 (s, 1 H). **36**: 1.4–1.6 (m, 9 H), 3.82 (m, 1 H, J = 7), 4.33 (q, 2 H, J = 7), 7.64 (s, 1 H), 7.74 (s, 1 H), 9.28 (s, 1 H).

The ribose-blocked nucleosides **3b** or **4b** were then added and the mixtures stirred at room temperature. Addition of 10% aqueous $NaHCO_3$ and $CHCl_3$ and separation of the organic layer, which was washed, dried, and evaporated, gave the acyladenosines **16b,c**, **19**,[14] **23a**, and **40c**.

6-*N*-(Benzyloxycarbonyl)-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyadenosine (16b): 95% yield from **3b** and **11b**; IR 1740 cm^{-1}; ^{1}H NMR δ 0.07 (s, 6 H), 0.13 (s, 6 H), 0.88 (s, 9 H), 0.93 (s, 9 H), 5.15 (s, 2 H), 6.25 (t, 1 H, J = 6), 7.2 (s, 5 H), 8.03 (s, 1 H), 8.53 (s, 1 H); UV λ_{max} 267 nm (ε 20 200). Anal. Calcd for $C_{30}H_{47}N_5O_5Si_2$: C, 58.7; H, 7.7; N, 11.4. Found: C, 58.4; H, 7.8; N, 11.3.

Carbamate **16b** can also be prepared by adding $AgNO_3$ (61 mg, 0.36 mmol) to a pyridine (20 mL) solution of the thiocarbamate **23a** (200 mg, 0.36 mmol) and benzyl alcohol (0.5 mL) and stirring overnight at room temperature. Filtering, evaporating, and chromatographing the residue (Et_2O/hexane, 70/30) gave **16b** in 50% yield.

2-Amino-6-[(benzyloxycarbonyl)amino]-9-[3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxy-β-D-*erythro*-pentofuranosyl]purine (40c). The diaminopurine **40b** was acylated with **11b** to give **39c** in 95% yield after chromatography (ethanol/$CHCl_3$, 3:97): IR 1760 cm^{-1}; ^{1}H NMR δ 0.03 (s, 12 H), 0.84 (s, 18 H), 5.16 (s, 2 H), 6.22 (t, 1 H, J = 6.5), 7.3 (s, 5 H), 7.83 (s, 1 H); UV λ_{max} 248 nm (ε10 200), 301 (11,200). Anal. Calcd for $C_{30}H_{48}N_6O_5Si_2$: C, 57.3; H, 7.7; N, 13.4. Found: C, 57.3; H, 7.6; N, 13.1.

6-*N*-(Benzyloxycarbonyl)-2'-deoxyadenosine (16c). 2'-Deoxyadenosine (5.00 g, 20.1 mmol) was added to 120 mmol of **11a** in 600 mL of acetonitrile and the mixture stirred for 72 h at room temperature. Saturated aqueous $NaHCO_3$ was added, the solvent was evaporated, and the residue was dissolved in $CHCl_3$, washed with water, dried, and evaporated. The residue, which contained **16a**, was dissolved at room temperature in 260 mL of THF/CH_3OH/H_2O (5:4:1) and 4.8 mL of 2 N NaOH, and the solution was stirred for 5 min and then quenched with Dowex AG-50 ion-exchange resin (pyridinium form). The resin was removed by filtration and washed with ethanol, and the combined filtrates were evaporated and chromatographed (ethanol/$CHCl_3$, 7:93) to give **16c**[1] in 47% yield. The benzyl carbamate **16c** can also be prepared from the thiocarbamate **23b**, according to the procedure for converting **23a** to **16a**, in 50% yield and from **3b** in 87% yield.[1]

Acylation of 3b with Chlorothioformates. Bis(*tert*-butyldimethylsilyl)deoxyadenosine **3b** (0.79 g, 1.6 mmol) was dissolved in 5 mL of pyridine and cooled to 0 °C, 12.0 mmol of either **20a** or **20b** was added, and the mixture was stirred at room temperature for 12 h. It was then poured into ice–water and extracted with $CHCl_3$, the $CHCl_3$ layer was dried and evaporated, and the residue was chromatographed ($CHCl_3$) to give **22b**: 79% yield; IR 1680 cm^{-1}; ^{1}H NMR δ 0.12 (s, 12 H), 0.90 (s, 18 H), 6.5 (t, 1 H, J = 6), 7.33 (s, 10 H), 8.43 (s, 1 H), 8.90 (s, 1 H); UV λ_{max} 251 nm (ε 17 000). Anal. Calcd for $C_{36}H_{49}N_5O_5S_2Si_2$: C, 57.5; H, 6.6; N, 9.3; S, 8.5. Found: C, 57.3; H, 6.7; N, 9.3; S, 8.6.

Compound **22a** was isolated in 80% yield: IR 1670 cm^{-1}; ^{1}H NMR δ 0.13 (s, 6 H), 0.17 (s, 6 H), 0.95 (s, 18 H), 2.3 (s, 6 H), 3.47 (t, 1 H, J = 6), 8.35 (s, 1 H), 8.80 (s, 1 H); UV λ_{max} 237 nm (ε 12 500), 273 (10 200). Anal. Calcd for $C_{25}H_{45}N_5O_5S_2Si_2$: C, 48.8; H, 7.4; N, 11.4. Found: C, 48.6; H, 7.1; N, 11.4.

3'5'-Bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxy-6-*N*-[(methylthio)carbonyl]adenosine (23a). The thiocarbamate **23a** was prepared by treating **22a** with sodium hydroxide according to the procedure for preparing **23b** and was isolated after chromatography ($CHCl_3$) in 70% yield: IR 1660 cm^{-1}; ^{1}H NMR δ 0.07 (s, 6 H), 0.12 (s, 6 H), 0.88 (s, 9 H), 0.93 (s, 9 H), 2.40 (s, 3 H), 6.40 (t, 1 H, J = 6), 8.25 (s, 1 H); UV λ_{max} 275 nm (ε 22 200). Anal. Calcd for $C_{24}H_{41}N_5O_4SSi_2$: C, 52.2; H, 7.5; N, 12.7. Found: C, 52.0; H, 7.5; N, 12.4. The thiocarbamate **23a** can also be prepared by refluxing **3b** with the tetrazole **24** (150 mol %) in THF for 15 h in 50% yield and by treating **3b** with the imidazolium salt **27b** (600 mol %) in CH_2Cl_2 for 12 h in 60% yield.

2'-Deoxy-6-*N*-[(methylthio)carbonyl]adenosine (23b). To 0.50 g (2.0 mmol) of 2'-deoxyadenosine in 40 mL of pyridine at 0 °C was added 2 mL of methyl chlorothioformate. The mixture was stirred overnight at room temperature then cooled to 0 °C, and water was added. The solution was evaporated, the residue was dissolved in $CHCl_3$ and washed with water, the $CHCl_3$ layer was dried and evaporated, and the residue was dissolved in 30 mL of ethanol and 20 mL of pyridine at 0 °C. After addition of 10 mL of 2 M NaOH and stirring for 45 min at 0 °C, the reaction was quenched with Dowex-AG 50 (pyridinium form). The resin was filtered and washed with ethanol, the combined filtrates were evaporated, and the residue was chromatographed (ethanol/

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$CHCl_3$, 10:90) to give **23b**: 50% yield; IR 1650 cm^{-1}; ^1H NMR δ ($CDCl_3/CD_3OD$) 2.17 (s, 3 H), 6.44 (t, 1 H, J = 6), 8.30 (s, 1 H), 8.65 (s, 1 H); UV λ_{max} 274 nm. Anal. Calcd for $C_{12}H_{15}N_5O_4S$: C, 44.3; H, 4.6; N, 21.5. Found: C, 43.8; H, 4.7; N, 21.7. **23b** can also be prepared from **23a** under standard[14] desilylation conditions in 90% yield.

3′,5′-Bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-6-*N*-(methoxycarbonyl)adenosine (29). The bis(thiocarbamate) **22b** (0.44 g, 0.58 mmol) was dissolved in 77 mL of $THF/CH_3OH/H_2O$ (5:4:1) at 0 °C, 3.7 mL of 2 M NaOH was added, the mixture was stirred for 10 min at 0 °C, and Dowex AG-50 ion-exchange resin (pyridinium form) was added. The resin was filtered and washed with ethanol, and the combined filtrates were evaporated. Chromatography (ether) gave a 70% yield of **29**: IR 1760 cm^{-1}; ^1H NMR δ 0.08 (s, 6 H), 0.12 (s, 6 H), 0.92 (s, 9 H), 0.95 (s, 9 H), 3.87 (s, 5 H), 6.45 (t, 1 H, J = 6), 8.23 (s, 1 H), 8.46 (s, 1 H); UV λ_{max} 266 nm (ϵ 17 900). Anal. Calcd for $C_{24}H_{54}N_5O_5Si_2$: C, 53.6; H, 8.1; N, 13.2. Found: C, 53.4; H, 8.1; N, 12.9.

N,N′-Bis[9-[3′,5′-bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-β-D-*erythro*-pentofuranosyl]purin-6-yl]urea (34). The bis(*tert*-butyldimethylsilyl)deoxyadenosine **3b** (0.51 g, 1.1 mmol) and the tetrazole **33** (0.60 g, 3.0 mmol) in 30 mL of THF were heated at 55 °C for 24 h. The solvent was evaporated, the residue was dissolved in $CHCl_3$ and washed with water, and the $CHCl_3$ solution was dried and evaporated. Chromatography of the residue (ether) gave **34**: 0.37 g (72%); IR 1720 cm^{-1}; ^1H NMR δ 0.13 (s, 12 H), 0.17 (s, 12 H), 0.98 (s, 36 H), 6.45 (t, 2 H, J = 6), 8.35 (s, 2 H), 8.67 (s, 2 H); UV λ_{max} 264 nm (ϵ 22 700), 282 (38 200), 290 (38 400); FDMS, m/e 985 (M^+), 506, 479, 449, 422. Anal. Calcd for $C_{45}H_{80}N_{10}O_7Si_4$: C, 54.8; H, 8.2; N, 14.2. Found: C, 54.8; H, 8.0; N, 14.1.

3′,5′-Bis-*O*-(*tert*-butyldimethylsilyl)-4-*O*-[(phenylthio)carbonyl]thymidine (37). To the bis(*tert*-butyldimethylsilyl)thymidine **1b** (1.10 g, 2.30 mmol) in 20 mL of pyridine at 0 °C was added phenyl chlorothioformate (4.0 g, 23 mmol). The mixture was allowed to come to room temperature, heated for 3 h at 50 °C, and poured into ice–water. The suspension was extracted with $CHCl_3$, the $CHCl_3$ was dried and evaporated, and the residue was chromatographed ($CHCl_3$) to give **37**: 0.89 g (64%); IR 1710, 1760, 1810 cm^{-1}; ^1H NMR δ 0.08 (s, 6 H), 0.10 (s, 6 H), 1.02 (s, 9 H), 1.05 (s, 9 H), 1.87 (s, 3 H), 6.13 (t, 1 H, J = 7), 7.30 (s, 6 H); UV λ_{max} 267 nm (ϵ 9900), 271 (9800). Anal. Calcd for $C_{29}H_{46}N_2O_6SSi_2$: C, 57.7; H, 7.6; N, 4.6. Found: C, 57.6; H, 7.7; N, 4.6.

9-[3′,5′-Bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-β-D-*erythro*-pentofuranosyl]-6-(phenylthio)-2-[bis[(phenylthio)carbonyl]amino]purine (38a). To the bis(*tert*-butyldimethylsilyl)deoxyguanosine **4b** (5.00 g, 10.1 mmol) in 20 mL of pyridine at 0 °C was added phenyl chlorothioformate (34.5 g, 200 mmol) in 20 mL of pyridine at 0 °C. The reaction mixture was stirred for 5 h at room temperature in the dark and then poured into ice–water. The water was extracted with $CHCl_3$, the $CHCl_3$ layer dried and evaporated, and the residue chromatographed ($CHCl_3$) to give **38a**[1] (7.38 g, 85%).

2-Amino-9-[3′,5′-bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-β-D-*erythro*-pentofuranosyl]-6-(phenylthio)purine (39a). To the thiocarbamate **38a** (9.36 g, 10.4 mmol), 300 mL of THF, and 100 mL of water at 0 °C was added 85 mL of 2 M NaOH, the heterogeneous mixture was stirred for 6 h at room temperature, and then acetic acid (20 g, 330 mmol) was added. The solvent was evaporated, the residue was dissolved in $CHCl_3$/water, and the $CHCl_3$ layer was dried and evaporated. Chromatography of the residue ($CHCl_3$) gave **39a**: 5.46 g (85%); ^1H NMR δ 0.08 (s, 6 H), 0.10 (s, 6 H), 0.9 (s, 18 H), 6.12 (t, 1 H, J = 6), 7.2–7.5 (m, 5 H), 7.71 (s, 1 H); UV λ_{max} 244 nm (ϵ 13 100), 252 (12 200), 315 (14 500). Anal. Calcd for $C_{28}H_{45}N_5O_3SSi_2$: C, 57.2; H, 7.7; N, 11.9. Found: C, 57.0; H, 7.7; N, 11.8.

2-Amino-9-[3′,5′-bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-β-D-*erythro*-pentofuranosyl]purine (40a). To the (phenylthio)guanosine **39a** (350 mg, 0.60 mmol) in 70 mL of methanol was added Raney nickel[26] (W-7, 2 g wet weight), and the mixture was refluxed for 6 h. The nickel was filtered out, the filtrate evaporated, and the residue recrystallized from ether/isooctane to give **40a**: 80% yield; ^1H NMR δ 0.08 (s, 6 H), 0.12 (s, 6 H), 0.93 (s, 18 H), 6.40 (t, 1 H, J = 7), 8.20 (s, 1 H), 8.88 (s, 1 H); UV λ_{max} 246 nm (ϵ 6300), 310 (7400). Anal. Calcd for $C_{22}H_{41}N_5O_3Si_2$: C, 55.1; H, 8.6; N, 14.6. Found: C, 54.9; H, 8.5; N, 14.7.

2,6-Diamino-9-[3′,5′-bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-β-D-*erythro*-pentofuranosyl]purine (40b). A bomb tube was charged with 40 mL of anhydrous methanol and saturated with anhydrous ammonia at 0 °C. The sulfide **39a** (380 mg) was added, the tube was sealed and heated at 150 °C for 24 h and then cooled to 0 °C, the solvent was evaporated, and the residue was chromatographed (ethanol/$CHCl_3$, 3:97) to give **40b**: 56% yield; ^1H NMR δ 0.08 (s, 6 H), 0.10 (s, 6 H), 0.90 (s, 18 H), 6.33 (t, 1 H, J = 7), 7.86 (s, 1 H); UV λ_{max} 258 nm (ϵ 9800), 281 (11 800). Anal. Calcd for $C_{22}H_{42}N_6O_3Si_2$: C, 53.4; H, 8.6; N, 17.0. Found: C, 53.3; H, 8.6; N, 16.9.

2-Amino-9-(2′-deoxy-β-D-*erythro*-pentofuranosyl)-6-(phenylthio)purine (39b). The sulfide **39b** was prepared in 90% yield by desilylating **39a** with tetrabutylammonium fluoride in THF[15] and chromatographing (ethanol/$CHCl_3$, 10:90): ^1H NMR δ 6.23 (t, 1 H, J = 7), 8.05 (s, 1 H); UV λ_{max} 245 nm (ϵ 12 900), 252 (11 900), 315 (13 600). Anal. Calcd for $C_{16}H_{17}N_5O_3S \cdot 0.75H_2O$: C, 51.5; H, 4.6; N, 18.8. Found: C, 51.9; H, 4.8; N, 18.6.

2′-Deoxy-6-*O*-methylguanosine (40d). The sulfide **39b** (130 mg, 0.36 mmol) was treated as described[27] by refluxing with sodium methoxide (120 mg, 2.22 mmol) in 25 mL of methanol for 18 h to give **40d**: 60% yield; glass, transition point 128–130 °C (lit.[27] mp 129–131 °C); ^1H NMR δ 4.05 (s, 3 H), 6.31 (t, 1 H, J = 6), 8.03 (s, 1 H).

2-[(Benzyloxycarbonyl)amino]-9-[3′,5′-bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-β-D-*erythro*-pentofuranosyl]-6-phenylthiopurine (41a). To thiocarbamate **38a** (3.06 g, 3.56 mmol) in 20 mL of THF was added a mixture of 40 mmol of tetraethylammonium hydroxide (22.24 g, of a 25% aqueous solution), benzyl alcohol (100 mL), and THF (300 mL) at 0 °C. The heterogeneous mixture was stirred for 24 h at 0 °C and then quenched with acetic acid (2.70 g, 45 mmol). Most of the solvent was evaporated (35 °C), and the residue was dissolved in $CHCl_3$ and washed with water. Evaporation of the solvent (50 °C, 20 μmHg) and chromatography of the residue ($CHCl_3$) gave **41a**: 75% yield; IR 1730 cm^{-1}; ^1H NMR δ 0.12 (s, 12 H), 0.93 (s, 18 H), 5.12 (s, 2 H), 6.33 (t, 1 H, J = 6), 8.08 (s, 1 H); FDMS, m/e 721 (M^+), 664 ($M^+ - 57$), 612 ($M^+ - SC_6H_5$), 586 ($M^+ - CO_2CH_2C_6H_5$); UV λ_{max} 243 nm (ϵ 20 000), 303 (17 100). Anal. Calcd for $C_{36}H_{51}N_5O_4SSi_2$: C, 59.9; H, 7.1; N, 9.7. Found: C, 59.7; H, 7.3; N, 9.4.

2-[(Methoxycarbonyl)amino]-9-[3′,5′-bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-β-D-*erythro*-pentofuranosyl]-6-(phenylthio)purine (41b). To thiocarbamate **38a** (0.62 g, 0.72 mmol) dissolved in 20 mL of THF, 16 mL methanol, and 4 mL of water at 0 °C was added 4 mL of 2.0 M NaOH. The solution is stirred for 40 min at 0 °C and quenched with Dowex AG-50 ion-exchange resin (pyridinium form). The resin was filtered off and washed with ethanol, the combined filtrate and washings were evaporated, and the residue was chromatographed ($CHCl_3$) to give **41b**: 80% yield; IR 1760 cm^{-1}; ^1H NMR δ 0.08 (s, 6 H), 0.10 (s, 6 H), 0.95 (s, 18 H), 3.7 (s, 3 H), 6.33 (t, 1 H, J = 6), 7.4 (m, 5 H), 8.06 (s, 1 H); UV λ_{max} 217 nm, 242, 302. Anal. Calcd for $C_{30}H_{47}N_5O_5SSi_2$: C, 55.8; H, 7.3; N, 10.8. Found: C, 55.5; H, 7.3; N, 10.5.

2-*N*-(Benzyloxycarbonyl)-3′,5′-bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyguanosine (43c). To thioguanosine **41a** (280 mg, 0.39 mmol) in 20 mL of CH_2Cl_2 at 0 °C was added MCPBA (85%; 0.32 g, 1.56 mmol) in 10 mL of CH_2Cl_2, and the solution was stirred overnight at 0 °C. The reaction mixture was poured into 20 mL of 5% sodium thiosulfate, and the organic layer was washed with 5% $NaHCO_3$ and water and dried. Evaporation of the CH_2Cl_2 and chromatography of the residue ($CHCl_3$/ethanol, 97:3) gave **43c**: 60% yield; IR 1700, 1770 cm^{-1}; ^1H NMR δ 0.17 (s, 6 H), 0.20 (s, 6 H), 1.00 (s, 9 H), 1.02 (s, 9 H), 5.35 (s, 2 H), 6.35 (t, 1 H, J = 6), 8.05 (s, 1 H); UV λ_{max} 258 nm (ϵ 15 500), 275 (sh, 11 200). Anal. Calcd for $C_{30}H_{47}N_5O_6Si_2$: C, 57.2; H, 7.5; N, 11.1. Found: C, 57.2; H, 7.6; N, 11.0.

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2-[(Benzyloxycarbonyl)amino]-9-[3′,5′-bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-β-D-*erythro*-pentofuranosyl]-purine (43a). Raney nickel[26] (W7, 1.5 g wet weight) was refluxed in 20 mL of acetone for 1 h, **41a** (160 mg, 0.22 mmol) was added, and the mixture was refluxed for 2 days. Cooling, filtering, and evaporating the filtrate left a residue which was chromatographed (ethanol/$CHCl_3$, 5:95) to give 80 mg of **43a**: 60% yield; IR 1740 cm^{-1}; ^1H NMR δ 0.09 (s, 6 H), 0.12 (s, 6 H), 0.92 (s, 18 H), 5.30 (s, 2 H), 6.49 (t, 1 H, J = 6), 7.4 (s, 5 H), 8.32 (s, 1 H), 9.00 (s, 1 H); UV λ_{max} 224 nm (ε 32 800), 247 (8300), 286 (9200). Anal. Calcd for $C_{30}H_{47}N_5O_5Si_2$: C, 58.7; H, 7.7; N, 11.4. Found: C, 58.6; H, 7.6; N, 11.1.

Reaction of 38a with Sodium Benzyl Oxide. Thiocarbamate **38a** (1.10 g, 1.20 mmol), dissolved in 40 mL of THF containing 14 mmol of sodium benzyl oxide, was stirred at 0 °C for 18 h and then quenched with Dowex AG-50 ion-exchange resin (pyridinium form). The resin was filtered off and washed with ethanol, and the combined filtrates were evaporated. Chromatography of the residue ($CHCl_3$ and then ethanol/$CHCl_3$, 5:95) gave **42a**: 41% yield; IR 1760 cm^{-1}; ^1H NMR δ 0.08 (s, 6 H), 0.10 (s, 6 H), 0.90 (s, 9 H), 0.91 (s, 9 H), 5.26 (s, 2 H), 5.60 (s, 2 H), 6.39 (t, 1 H, J = 6.5), 7.4 (m, 10 H), 8.09 (s, 1 H); UV λ_{max} 257 nm (ε 15 500), 267 (15 600). Anal. Calcd for $C_{37}H_{53}N_5O_6Si_2$: C, 61.7; H, 7.4; N, 9.7. Found: C, 61.8; H, 7.3; N, 9.6.

The partially desilylated products **42b** and **42c** were also obtained. **42b**: 30% yield; IR 1750 cm^{-1}; ^1H NMR δ 0.12 (s, 6 H), 0.95 (s, 9 H), 5.20 (s, 2 H), 5.53 (s, 2 H), 6.20 (t, 1 H, J = 6.5), 7.30 (s, 10 H), 7.87 (s, 1 H); UV λ_{max} 257 nm (ε 13 100), 267 (13 500). Anal. Calcd for $C_{31}H_{39}N_5O_6Si$: C, 61.5; H, 6.5; N, 11.6. Found: C, 61.2; H, 6.5; N, 11.5. **42c** was not obtained free from **42b** (10% yield).

3′,5′-Bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-6-*O*-methyl-2-*N*-(methoxycarbonyl)guanosine (42e). Thiocarbamate **38a** (3.55 g, 4.1 mmol), sodium methoxide (2.0 g, 37 mmol) in CH_3OH (10 mL), and THF (100 mL) were mixed at 0 °C. The mixture was allowed to come to room temperature, stirred for 2 days, and cooled to 0 °C, and acetic acid (2.2 g, 37 mmol) was added. The solvent was evaporated, the residue was taken up in $CHCl_3/H_2O$, the $CHCl_3$ was separated, dried, and evaporated, and the residue was chromatographed ($CHCl_3$) to give **42e**: 1.60 g (68%); IR 1750 cm^{-1}; ^1H NMR δ 0.07 (s, 6 H), 0.11 (s, 6 H), 0.91 (s, 18 H), 3.81 (s, 3 H), 4.14 (s, 3 H), 6.41 (t, 1 H, J = 6), 8.13 (s, 1 H); UV λ_{max} 255 nm (ε 13 400), 266 (14 100). Anal. Calcd for $C_{25}H_{45}N_5O_6Si_2$: C, 52.9; H, 8.0; N, 12.3. Found: C, 53.0; H, 7.9; N, 12.0.

9-[3′,5′-Bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-β-D-*erythro*-pentofuranosyl]-6-(phenylthio)-2-ureidopurine (41d). Thiocarbamate **38a** (520 mg, 0.60 mmol) was treated with 30 mL of ethanolic ammonia (saturated at 0 °C) at room temperature overnight. Evaporation of the solvent and chromatography (ethanol/$CHCl_3$, 2:98) gave **41d**: 290 mg (77%); IR 1690 cm^{-1}; ^1H NMR δ 0.11 (s, 12 H), 0.92 (s, 18 H), 6.34 (t, 1 H, J = 6, 7.4 (m, 5 H), 8.26 (s, 1 H); UV λ_{max} 230 nm (ε 16 400), 293 (18 200). Anal. Calcd for $C_{29}H_{46}N_6O_4SSi_2$: C, 55.2; H, 7.4; N, 13.3. Found: C, 55.1; H, 7.4; N, 13.3.

6-Methoxy-9-[3′,5′-bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-β-D-*erythro*-pentofuranosyl]-2-ureidopurine (41e). A solution of 20 mL of concentrated aqueous ammonia and **42e** (0.56 g, 0.98 mmol), dissolved in 20 mL of isopropyl alcohol, was heated in a sealed tube at 50 °C for 24 h. The solvent was evaporated and the residue chromatographed (ethanol/$CHCl_3$, 2:98) to give **41e**: 70% yield; IR 1690 cm^{-1}; ^1H NMR δ 0.11 (s, 12 H), 0.89 (s, 18 H), 2.38 (t, 2 H, J = 6), 4.02 (s, 3 H), 6.28 (t, 1 H, J = 6), 8.08 (s, 1 H); UV λ_{max} 254 nm (ε 14 300), 276 (14 200). Anal. Calcd for $C_{24}H_{44}N_6O_5Si_2$: C, 52.1; H, 8.0; N, 15.2. Found: C, 51.9; H, 8.1; N, 14.9.

2-[(Methoxycarbonyl)amino]-6-(methylthio)-9-[3′,5′-bis-*O*-(*tert*-butyldimethylsilyl)-2′-deoxy-β-D-*erythro*-pentofuranosyl]purine (41c). Crude thioether thiocarbamate **38b** was prepared from **4b** and methyl chlorothioformate according to the procedure for the phenyl derivative **38a**. To this crude material (**38b**, 0.60 g) dissolved in 100 mL of THF/CH_3OH/H_2O (5:4:1) at 0 °C was added 5 mL of 2 M NaOH. After 3 h at 0 °C, Dowex AG-50 ion-exchange resin (pyridinium form) was added. The resin was filtered off and washed with ethanol, the combined filtrates were evaporated, and the residue was chromatographed ($CHCl_3$/isooctane, 70:30) to give **41c** in 10% yield from **4b**: IR 1750 cm^{-1}; ^1H NMR δ 0.1 (s, 12 H), 0.9 (s, 18 H), 2.6 (s, 3 H), 3.8 (s, 3 H), 6.4 (t, 1 H, J = 6), 8.0 (s, 1 H), UV λ_{max} 244 nm (ε 24 200), 294 (15 600), 302 (15 100). Anal. Calcd for $C_{25}H_{45}N_5O_5SSi_2$: C, 51.4; H, 7.8; N, 12.0. Found: C, 51.2; H, 7.7; N, 11.9.

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