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SYNTHESIS OF BENZYL AND BENZYLOXYCARBONYL BASE-BLOCKED 2'-DEOXYRIBONUCLEOSIDES

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Abstract

Acylimidazolium salts, particularly benzyloxycarbonylimidazolium salts, are shown to be effective agents for the direct N-protection of nucleoside bases as their acyl derivatives. These acyl nucleosides are also available in two steps via thiocarbamate intermediates. In addition, chlorothioformates are shown to be effective for converting the 6-oxygen of 2'-deoxyguanosine to a thioether, which then can be transformed to a number of 6-substituted 2'-deoxyguanosines.

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Introduction

In our synthetic efforts directed towards oligonucleotides¹, 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 derivatives², although there are a few examples of carbamates³⁻⁶ and one example of the N,N-dimethylaminomethylene 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 shown¹ 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^{9,10,11} 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. Recently¹² substituted phenyl groups have been introduced to block these positions, and in our previous work¹ we used a benzyl group to block the 6-O of guanosine. 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 is described here.

Results and Discussion

Acylation with Benzyl Chloroformate. The Cbz group is most commonly introduced using benzyl chloroformate (5) under aqueous alkaline conditions. This procedure is not applicable to acylation of nucleosides because of their tendency to undergo ring opening reactions¹³ 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 $-20^\circ C$ benzyl chloroformate will react with nucleosides 1a, 3a, and 4a to give moderate yields of ribose-O-acylated nucleosides. With the ribose-blocked nucleosides 3b or 4b under these conditions no reaction occurs. 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 towards nucleophilic attack by chloride ion (Scheme I). In the case of cytidine, the most easily acylated nucleoside, acylation is competitive with this destruction of the benzyl chloroformate, whereas in the case of the less nucleophilic adenosine and guanosines, 3b and 4b, benzyl chloride formation occurs to the exclusion of acylation. To test this hypothesis, benzyl chloroformate was allowed to

react with 2a in the presence of the highly hindered amine 1,2,2,6,6-penta-methylpiperidine which should be sterically incapable of forming an acylammonium complex. Indeed, benzyl chloroformate was found to be stable under these conditions, however acylation 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 imidazolidine 10 is readily obtained as a low melting crystalline solid from benzyl chloroformate and imidazole, however this imidazolidine is a poor acylating agent. Alkylation of 10 with either trimethyl or triethyloxonium tetrafluoroborate gave the stable acylimidazolium salts 11a and 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 b in CH_2Cl_2 to produce the Cbz-adenosine 16b in 95% yield. 2'-Deoxyadenosine (2a) itself reacts with 11a or b to give the tris-acyladenosine 16a. Both 16a and 16b may be converted to the hydroxy-free acyladenosine 16c under standard conditions,^{14,15} however the conversion of 16a to 16c proceeds in only 50% yield due to the large amount of 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, non-basic 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 ribose-blocked adenosine to give only the mono acylated nucleosides 16 and 19, respectively, with no detectable bis-acylation.

2'-Deoxycytidine also reacts with 11a or b 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 deoxyribose-blocked guanosine 4b fails to react with either 11a or b at room temperature. In refluxing CH₂Cl₂, a benzyloxycarbonylguanine of unknown structure was isolated from which the deoxy sugar had been lost.

Acyltriazolium salts have also been used as acylating agents.¹⁸ Benzyloxycarbonyltriazole (14), easily prepared from benzyl chloroformate and triazole, was alkylated to give a mixture of the two possible regioisomers 15. These reacted with the adenosine 3b and the guanosine 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 ribose blocked guanosine 4b nor any of the 2-aminopurines subsequently described reacted with any of the acylimidazolium or triazolium salts or acyltetrazoles to give acyl nucleosides; only educt or polar, alkylated products were observed. The 2,6-diaminopurine 40b reacts with the benzyloxycarbonylimidazolium 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 a 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 susceptible to nucleophilic displacement as in the benzyloxy series.

This approach was first investigated with adenosine derivatives (Scheme III). The bis-silyl ether of adenosine (3b) was treated with methyl chlorothioformate or phenyl chlorothioformate and gave the bis-acyladenosines (22a, b) in high yield. The bis-methylthiocarbamate 22a can be selectively hydrolyzed under alkaline conditions to the mono-thiocarbamate 23a which can be desilylated under standard conditions¹⁴ to yield the mono-thiocarbamate 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 acyltetrazoles⁵ have been used to selectively acylate adenosine derivatives, 5-methylthiocarbonyltetrazole (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 adenosine 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 have 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 11b is treated with methanolic aqueous sodium hydroxide 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 which is trapped

by the most reactive nucleophile present to give the observed product. 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. 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 then 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 , mono-thiocarbamates 23a and b are converted to the benzyl carbamates 16b and 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 adenosine 3a and b. This process is not nearly as efficient as the acylimidazolium salt method for the preparation of acyl adenosines, however it was still considered a viable route to acyl guanosines, as discussed below.

The Reaction of Phenyl Chlorothioformate with Guanosine. Chlorothioformates did not react with guanosine derivatives in a fashion analogous to adenosine. The guanosine silyl ether 4b, when allowed to react with phenyl chlorothioformate, gave the 6-phenylthioguanosine 38a. 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 concentration as well as reaction time since 38a is not stable to the reaction conditions. 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 guanosine 4b also reacts with methyl chlorothioformate to give the 6-methylthioguanosine 38b, but seems to be limited to purines as the thymidine 1b gives the 6-O-qcylthymine 37 with phenyl chlorothioformate.

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-chloro¹⁹ or 6-thioguanosine²⁰ can be elaborated to a large variety of derivatives. This is not the case in the 2'-deoxyribose series 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-mesylate¹² and the nitrotriazolide,⁹ however their synthetic scope has not been investigated.

The bis-thiocarbamate 38a can be hydrolyzed to the 6-phenylthioguanosine 39a. When treated with Raney Nickel, 39a is cleanly desulfurized to give the isoadenosine 40a. Similarly, the diaminopurine 40b can be obtained in 80% yield from 38a and ethanolic ammonia at 150°. 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 6-O-methyl-2'-deoxyguanosine 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 aqueous sodium methoxide to give the benzyl or methyl carbamates 41a and 41b. Likewise the methylthioguanosine 38b can be treated with aqueous sodium methoxide to give the methyl carbamate 41c. With 38a and either anhydrous sodium methoxide or sodium benzyloxide, 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 41d 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 oligonucleotided 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 and 41b failed. When treated with deactivated Raney Nickel 41a gives the isoadenosine 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 e 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 45b 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.

Conclusion

Acylimidazolium salts have been found to be effective acylating agents for adenosines but not for guanosines. For guanosines, reaction with chlorothioformates provided versatile intermediates for blocked derivatives. Thus

the guanosine thioether-thiocarbamate 38a, which is readily prepared from 2'-deoxyguanosine and phenyl chlorothioformate, is a useful intermediate for the preparation of a number of C-6 and 2-N substituted 2'-deoxyguanosines.

Experimental Section

Melting points were obtained with a Buchi (capillary) apparatus and are uncorrected. IR spectra were determined as KBr pellets with a Perkin-Elmer 137 spectrophotometer using 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 ppm (δ) downfield from Me_4Si . The ^1H NMR spectra reported do not contain the resonances for the 3', 4', and 5' 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 with an Altex stainless steel column ($3.2 \times 250\text{ mm}$, 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 nm. The solvent systems were acetonitrile with varying amounts of water. Column chromatography (CC) 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) and 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 ($20\text{-}26^\circ$). Organic layers were dried over MgSO_4 and evaporated with a Berkeley rotary evaporator using 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 4Å 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 conc. aq. HF and rendered anhydrous by repeated addition and evaporation of pyridine.

The silyl ethers 3b and 4b,¹⁴ benzoylimidazole,²¹ isopropyl chlorothioformate, phenyl chlorothioformate²² and tetrazole²³ 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 stirring overnight, the suspensions were filtered and evaporated and the residue 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 (110 mol%) in THF and isolated as above. The tetrazole 33 was sublimed (90°C, 20 μM Hg).

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 triethyloxonium²⁴ or trimethyloxonium²⁵ tetrafluoroborate (95 mol%). The mixture was stirred at room temperature from 2 to 12 h to give solutions of the

acylimidazolium salts which were characterized by ^1H NMR.

11a: (CD_3CN) δ 3.91 (s, 3H), 5.50 (s, 2H), 7.45 (s, 6H), 7.75 (s, 1H), 9.05 (s, 1H)

11b: (CDCl_3) 1.47 (t, 3H, $J=7$), 4.20 (q, 2H, $J=7$), 5.42 (s, 2H), 7.3 (m, 6H), 7.65 (s, 1H), 8.98 (s, 1H).

15: (CD_3CN) δ 3.93 (s, 1/3 H), 4.06 (s, 2/3 H), 5.53 (s, 2H), 7.4 (s, 5H), 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, 3H), 3.93 (s, 3H), 7.45 (s, 1H), 7.78 (s, 1H), 9.10 (s, 1H).

28: (CD_3CN) δ 2.63 (s, 3H), 4.00 (s, 3H), 8.63 (s, 1H), 9.86 (s, 1H).

32: (CD_3CN) δ 3.96 (s, 3H), 7.5 (s, 6H), 7.81 (s, 1H), 9.14 (s, 1H).

36: 1.4-1.6 (m, 9H), 3.82 (m, 1H, $J=7$), 4.33 (q, 2H, $J=7$), 7.64 (s, 1H), 7.74 (s, 1H), 9.28 (s, 1H).

The ribose-blocked nucleosides 3b or 4b were then added and the mixtures stirred at room temperature. Addition of 10% aq. NaHCO_3 and CHCl_3 and separation of the organic layer which was washed, dried, and evaporated, gave the acyladenosines 16b, 16c, 19, ¹⁴23a, and 39c.

6-N-Benzoyloxycarbonyl-bis-3',5'-O-(tert-butyldimethylsilyl)-2'-deoxyadenosine

(16b): 95% yield from 3b and 11b; IR 1740 cm^{-1} ; ^1H NMR 0.07 (s, 6H), 0.13 (s, 6H), 0.88 (s, 9H), 0.93 (s, 9H), 5.15 (s, 2H), 6.25 (t, 1H, $J=6$), 7.2 (s, 5H), 8.03 (s, 1H), 8.53 (s, 1H). UV λ_{max} (nm (ϵ)) 267 (20,200). Anal. Calcd for $\text{C}_{30}\text{H}_{47}\text{N}_5\text{O}_5\text{Si}_2$: 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 mmole) to a pyridine (20 mL) solution of the thiocarbamate 23a (200 mg, 0.36 mmole) 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.

6-N-Benzoyloxycarbonyl-2,6-diamino-9-(bis-3',5'-O-tert-butyldimethylsilyl)-2'-deoxy- β -D-erythropentofuranosyl)purine (40c). The diaminopurine 40b was

acylated with 11b to give 39c in 95% yield after chromatography (ethanol/CHCl₃, 3/97): IR 1760 cm⁻¹; ¹H NMR δ 0.03 (s, 12H), 0.84 (s, 18H), 5.16 (s, 2H), 6.22 (t, 1H, J=6.5), 7.3 (s, 5H), 7.83 (s, 1H); UV λ_{max} (nm (ε)) 248 (10,200), 301 (11,200). Anal. Calcd for C₃₀H₄₈N₆O₅Si₂: C, 57.3; H, 7.7; N, 13.4. Found: C, 57.3; H, 7.6; N, 13.1

6-N-Benzoyloxycarbonyl-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. Sat. aq. NaHCO₃ was added, the solvent was evaporated, and the residue was dissolved in CHCl₃ and washed with water, dried, and evaporated. The residue, which contained 16a was dissolved at room temperature in 260 mL of THF/CH₃OH/H₂O (5/4/1) and 4.8 mL of 2 N NaOH and the solution stirred for 5 min 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/CHCl₃, 7:93) to give 16c¹ 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. The ribose-blocked adenosine 3b (0.79 g, 1.6 mmol) was dissolved in 5 mL of pyridine, cooled to 0°C, 12.0 mmol of either 20a or b was added, and the mixture stirred at room temperature for 12 h. It was then poured into ice water and extracted with CHCl₃, the CHCl₃ layer was dried and evaporated, and the residue was chromatographed (CHCl₃) to give 22b in 79% yield: IR 1680 cm⁻¹; ¹H NMR δ 0.12 (s, 12H), 0.90 (s, 18H), 6.5 (t, 1H, J=6), 7.33 (s, 10H), 8.43 (s, 1H), 8.90 (s, 1H); UV λ_{max} (nm (ε)) 251 (17,000). Anal. Calcd for C₃₆H₄₉N₅O₅S₂Si₂: 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.

22a was isolated in 80% yield: IR 1670 cm⁻¹; ¹H NMR δ 0.13 (s, 6H), 0.17

(s, 6H), 0.95 (s, 18H), 2.3 (s, 6H), 3.47 (t, 1H, J=6), 8.35 (s, 1H), 8.80 (s, 1H); UV λ_{max} (nm (ϵ)) 237 (12,500), 273 (10,200). Anal. Calcd for $\text{C}_{25}\text{H}_{45}\text{N}_5\text{O}_5\text{S}_2\text{Si}_2$: C, 48.8; H, 7.4; N, 11.4. Found: C, 48.6; H, 7.1; N, 11.4.

6-N-Methylthiocarbonyl-bis-3',5'-O-(tert-butyl dimethylsilyl)-2'-deoxy-
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} ; $^1\text{H-NMR}$ δ 0.07 (s, 6H), 0.12 (s, 6H), 0.88 (s, 9H), 0.93 (s, 9H), 2.40 (s, 3H), 6.40 (t, 1H, J=6), 8.25 (s, 1H); UV λ_{max} (nm (ϵ)) 275(22,200). Anal. Calcd for $\text{C}_{24}\text{H}_{41}\text{N}_5\text{O}_4\text{SSi}_2$: 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.

6-N-Methylthiocarbonyl-2'-deoxyadenosine (23b). To 0.50 g 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 2M 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/ CHCl_3 , 10/90) to give 23b in 50% yield: IR 1650 cm^{-1} ; $^1\text{H-NMR}$ δ ($\text{CDCl}_3/\text{CD}_3\text{OD}$) 2.17 (s, 3H), 6.44 (t, 1H, J=6), 8.30 (s, 1H), 8.65 (s, 1H); UV λ_{max} (nm) 274. Anal. Calcd for $\text{C}_{12}\text{H}_{15}\text{N}_5\text{O}_4\text{S}$: 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 standard¹⁵ desilylation conditions in 90% yield.

6-N-Methoxycarbonyl-bis-3',5'-O-(tert-butyldimethylsilyl)-2'-deoxyadenosine

(29). The bis-thiocarbamate 22b (0.44 g, 0.58 mmol) was dissolved in 77 mL of THF/CH₃OH/H₂O (5/4/1) at 0°C, 3.7 mL of 2M 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, 6H), 0.12 (s, 6H), 0.92 (s, 9H), 0.95 (s, 9H), 3.87 (s, 5H), 6.45 (t, 1H, J=6), 8.23 (s, 1H), 8.46 (s, 1H); UV λ_{max} (nm (ε)) 266 (17,900). Anal. Calcd for C₂₄H₅₄N₅O₅Si₂: C, 53.6; H, 8.1; N, 13.2. Found: C, 53.4; H, 8.1; N, 12.9.

Carbonyl-bis-6-N-(bis-3',5'-O-(tert-butyldimethylsilyl)-2'-deoxyadenosine)

(34). The adenosine 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 CHCl₃ and washed with water, and the CHCl₃ 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, 12H), 0.17 (s, 12H), 0.98 (s, 36H), 6.45 (t, 2H, J=6), 8.35 (s, 2H), 8.67 (s, 2H); UV λ_{max} (nm (ε)) 264 (22,700), 282 (38,200), 290 (38,400); FDMS (m/e 985 (M⁺), 506, 479, 449, 422. Anal. Calcd for C₄₅H₈₀N₁₀O₇Si₄: C, 54.8; H, 8.2; N, 14.2. Found: C, 54.8; H, 8.0; N, 14.1.

4-O-(Phenylthiocarbonyl)-bis-3',5'-O-(tert-butyldimethylsilyl)-thymidine (37).

To the thymidine 1b (1.10 g, 2.30 mmol) in 20 mL of pyridine at 0°C is added phenyl chlorothioformate (4.0 g, 23 mmol). The mixture was allowed to come to room temperature, then heated for 3 h at 50°C and poured into ice water. The suspension was extracted with CHCl₃, the CHCl₃ was dried and evaporated and the residue was chromatographed (CHCl₃) to give 37 (0.89 g, 64%): IR 1710, 1760, 1810 cm⁻¹; ¹H-NMR δ 0.08 (s, 6H), 0.10 (s, 6H), 1.02 (s, 9H), 1.05 (s, 9H), 1.87 (s, 3H), 6.13 (t, 1H, J=7), 7.30 (s, 6H); UV λ_{max} (nm (ε)) 267 (9,900), 271 (9,800).

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.

6-Deoxy-6-phenylthio-bis-2-N,N-(phenylthiocarbonyl)-bis-3',5'-O-(tert-butyl-dimethylsilyl)-2'-deoxyguanosine (38a). To the ribose-blocked guanosine 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 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 38a¹ (7.38 g, 85%).

6-Deoxy-6-phenylthio-bis-3',5'-O-tert-butyl dimethylsilyl)-2'-deoxyguanosine (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 2M NaOH, and the heterogeneous mixture was stirred for 6 h at room temperature then acetic acid (20 g, 330 mmol) was added. The solvent was evaporated, the residue dissolved in $CHCl_3$ /water, and the $CHCl_3$ layer dried and evaporated. Chromatography of the residue ($CHCl_3$) gave 39a (5.46 g, 85%): ¹H-NMR δ 0.08 (s, 6H), 0.10 (s, 6H), 0.9 (s, 18H), 6.12 (t, 1H, J=6), 7.2-7.5 (m, 5H), 7.71 (s, 1H); UV λ_{max} (nm (ϵ)) 244 (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.

Bis-3',5'-O-(tert-Butyldimethylsilyl)-2'-deoxyisoadenosine (40a). To the guanosine 39a (350 mg, 0.60 mmol) in 70 mL of methanol was added Raney nickel²⁶ (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 in 80% yield: ¹H-NMR δ 0.08 (s, 6H), 0.12 (s, 6H), 0.93 (s, 18H), 6.40 (t, 1H, J=7), 8.20 (s, 1H), 8.88 (s, 1H); UV λ_{max} (nm (ϵ)) 246 (6,300), 310 (7,400). 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-(bis-3',5'-O-(tert-butylidimethylsilyl)-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 then cooled to 0°C, the solvent was evaporated, and the residue was chromatographed (ethanol/CHCl₃, 3/97) to give 40b in 56% yield: ¹H NMR δ 0.08 (s, 6H), 0.10 (s, 6H), 0.90 (s, 18H), 6.33 (t, 1H, J=7), 7.86 (s, 1H); UV λ_{max} 258 (9,800), 281 (11,800). Anal. Calcd for C₂₂H₄₂N₆O₃Si₂: C, 53.4; H, 8.6; N, 17.0. Found: C, 53.3; H, 8.6; N, 16.9.

6-Deoxy-6-phenylthio-2'-deoxyguanosine (39b). The sulfide 39b was prepared in 90% yield by desilylating 39a with tetrabutylammonium fluoride in THF¹⁵ and chromatographing (ethanol/CHCl₃, 10/90): ¹H-NMR δ 6.23 (t, 1H, J=7), 8.05 (s, 1H); UVλ_{max} (nm (ε)) 245 (12,900), 252 (11,900), 315 (13,600). Anal. Calcd for C₁₆H₁₇N₅O₃S 0.75 H₂O: C, 51.5; H, 4.6; N, 18.8. Found: C, 51.9; H, 4.8; N, 18.6.

6-O-Methyl-2'-deoxyguanosine (40d). The sulfide 39b (130 mg, 0.36 mmol) was treated as described²⁷ by refluxing with sodium methoxide (120 mg, 2.22 mmol) in 25 mL of methanol for 18 h to give 40d in 60% yield: glass, transition point 128-130°C (lit.²⁷ mp 129-131°C); ¹H-NMR δ 4.05 (s, 3H), 6.31 (t, 1H, J=6), 8.03 (s, 1H).

6-Deoxy-6-phenylthio-2-N-benzyloxycarbonyl-bis-3',5'-O-(tert-butylidimethylsilyl)-2'-deoxyguanosine (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% aq. solution), benzyl alcohol (100 mL) and THF (300 mL) at 0°C. The heterogeneous mixture is stirred for 24 h at 0°C then quenched with acetic acid (2.70 g, 45 mmol). Most of the solvent was evaporated (35°C) and the residue was dissolved in CHCl₃ and washed with water. Evaporation of the solvent (50°C,

20 μ M Hg) and chromatography of the residue (CHCl_3) gave 41a in 75% yield:

IR 1730 cm^{-1} ; $^1\text{H-NMR}$ δ 0.12 (s, 12H), 0.93 (s, 18H), 5.12 (s, 2H), 6.33 (t, 1H, $J=6$), 8.08 (s, 1H); FDMS (m/e) 721 (M^+), 664 (M^+-57), 612 ($M^+-\text{SC}_6\text{H}_5$), 586 ($M^+-\text{CO}_2\text{CH}_2\text{C}_6\text{H}_5$); UV λ_{max} (nm (ϵ)) 243 (20,000), 303 (17,100). Anal. Calcd for $\text{C}_{36}\text{H}_{51}\text{N}_5\text{O}_4\text{SSi}_2$: C, 59.9; H, 7.1; N, 9.7. Found: C, 59.7; H, 7.3; N, 9.4.

6-Deoxy-6-phenylthio-2-N-methoxycarbonyl-bis-3',5'-O-(tert-butyldimethylsilyl)-2'-deoxyguanosine (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} ; $^1\text{H-NMR}$ δ 0.08 (s, 6H), 0.10 (s, 6H), 0.95 (s, 18H), 3.7 (s, 3H), 6.33 (t, 1H, $J=6$), 7.4 (m, 5H), 8.06 (s, 1H); UV λ_{max} (nm) 217, 242, 302. Anal. Calcd for $\text{C}_{30}\text{H}_{47}\text{N}_5\text{O}_5\text{SSi}_2$: C, 55.8; H, 7.3; N, 10.8. Found: C, 55.5; H, 7.3; N, 10.5.

2-N-Benzyloxycarbonyl-bis-3',5'-O-(tert-butyldimethylsilyl)-2'-deoxyguanosine (43c). To thioguanosine 41a (280 mg, 0.39 mmol) in 20 mL CH_2Cl_2 at 0°C was added MCPBA (85%, 0.32 g, 1.56 mmol) in 10 mL 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 , water, and dried. Evaporation of the CH_2Cl_2 and chromatography of the residue (CHCl_3 /ethanol, 97/3) gave 43c: 60% yield; IR $1700, 1770\text{ cm}^{-1}$; $^1\text{H-NMR}$ δ 0.17 (s, 6H), 0.20 (s, 6H), 1.00 (s, 9H), 1.02 (s, 9H), 5.35 (s, 2H), 6.35 (t, 1H, $J=6$), 8.05 (s, 1H); UV λ_{max} (nm (ϵ)) 258 (15,500), 275 (sh, 11,200). Anal. Calcd for $\text{C}_{30}\text{H}_{47}\text{N}_5\text{O}_6\text{Si}_2$: C, 57.2; H, 7.5; N, 11.1. Found: C, 57.2; H, 7.6; N, 11.0.

2-N-Benzyloxycarbonyl-bis-3',5'-O-(tert-butyldimethylsilyl)-2'-deoxyiso-adenosine (43a). Raney nickel²⁶ (W7, 1.5 g wet weight) was refluxed in 20 mL

of acetone for 1 h then 41a (160 mg, 0.22 mmol) was added and the mixture refluxed for 2 days. Cooling, filtering, and evaporating the filtrate left a residue which was chromatographed (ethanol/CHCl₃, 5/95) to give 80 mg of 43a, 60% yield; IR 1740 cm⁻¹; ¹H-NMR δ 0.09 (s, 6H), 0.12 (s, 6H), 0.92 (s, 18H), 5.30 (s, 2H), 6.49 (t, 1H, J=6), 7.4 (s, 5H), 8.32 (s, 1H), 9.00 (s, 1H); UV λ_{max} (nm (ε)) 224 (32,800), 247 (8,300), 286 (9,200). Anal. Calcd for C₃₀H₄₇N₅O₅Si₂: C, 58.7; H, 7.7; N, 11.4. Found: C, 58.6; H, 7.6; N, 11.1.

Reaction of 38a with Sodium Benzyloxide. Thiocarbamate 38a (1.10 g, 1.20 mmol), dissolved in 40 mL of THF containing 14 mmol of sodium benzyloxide, was stirred at 0°C for 18 h 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 (CHCl₃ then ethanol/CHCl₃, 5/95) gave 42a: 41% yield; IR 1760 cm⁻¹; ¹H-NMR δ 0.08 (s, 6H), 0.10 (s, 6H), 0.90 (s, 9H), 0.91 (s, 9H), 5.26 (s, 2H), 5.60 (s, 2H), 6.39 (t, 1H, J=6.5), 7.4 (m, 10H), 8.09 (s, 1H); UV λ_{max} (nm (ε)) 257 (15,500), 267 (15,600). Anal. Calcd for C₃₇H₅₃N₅O₆Si₂: 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, 6H), 0.95 (s, 9H), 5.20 (s, 2H), 5.53 (s, 2H), 6.20 (t, 1H, J=6.5), 7.30 (s, 10H), 7.87 (s, 1H); UV λ_{max} (nm (ε)) 257 (13,100), 267 (13,500). Anal. Calcd for C₃₁H₃₉N₅O₆Si: 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).

6-O-Methyl-2-N-methyloxycarbonyl-bis-3',5'-O-(tert-butyltrimethylsilyl)-2'-deoxyguanosine (42e). Thiocarbamate 38a (3.55 g, 4.1 mmol), sodium methoxide (2.0 g, 37 mmol) in CH₃OH (10 mL), and THF (100 mL) were mixed at 0°C. The mixture was allowed to come to room temperature and stirred for two days, then

cooled to 0°C and acetic acid (2.2 g, 37 mmol) was added. The solvent was evaporated, the residue was taken up in $\text{CHCl}_3/\text{H}_2\text{O}$, 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} ; $^1\text{H-NMR}$ δ 0.07 (s, 6H), 0.11 (s, 6H), 0.91 (s, 18H), 3.81 (s, 3H), 4.14 (s, 3H), 6.41 (t, 1H, $J=6$), 8.13 (s, 1H); UV λ_{max} (nm (ϵ)) 255 (13,400), 266 (14,100). Anal. Calcd for $\text{C}_{25}\text{H}_{45}\text{N}_5\text{O}_6\text{Si}_2$: C, 52.9; H, 8.0; N, 12.3. Found: C, 53.0; H, 7.9; N, 12.0.

6-Deoxy-phenylthio-2-N-carbamyl-bis-3',5'-O-(tert-butyltrimethylsilyl)-2'-deoxy-guanosine (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} ; $^1\text{H-NMR}$ δ 0.11 (s, 12H), 0.92 (s, 18H), 6.34 (t, 1H, $J=6$), 7.4 (m, 5H), 8.26 (s, 1H); UV λ_{max} (nm (ϵ)) 230 (16,400), 293 (18,200). Anal. Calcd for $\text{C}_{29}\text{H}_{46}\text{N}_6\text{O}_4\text{SSi}_2$: C, 55.2; H, 7.4; N, 13.3. Found: C, 55.1; H, 7.4; N, 13.3.

6-O-Methyl-2-N-carbamyl-bis-3',5'-O-(tert-butyltrimethylsilyl)-2'-deoxy-guanosine (41e). A solution of 20 mL of conc. aq. 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} ; $^1\text{H-NMR}$ δ 0.11 (s, 12H), 0.89 (s, 18H), 2.38 (t, 2H, $J=6$), 4.02 (s, 3H), 6.28 (t, 1H, $J=6$), 8.08 (s, 1H); UV λ_{max} (nm (ϵ)) 254 (14,300), 276 (14,200). Anal. Calcd for $\text{C}_{24}\text{H}_{44}\text{N}_6\text{O}_5\text{Si}_2$: C, 52.1; H, 8.0; N, 15.2. Found: C, 51.9; H, 8.1; N, 14.9.

6-Deoxy-6-methylthio-2-N-methoxycarbonyl-bis-3',5'-O-(tert-butyltrimethylsilyl)-2'-deoxyguanosine (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 2M 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 4lc in 10% yield from

4b: IR 1750 cm^{-1} ; $^1\text{H-NMR}$ δ 0.1 (s, 12H), 0.9 (s, 18H), 2.6 (s, 3H), 3.8 (s, 3H), 6.4 (t, 1H, $J=6$), 8.0 (s, 1H), UV λ_{max} (nm (ϵ)) 244 (24,200), 294 (15,600), 302 (15,100). Anal. Calcd for $\text{C}_{25}\text{H}_{45}\text{N}_5\text{O}_5\text{SSi}_2$: C, 51.4; H, 7.8; N, 12.0. Found: C, 51.2; H, 7.7; N, 11.9.

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Table I. Characterization of New Activated Carbonyl Compounds, $X-\overset{\text{O}}{\underset{\text{Y}}{\text{C}}}$

Compound	X	Y	yield %	mp, °C	recryst. solvent	Anal.						¹ H-NMR, δ
						C	H	N	C	H	N	
14 ~~	C ₆ H ₅ CH ₂		30	49-50	Et ₂ O	C ₁₀ H ₉ N ₃ O ₂						5.48 (s, 2H), 7.14 (s, 5H) 8.03 (s, 1H), 8.78 (s, 1H)
						59.0	4.5	20.7	59.2	4.6	20.5	
24 ~~	CH ₃ S		91	47-48	Et ₂ O	C ₃ H ₄ N ₄ OS						1.69 (s, 3H), 9.5 (s, 1H)
						25.0	2.8	38.9	25.2	2.8	38.9	
25 ~~	CH ₃ S		40	30	Et ₂ O	C ₅ H ₆ N ₂ OS						2.55 (s, 3H), 7.0 (s, 1H) 7.37 (s, 1H), 8.07 (s, 1H)
						42.2	4.3	19.7	42.6	4.4	19.5	
26 ~~	CH ₃ S		50	49-50	pet. ether	C ₄ H ₅ N ₃ OS						2.55 (s, 3H), 7.98 (s, 1H) 8.83 (s, 1H)
						33.6	3.5	29.4	33.4	3.6	29.5	
31 ~~	C ₆ H ₅ S		38	65-68	hexane	C ₁₀ H ₈ N ₂ OS						7.03 (s, 1H), 7.43 (s, 6H) 8.13 (s, 1H)
						58.8	4.0	13.7	59.0	4.1	13.6	
33 ~~	C ₆ H ₅ S		90	105-107 (dec)	CH ₂ Cl ₂ / isooctane	C ₈ H ₆ N ₄ OS						7.57 (s, 5H), 9.17 (s, 1H)
						46.6	2.9	27.2	46.9	2.9	27.2	
35 ~~	(CH ₃) ₂ CHS		40	< 20	isooctane	C ₇ H ₁₀ N ₂ OS						1.44 (d, 6H, J=7), 3.87 (m, 1H, J=7), 7.07 (s, 1H) 7.42 (s, 1H), 8.17 (s, 1H)
						49.4	5.9	16.4	49.2	5.9	16.3	

Scheme I.

Scheme II. Carbamates From Chlorothioformates

Scheme III. Reactions of Deoxyadenosine Thiocarbamates

Scheme IV. Blocked Deoxyguanosine Derivatives

Chart I. Some Activated Carbonyl Reagents

Scheme I

Scheme II.

Scheme IV.

	<u>X</u>	<u>Y</u>
10	$\text{C}_6\text{H}_5\text{CH}_2\text{O}$	$-\text{N} \begin{array}{c} \diagup \text{N} \\ \diagdown \end{array}$
11a	$\text{C}_6\text{H}_5\text{CH}_2\text{O}$	$-\text{N} \begin{array}{c} \diagup \text{N}^+-\text{CH}_3 \\ \diagdown \end{array}$
11b	$\text{C}_6\text{H}_5\text{CH}_2\text{O}$	$-\text{N} \begin{array}{c} \diagup \text{N}^+-\text{C}_2\text{H}_5 \\ \diagdown \end{array}$
12	C_6H_5	$-\text{N} \begin{array}{c} \diagup \text{N} \\ \diagdown \end{array}$
13	C_6H_5	$-\text{N} \begin{array}{c} \diagup \text{N}^+-\text{CH}_3 \\ \diagdown \end{array}$
15	$\text{C}_6\text{H}_5\text{CH}_2\text{O}$	$-\text{N} \begin{array}{c} \diagup \text{N}^+-\text{CH}_3 \\ \diagdown \end{array}$
27	CH_3S	$-\text{N} \begin{array}{c} \diagup \text{N}^+-\text{CH}_3 \\ \diagdown \end{array}$
28	CH_3S	$-\text{N} \begin{array}{c} \diagup \text{N}^+-\text{CH}_3 \\ \diagdown \end{array}$
32	$\text{C}_6\text{H}_5\text{S}$	$-\text{N} \begin{array}{c} \diagup \text{N}^+-\text{CH}_3 \\ \diagdown \end{array}$
36	$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{CH} \\ \diagup \\ \text{CH}_3 \end{array}$	$-\text{N} \begin{array}{c} \diagup \text{N}^+-\text{C}_2\text{H}_5 \\ \diagdown \end{array}$

Chart I.

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