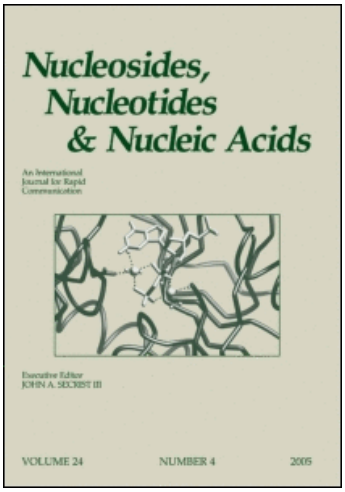

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SYNTHESES OF NOVEL SUBSTITUTED-BORANOPHOSPHATE NUCLEOSIDES

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ABSTRACT

A number of substituted (borano) nucleic acids, 3′-[diethylphosphite-(cyano, carboxy, or carbamoyl) borano] deoxynucleosides (**3a–4c**) and 5′-[diethylphosphite(cyano or carboxy) borano] deoxynucleosides (**6a–7d**) were prepared by a variety of synthetic procedures. The syntheses of the pyrophosphates (**2a–2c**), as precursors for **3a–4c**, are also described.

INTRODUCTION

There is abundant evidence that boron containing bio-molecules are playing an increasingly important role in areas of pharmacology, medicine, biochemistry and nutrition. It has been shown in model studies that boron analogues of nucleosides,[1] nucleotides,[2–7] amino acids[8–10] and nucleic acids possess potent anticancer,[11–13] anti-inflammatory,[14] hypolipidaemic, and anti-osteoporotic[15] properties. In addition, important new diagnostic

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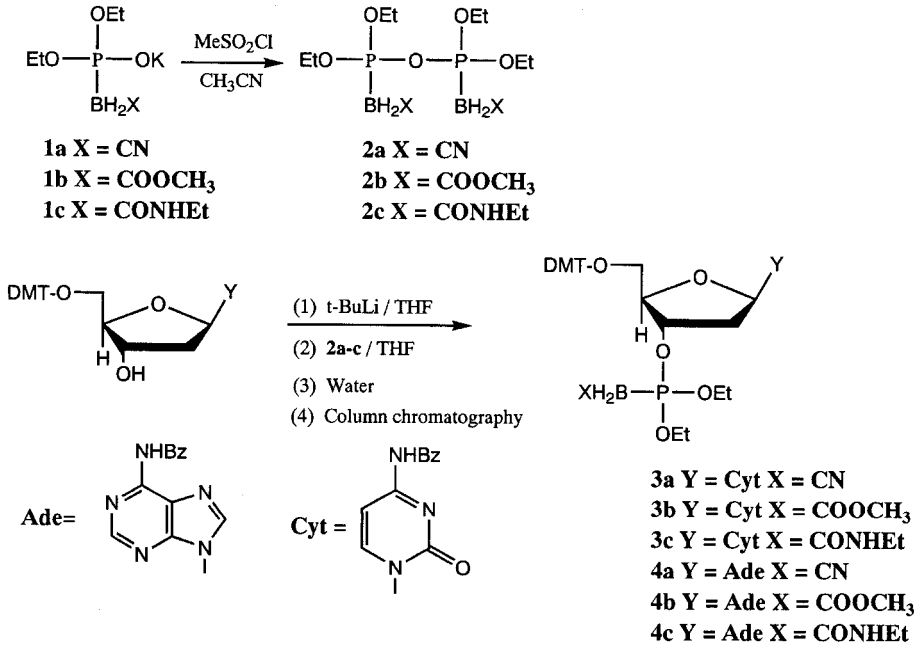
applications have been reported in the areas of polymerase chain reaction (PCR) sequencing and DNA diagnostics using boronated DNA such as oligonucleotides in which a non-bridging oxygen atom on a phosphorus is replaced by a borane (BH_3) group.[2,4,15–17] The versatility of the BH_3 group is due to the fact that it is isoelectronic with an oxygen atom, while the BH_3^- is isoelectronic and isostructural with a methyl group. Therefore, modifications of the phosphate backbones of oligonucleotides by substitution of a BH_3 group for an oxygen or a methyl group in methyl phosphonates have produced a number of useful compounds. It has been shown that incorporation of boranophosphates into DNA causes an increase in the resistance to *exo*- and *endo*-nucleases[3,18a] as compared to non-modified DNA. There are also notable applications of the α-boranotriphosphates in PCR sequencing[18a] and nucleic acid detection.[18b]

Although considerable effort and progress has been made with the boranophosphate linkage, numerous limitations are inherent in the use of the BH_3 moiety, especially in chemical syntheses. The highly reducing nature of this group can cause base degradation and it has been reported that the borane group is incompatible with some commonly used protecting groups in modified oligonucleotide synthesis.[4,19] Likewise, the BH_3 moiety has severe toxicity implications in that borohydrides, boranocarbonates, and amine-boranes typically have LD_{50} values in the tens of mg/kg by I.P. injection in mice. We have been intensively investigating the syntheses and properties of biologically important molecules that contain substituted-boranes of the form BH_2X, (X = COOR, C(O)NHR, CN, COOH). The use of these substituted-boranes in oligonucleotide modification may ameliorate some of the problems found with the unsubstituted boranonucleic acids. Since the boron analogue of glycine, H_3NBH_2COOH was found to have a very low toxicity ($LD_{50} > 2000$ mg/kg),[20] it has been predicted that the use of substituted boranonucleosides should result in less toxic products.

Herein we report the syntheses and characterization of modified oligonucleotides containing P-BH_2X (X = CN, COOMe and CONHEt) linkages.

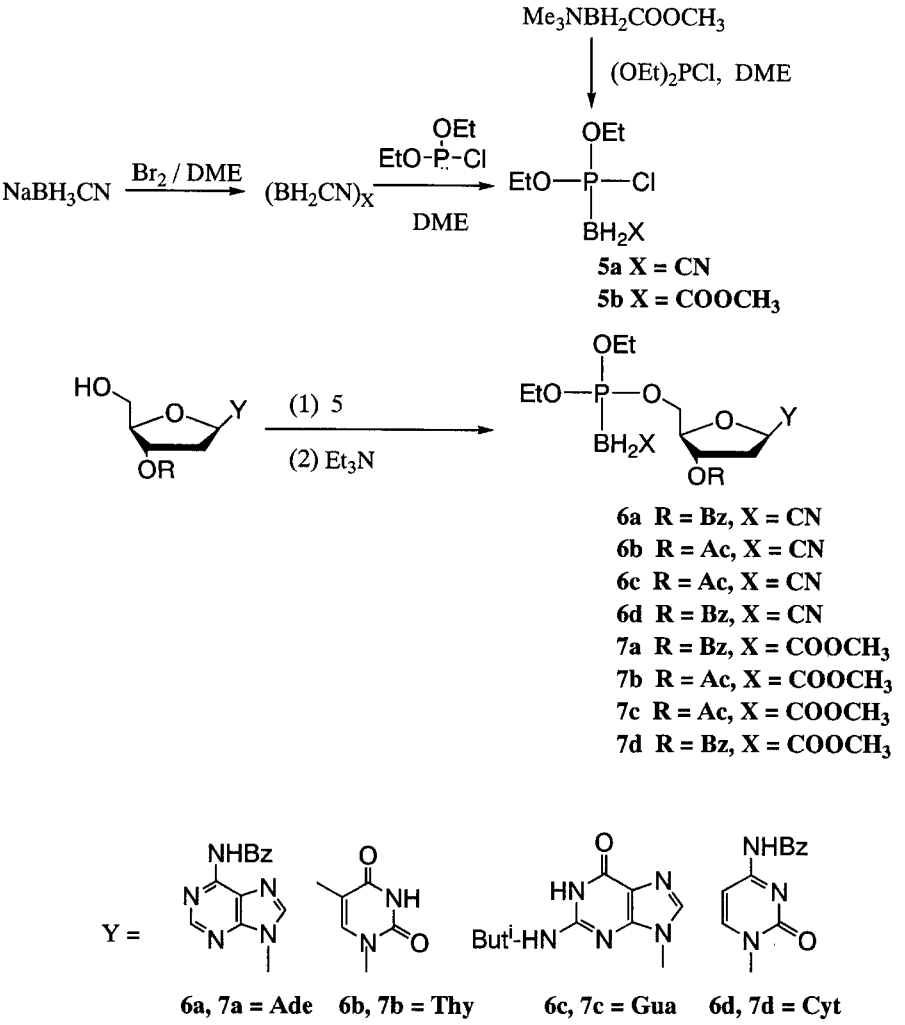
DISCUSSION

A number of 3′- or 5′-boranophosphate esters of several different deoxynucleosides were synthesized as outlined in Schs. 1–3. The site of phosphorylation was controlled by using either 5′-O- or 3′-O-protecting groups on the nucleoside precursors. The 3′-[diethylphosphite (cyano-, carbomethoxy- or carbamoyl-)borano]-5′-dimethoxytrityl-N^4-benzoyl-deoxycytidines (**3a–c**) and 3′-[diethylphosphite (cyano-, carbomethoxy- or carbamoyl-)borano]-5′-dimethoxytrityl-N^4-benzoyl-deoxyadenosines (**4a–c**) were obtained in good yields (76%–78%) from the reaction of the 5′-O- and



Scheme 1. Synthetic scheme for the preparation of tetraethyl substituted-boranopyrophosphates and the corresponding nucleosides.

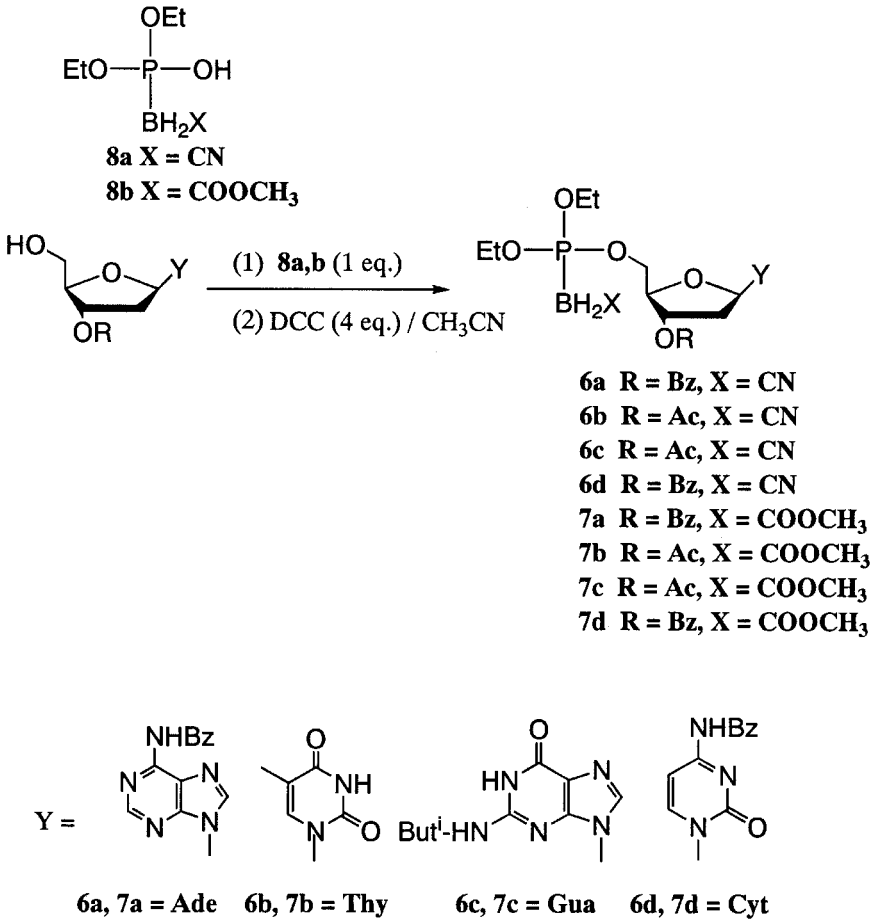
N^4-protected deoxycytidine, or the similarly protected deoxyadenosine, with tetraethyl(dicyano-, dicarbomethoxy-, or dicarbamoyl)boranopyrophosphate (**2a–c**). The pyrophosphate precursors were obtained in moderate yield (61%–70%) from the condensation reaction of the corresponding $K[(EtO)_2(O)(BH_2X)]$ {X = CN (**1a**), COOMe (**1b**), and CONHEt (**1c**)}using $MeSO_2Cl$ as the coupling agent, as shown in Sch. 1.[21] Protection of the base nitrogens in all of the deoxynucleosides was necessary to prevent boronation of the bases, a common phenomenon that was observed in the reaction of unprotected nucleosides with Ph_3PBH_2CN.[3c] With nitrogen protection, the ^{31}P and ^{11}B NMR spectra exhibited the proper P-B couplings, indicating that bond remains intact during the complete reaction sequence shown in Sch. 1. The reaction of the deoxynucleoside with the tetraethylboranopyrophosphates resulted in a downfield shift of the ^{31}P NMR resonance as a quartet by about 11 to 18 ppm (from $\delta = 80$ to 101 ppm for **2a–2c** to $\delta = 68$ to 85 ppm for **3a–4c**), with the position of the ^{11}B doublet showing little change. This is not surprising since the immediate bonding environment around the boron changes much less than that around the phosphorus during the course of the reactions. Advantage of this shift can be taken in that the shift in the ^{31}P NMR signal provides a simple way of measuring the extent of the reaction, while the ^{11}B NMR spectra can be used to monitor the integrity of the P-B



Scheme 2. Synthetic scheme for the preparation of diethylchlorophosphite-cyanoborane and diethylchlorophosphite-carbomethoxyborane and the corresponding nucleosides.

bond. The ^{1}H and ^{13}C NMR spectra and IR spectra of **3a–4c** are consistent with their formulations.

Imamoto and coworkers showed that the deprotection of 3′-(dimethylphosphiteborano)-5′-dimethoxytrityldeoxythymidine could be accomplished by reacting it with $HOAc/H_2O$ without the cleavage of the B-P bond.[21] On the other hand, Caruthers and coworkers report that the boranophosphate linkage was incompatible with DMT deprotection procedures.[19] Nonetheless, the ^{31}P, ^{11}B and ^{1}H NMR spectral evidences in our laboratories show that the DMT protecting group can be removed with $HOAc/H_2O$ without the disruption of the P-B bond.



Scheme 3. Synthetic scheme for the preparation of diethylphosphitecyano or carbomethoxyborane and the corresponding nucleosides.

The N-protected-3′-O-protected-5′-diethylphosphite(cyano- or carbomethoxy-)borano-2′-deoxynucleosides (**6a–7d**) were synthesized by two methods. The first involved the reaction of $(EtO)_2PCl(BH_2X)$ [X = CN (**5a**) and $COOCH_3$ (**5b**)] with the particular nucleoside, in the presence of Et_3N, as outlined in Sch. 2. The yields varied from a high of 91% for N^6, 3′-O-dibenzoyl-5′-diethylphosphitecyanoborano-deoxyadenosine (**6a**) to a low of 45% for 3′-O-acetyl-5′-diethylphosphitecarbo-methoxyborano-2′-deoxythymidine (**7b**). In general, use of the benzoyl-protected adenosine and cytidine nucleosides resulted in substantially higher yields than did the acetyl-protected thymidine and guanosine ones. The diethylchlorophosphitecyanoborane (**5a**) precursor was prepared by the reaction of sodium cyanoborohydride and bromine to give the cyanoborane polymer that was

refluxed with diethylchlorophosphite to give the desired compound in 65% yield. Diethylchlorophosphitecarbomethoxyborane (**5b**) was prepared, in 68% yield, by amine exchange reaction[22] as shown in Sch. 2. The ^{11}B proton-decoupled NMR spectra of **5a** and **5b** showed doublets at $\delta -42.18$ and $\delta -36.21$, respectively, while the ^{31}P NMR spectra consisted of quartets at δ 90.2 (**5a**) and δ 96.4 (**5b**). The IR spectra of **5a** and **5b** both showed singlets at 2470 and 2395 cm^{-1} for the B-H stretches, as well as the expected CN stretch at 2195 cm^{-1} for **5a** or the C=O stretch at 1658 cm^{-1} for **5b**. These phosphitylating agents were isolated as colorless oils. Both decomposed slowly to give dimethylphosphate, but were hydrolytically stable for a few days. However, they decomposed violently at 107°C. Because of the moisture sensitivity of the diethylchlorophosphite precursors and the disappointing yields in certain of the deoxynucleosides (**6b, c, 7b–d**), an alternative synthesis of the 3′-O-protected nucleosides was carried out and is shown in Sch. 3. This route involved the reaction of the diethylphosphite(cyano- or carbomethoxy)borane (**8a, b**)[23] with the nucleosides in the presence of the coupling agent, dicyclohexylcarbodiimide (DCC).[10] With the exception of **7d**, the yields in Sch. 3 are about the same as that found from the route given in Sch. 2. The yield for **7d** increased from 46% in Sch. 2 to more than 78% in Sch. 3, which is more in-line with the results found for the other benzoyl-protected nucleosides. The spectral, analytical and physical data for the analogous products from the two synthetic routes were essentially identical, thus confirming the formulations of compounds **6a–7d**.

EXPERIMENTAL

Materials and Methods

All solvents, chemicals and reagents were of analytical grade and used without further purification unless otherwise noted. Baker analyzed silica gel (60–200 mesh) was used for flash column chromatography. The nucleosides, 5′-dimethoxytrityl-N^4-benzoyl-deoxycytidine (Bz-DMT-deoxycytidine), 5′-dimethoxytrityl-N^4-benzoyl-deoxyadenosine (Bz-DMT-deoxyadenosine), N^6, 3′-O-dibenzoyl-2′-deoxyadenosine, 3′-acetylthymidine, N^2-isobutyryl-3′-acetyl-2′-deoxyguanosine, N^4, 3′-O-dibenzoyl-2′-deoxycytidine and 3′-acetylthymidine were obtained from Sigma-Aldrich and used without further purification. The boranophosphate esters were synthesized by literature methods[23] or by those described in this report. All experiments were carried out in Pyrex glass round-bottom 2-necked flasks of 100 mL capacity, each containing a magnetic stirring bar and nitrogen inlet. All known compounds were identified by comparing their IR and NMR spectra with those of authentic samples.

Spectroscopic and Analytical Procedures. Proton, boron-11, carbon-13 and phosphorus-31 NMR spectra were obtained on a Varian Fourier-transform NMR spectrometer at 200, 64.2, 50.3 and 81.20 MHz respectively. Infrared spectra were recorded using a Nicolet Magna 550 FT-IR spectrophotometer. Elemental analyses were obtained in house using Perkin Elmer 2400 CHNS elemental analyzer.

Syntheses of Tetraethyl Di(cyano or Carboxy or Carbamoyl) Boranopyrophosphates (2a–c). The diboranopyrophosphates, **2a–c**, were synthesized by the condensation dimerization of their corresponding monoboranophosphites, **1a–c**, as shown in Sch. 1. Specifically, methane sulfonylchloride was added to a solution of the potassium salt of the particular diethylphosphiteborane[23] in acetonitrile (50 mL) at 0°C and the mixture was stirred at room temperature for 4 h. The precipitate that was formed in the reaction (KCl) was removed by filtration, and the filtrate was concentrated under reduced pressure. The resulting residue was then passed through a short column of silica gel with ethyl acetate as an eluent to isolate the corresponding diboranopyrophosphates as oils in 61–70% yields. The specific quantitative information, including yields, and compound characterizations are as follows.

Tetraethyl Dicyanoboranopyrophosphate (2a). The reaction of 0.96 g (8.34 mmol) of methane sulfonylchloride and 3.0 g (13.9 mmol) of $(EtO)_2$-(KO)P(BH_2CN) gave 3.25 g (9.7 mmol, 69.5% yield) of $[(EtO)_2P(BH_2CN)]_2O$ (**2a**). Physical properties and characterization are: dec. 120°C; ^{1}H NMR (DMSO, relative to Me_4Si) δ 1.20 (t, 12H), 3.85 (m, 8H); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −40.58 (d, $^1J_{BP} = 160.4$ Hz); ^{13}C NMR (DMSO, relative to Me_4Si) δ 16.90 (CH_3), 57.71(CH_2); ^{31}P NMR (DMSO, relative to H_3PO_4) δ 80.21 (q, $J_{PB} = 163$ Hz); IR (cm^{-1}, KBr pellet) 2409, 2361 ν(BH); 2209 ν(CN). Anal. Calcd for $C_{10}H_{24}P_2O_5B_2N_2$: C, 35.74; H, 7.20; N, 8.33. Found: C, 35.01; H, 7.90; N, 8.56.

Tetraethyl Dicarbomethoxyboranopyrophosphate (2b). The reaction of 0.84 g (7.26 mmol) of methane sulfonylchloride and 3.0 g (12.1 mmol) of $(EtO)_2$(KO)P(BH_2COOMe) gave 2.99 g (7.4 mmol, 61.4% yield) of $[(EtO)_2$-$P(BH_2COOMe)]_2O$ (**2b**). Physical properties and characterization are: dec. 122°C; ^{1}H NMR (DMSO, relative to Me_4Si) δ 1.22 (t, 12H), 3.83 (m, 8H), 4.01(s 6H); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −34.28 (d, $^1J_{BP} = 161.8$ Hz); ^{13}C NMR (DMSO, relative to Me_4Si) δ 17.20 (CH_3), 57.72 (CH_2), 54.01 (OCH_3), 178.00 (C=O); ^{31}P NMR (DMSO, relative to H_3PO_4) δ 97.81 (q, $J_{PB} = 161.5$ Hz); IR (cm^{-1}, KBr pellet) 2358, 2419 ν(BH), 1660 (ν, C=O). Anal. Calcd for $C_{12}H_{30}P_2O_9B_2$: C, 35.82; H, 7.5. Found: C, 35.71; H, 7.9.

Tetraethyl Dicarbamoylboranopyrophosphate (2c). The reaction of 0.79 g (6.84 mmol) of methane sulfonylchloride and 3.0 g (11.4 mmol) of $(EtO)_2(KO)P(BH_2CONHEt)$ gave 3.10 g (7.2 mmol, 63.5% yield) of $[(EtO)_2P(BH_2CONHEt)]_2O$ (**2c**). Physical properties and characterization are: dec. 123°C; ^1H NMR (DMSO, relative to Me_4Si) δ 0.90(t, 6H), 1.21 (t, 12H), 2.01(m, 4H), 3.84(m, 8H); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −32.33 (d, $^1J_{BP} = 162.5$ Hz); ^{13}C NMR (DMSO, relative to Me_4Si) δ 15.00, 16.90 (CH_3), 42.00, 57.71 (CH_2), 180.00 (C=O); ^{31}P NMR (DMSO, relative to H_3PO_4) δ 101 (q, $J_{PB} = 162.4$ Hz); IR (cm^{-1}, KBr pellet) 2412, 2368 ν(BH). Anal. Calcd for $C_{14}H_{36}P_2O_7B_2N_2$: C, 39.25; H, 8.41; N, 6.54. Found: C, 39.15; H, 8.43; N, 6.51.

Syntheses of 3′-[diethylphosphite (Cyano, Carbomethoxy, or Carbamoyl) Borano]-5′-dimethoxytrityl-N^4-benzoyl-(deoxycytidines or Deoxyadenosines) (3a–4c). Bz-DMT-deoxycytidine or Bz-DMT-deoxyadenosine was dissolved in 15 mL of THF, the solution was cooled to –78°C and stirred for 30 min, after which *t*-BuLi was added to the reaction mixture and the stirring continued for an additional 30 min. The particular diboranopyrophosphate (**2a–c**), dissolved in 10 ml of THF, was then added and the reaction mixture was stirred for 18 h. The solvent was removed under reduced pressure to obtain a white residue to which 25 mL of water was added and solution was stirred for 5 h. The crude solid was obtained by filtration and was purified by chromatography to give the corresponding compounds. See Sch. 1. The specific quantitative information, including yields, and product characterizations are as follows.

3′-(Diethylphosphitecyanoborano)-5′-dimethoxytrityl-N^4-benzoyl-deoxycytidine (3a). The reaction between 0.25 g (0.4 mmol) of Bz-DMT-deoxycytidine, *t*-BuLi (1.0 mL of 1.5 M *t*-BuLi in hexane, 1.5 mmol) and 0.2 g (0.5 mmol) of $[(EtO)_2P(BH_2CN)]_2O$ (**2a**) gave 0.24 g (0.38 mmol, 75.7% yield) of **3a**. Spectroscopic and Analytical Data: ^1H NMR (DMSO, relative to Me_4Si) δ 8.23 (m, 5H, Ar-H), 7.69(br, 13H, Ar-H), 7.65 (d, 2H, H-5, H-6), 6.18 (t, 1H, H-1′), 2.21, 2.15 (m, 2H, H-2′), 4.00 (m, 1H, H-3′), 5.37 (m, 1H, H-4′), 3.67, 4.05 (m, 2H, H-5′), 3.95 (q, 4H), 1.30 (t, 6H); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ –39.63 (d, $^1J_{BP} = 178.6$ Hz); ^{31}P NMR (DMSO, relative to H_3PO_4) δ 68.12 (q, $J_{PB} = 163$ Hz); ^{13}C NMR (DMSO, relative to Me_4Si): δ 14.00 (CH_3), 20.00 (CH_2), 58.40 (OCH_2), 54.90, 58.10 (OCH), 53.40 (OCH_3), 171.00 (C=O), 127.90 (aromatic); IR (cm^{-1}, KBr pellet) 2762, 2701 ν(BH); 2295 ν(CN). Anal. Calcd for $C_{42}H_{46}O_9N_4BP$: C, 63.63; H, 5.80; N, 7.07. Found: C, 62.89; H, 6.10; N, 6.42.

3′-(Diethylphosphitecarbomethoxyborano)-5′-dimethoxytrityl-N^4-benzoyl-deoxycytidine (3b). The reaction between 0.20 g (0.32 mmol) of Bz-DMT-deoxycytidine, *t*-BuLi (1.0 mL of 1.5 M *t*-BuLi in hexane, 1.5 mmol) and 0.2 g

(0.4 mmol) of $[(EtO)_2P(BH_2COOMe)]_2O$ (**2b**) gave 0.21 g (0.31 mmol, 78.0% yield) of **3b**. Spectroscopic and Analytical Data: ^1H NMR (DMSO, relative to Me_4Si) δ 8.23 (m, 5H, Ar-H), 7.71(br, 13H, Ar-H), 7.65 (d, 2H, H-5, H-6), 6.19 (t, 1H, H-1′), 3.80 (s, 3H), 2.21, 2.14 (m, 2H, H-2′), 3.90 (m, 1H, H-3′), 5.37 (m, 1H, H-4′), 3.66, 4.01 (m, 2H, H-5′), 3.98 (q, 4H), 1.20 (t, 6H); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −32.21 (d, $^1J_{BP} = 176.6$ Hz); ^{31}P NMR (DMSO, relative to H_3PO_4) δ 80.12 (q, $J_{PB} = 164.5$ Hz); ^{13}C NMR (DMSO, relative to Me_4Si): δ 16.00 (CH_3), 18.00 (CH_2), 61.50 (OCH_2), 53.40, 59.10 (OCH), 53.00, 58.00 (OCH_3), 168.00, 171.00 (C=O), 128.50 (aromatic); IR (cm^{-1}, KBr pellet) 2758, 2711 ν(BH), 1667 (ν, C=O). Anal. Calcd for $C_{43}H_{49}O_{11}N_3BP$: C, 62.54; H, 5.93; N, 5.09. Found: C, 62.50; H, 5.98; N, 5.06.

3′-(Diethylphosphitecarbamoylborano)-5′-dimethoxytrityl-N^4-benzoyl-deoxycytidine (3c). The reaction between 0.25 g (0.4 mmol) of Bz-DMT-deoxycytidine, *t*-BuLi (1.0 mL of 1.5 M *t*-BuLi in hexane, 1.5 mmol) and 0.25 g (0.5 mmol) of $[(EtO)_2P(BH_2CONHEt)]_2O$ (**2c**) gave 0.26 g (0.39 mmol, 77.5% yield) of **3c**. Spectroscopic and Analytical Data: ^1H NMR (DMSO, relative to Me_4Si) δ 8.23 (m, 5H, Ar-H), 7.68 (br, 13H, Ar-H), 7.65 (d, 2H, H-5, H-6), 6.20 (t, 1H, H-1′), 2.22, 2.15 (m, 2H, H-2′), 2.10 (m, 2H), 4.00 (m, 1H, H-3′), 5.35 (m, 1H, H-4′), 3.65, 4.02 (m, 2H, H-5′), 3.95 (q, 4H), 1.31 (t, 6H), 0.90 (t, 3H); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −30.05 (d, $^1J_{BP} = 177.6$ Hz); ^{31}P NMR (DMSO, relative to H_3PO_4): δ 84.32 (q, $J_{PB} = 160.5$ Hz); ^{13}C NMR (DMSO, relative to Me_4Si) δ 14.00, 17.00 (CH_3), 20.00, 38.00 (CH_2), 60.00 (OCH_2), 55.00, 57.00 (OCH), 59.00 (OCH_3), 176.00 (C=O), 130.00 (aromatic); IR (cm^{-1}, KBr pellet) 2751, 2718 ν(BH). Anal. Calcd for $C_{44}H_{52}O_{10}N_4BP$: C, 63.01; H, 6.21; N, 6.68. Found: C, 62.99; H, 6.26; N, 6.64.

3′-(Diethylphosphitecyanoborano)-5′-dimethoxytrityl-N^4-benzoyl-deoxy-adenosine (4a). The reaction between 0.263 g (0.4 mmol) of Bz-DMT-deoxyadenosine, *t*-BuLi (1.0 mL of 1.5 M *t*-BuLi in hexane, 1.5 mmol) and 0.20 g (0.5 mmol) of $[(EtO)_2P(BH_2CN)]_2O$ (**2a**) gave 0.25 g (0.39 mmol, 77.4% yield) of **4a**. Spectroscopic and Analytical Data: ^1H NMR (DMSO, relative to Me_4Si) δ 8.21 (m, 5H, Ar-H), 8.12(d, 1H, H-8), 7.80 (d, 1H, H-2), 7.69 (br, 13H, Ar-H), 6.14 (t, 1H, H-1′), 2.21, 2.14 (m, 2H, H-2′), 4.01 (m, 1H, H-3′), 5.34 (m, 1H, H-4′), 3.65, 4.03 (m, 2H, H-5′), 3.92 (q, 4H), 1.30 (t, 6H); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −40.01 (d, $^1J_{BP} = 179.6$ Hz); ^{31}P NMR (DMSO, relative to H_3PO_4) δ 69.23 (q, $J_{PB} = 162$ Hz); ^{13}C NMR (DMSO, relative to Me_4Si): δ 14.20 (CH_3), 19.00 (CH_2), 59.40 (OCH_2), 55.00, 58.40(OCH), 52.40 (OCH_3), 170.00 (C=O), 128.00 (aromatic); IR (cm^{-1}, KBr pellet) 2765, 2711 ν(BH); 2291 ν(CN). Anal. Calcd for $C_{43}H_{47}O_8N_6BP$: C, 63.15; H, 5.75; N, 10.28. Found: C, 63.10; H, 5.81; N, 10.45.

3′-(Diethylphosphitecarbomethoxyborano)-5′-dimethoxytrityl-N^4-benzoyl-deoxyadenosine (4b). The reaction between 0.21 g (0.32 mmol) of Bz-DMT-deoxyadenosine, *t*-BuLi (1.0 mL of 1.5 M *t*-BuLi in hexane, 1.5 mmol) and 0.20 g (0.4 mmol) of $[(EtO)_2P(BH_2COOMe)]_2O$ (**2b**) gave 0.22 g (0.31 mmol, 78% yield) of **4b**. Spectroscopic and Analytical Data: ^{1}H NMR (DMSO, relative to Me_4Si) δ 8.24 (m, 5H, Ar-H), 8.14 (d, 1H, H-8), 7.90 (d, 1H, H-2), 7.65 (br, 13H, Ar-H), 6.19 (t, 1H, H-1′), 3.80 (s, 3H), 2.21, 2.13 (m, 2H, H-2′), 3.90 (m, 1H, H-3′), 5.38 (m, 1H, H-4′), 3.69, 4.02 (m, 2H, H-5′), 3.99 (q, 4H), 1.30 (t, 6H); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −34.02 (d, $^1J_{BP} = 175.6$ Hz); ^{31}P NMR (DMSO, relative to H_3PO_4) δ 82.46 (q, $J_{PB} = 163.9$ Hz); ^{13}C NMR (DMSO, relative to Me_4Si): δ 15.00 (CH_3), 20.00 (CH_2), 60.90 (OCH_2), 53.40, 58.50 (OCH), 54.00, 56.00 (OCH_3), 170.00 (C=O), 129.00 (aromatic); IR (cm^{-1}, KBr pellet) 2754, 2719 ν(BH), 1668 (ν, C=O). Anal. Calcd for $C_{44}H_{50}O_{10}N_5BP$: C, 62.12; H, 5.88; N, 8.23. Found: C, 62.08; H, 5.91; N, 8.19.

3′-(Diethylphosphitecarbamoylborano)-5′-dimethoxytrityl-N^4-benzoyl-deoxyadenosine (4c). The reaction between 0.26 g (0.4 mmol) of Bz-DMT-deoxyadenosine, *t*-BuLi (1.0 mL of 1.5 M *t*-BuLi in hexane, 1.5 mmol) and 0.25 g (0.5 mmol) of $[(EtO)_2P(BH_2CONHEt)]_2O$ (**2c**) gave 0.27 g (0.39 mmol, 78% yield) of **4c**. Spectroscopic and Analytical Data: ^{1}H NMR (DMSO, relative to Me_4Si) δ 8.23 (m, 5H, Ar-H), 8.12 (d, 1H, H-8), 7.50 (d, 1H, H-2), 7.65 (br, 13H, Ar-H), 6.22 (t, 1H, H-1′), 2.20, 2.16 (m, 2H, H-2′), 1.80 (m, 2H), 4.10 (m, 1H, H-3′), 5.34 (m, 1H, H-4′), 3.65, 4.02 (m, 2H, H-5′), 3.95 (q, 4H), 1.31 (t, 6H), 0.90 (t, 3H); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −31.62 (d, $^1J_{BP} = 176.2$ Hz); ^{31}P NMR (DMSO, relative to H_3PO_4) δ 85.24 (q, $J_{PB} = 161.3$ Hz); ^{13}C NMR (DMSO, relative to Me_4Si): δ 14.00, 16.70 (CH_3), 20.00, 34.00 (CH_2), 62.40 (OCH_2), 54.00, 57.00 (OCH), 58.00 (OCH_3), 172.00 (C=O), 129.50 (aromatic); IR (cm^{-1}, KBr pellet) 2755, 2721 ν(BH). Anal. Calcd for $C_{45}H_{53}O_9N_6BP$: C, 62.57; H, 6.14; N, 9.73. Found: C, 62.61; H, 6.10; N, 9.72.

Synthesis of Diethylchlorophosphitecyanoborane (5a). A 39.9 mmol sample of bromine (6.24 g) was added drop-wise, with stirring, to a solution of sodium cyanoborohydride, (5 g, 79.0 mmol) in anhydrous dimethoxy ethane (DME) (80 mL). The solution was then filtered, the filtrate mixed with diethylchlorophosphite (12.52 g, 80.0 mmol) under nitrogen and heated to reflux for 2 days. The reaction mixture was again filtered and the solvent was removed from the filtrate under reduced pressure to produce an oil. The oil was extracted into ether and pentane mixture (3:1) and the solvent mixture was removed under reduced pressure to isolate diethylchlorophosphitecyanoborane (**5a**) as colorless oil in 65% yield (10.20 g, 52.2 mmol). Spectroscopic and Analytical Data: ^{1}H NMR (DMSO, relative to Me_4Si): δ 1.34 (t, 6H, CH_3), 4.22 (m, 4H, CH_2); ^{13}C NMR (DMSO, relative to Me_4Si):

δ 17.50 (CH_3), 63.70 (OCH_2); ^{31}P NMR (DMSO, relative to H_3PO_4): δ 90.20 (q, $J_{PB} = 141.80$ Hz); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −42.18 (d, $^1J_{BP} = 139.6$ Hz); IR (cm^{-1}, KBr pellet) 2470, 2395 ν(BH); 2192 ν(CN). Anal. Calcd for $C_5H_{12}O_2NBPCl$: C, 30.42; H, 6.09; N, 7.09. Found: C, 31.01; H, 5.99; N, 6.98.

Diethylchlorophosphitecarbomethoxyborane (5b). A 40.0 mmol sample of diethylchlorophosphite (6.26 g) and trimethylamine-carbomethoxyborane (5.24 g, 40 mmol) were dissolved in anhydrous DME (80 mL) and heated to reflux for 2 days. The solvent was removed under reduced pressure to give an oil. The oil was extracted into ether and pentane mixture (3:1) and the solvent mixture was removed under reduced pressure to give diethylchlorophosphitecarbomethoxyborane (**5b**) (6.20 g, 27.1 mmol) in 68% yield as a colorless oil. Spectroscopic and Analytical Data: ^{1}H NMR (DMSO, relative to Me_4Si): δ 1.35 (t, 6H, CH_3), 3.90 (s, 3H), 4.18 (m, 4H, CH_2); ^{13}C NMR (DMSO, relative to Me_4Si): δ 17.50 (CH_3), 54.00 (OCH_3), 63.70 (OCH_2), 176.00 (C=O); ^{31}P NMR (DMSO, relative to H_3PO_4): δ 103.40 (q, $J_{PB} = 142.38$ Hz); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −35.09 (d, $^1J_{BP} = 137.5$ Hz); IR (cm^{-1}, KBr pellet) 2470, 2395 ν(BH); 1658 ν(C=O). Anal. Calcd for $C_6H_{15}O_4BPCl$: C, 31.51; H, 6.56. Found: C, 31.41; H, 6.60.

Syntheses of N-protected-3′-O-protected-5′-[diethylphosphite (cyano or carbomethoxy) borano]deoxynucleosides (6a–7d). The N-protected-3′-O-protected-5′-diethylphosphitecyanoboranodeoxynucleosides (**6a–6d**) were prepared from the reaction of the particular nucleosides with diethylchlorophosphite(cyano or carbomethoxy)borane in the presence of triethylamine. Specifically, the nucleoside, phosphiteborane and triethylamine were dissolved in anhydrous THF and the mixture was stirred at room temperature for 6 h. After removing the insoluble materials by filtration, the solvent in the filtrate was removed under reduced pressure and the resulting residue was redissolved in dichloromethane (20 mL) and washed with water (5 × 15 mL). The organic layer in the extract was dried with $MgSO_4$, filtered and concentrated under reduced pressure to produce a solid residue that was purified by flash chromatography on silica gel using a solvent mixture of ethyl acetate: hexane (9:1) to isolate the corresponding phosphiteboranonucleosides (**6a–7d**) as colorless oils in 45–90% yields. The quantitative information, including, yields, and product characterizations are as follows.

N^6-3′-O-dibenzoyl-5′-diethylphosphitecyanoboranodeoxyadenosine (6a). The reaction between 0.027 g (0.06 mmol) of N^6, 3′-O-dibenzoyl-2′-deoxyadenosine, 0.012 g (0.06 mmol) of diethylchlorophosphitecyanoborane (**5a**) and 6.0 mg (0.06 mmol) of Et_3N produced 0.031 g (0.054 mmol, 90.7% yield) of N^6-3′-O-dibenzoyl-5′-diethylphosphitecyanoboranodeoxyadenosine (**6a**). Spectroscopic and Analytical Data: ^{1}H NMR (DMSO, relative to Me_4Si):

δ 1.39, 1.40 (t, 6H, CH_3), 1.00–1.60 (br, 2H, BH_2), 2.41–2.60 (m, 2H, H-2′), 3.91–4.12 (m, 2H, H-5′), 4.12–4.14 (m, 1H, H-4′), 4.26 (m, 4H, OCH_2), 4.81–5.00 (m, 1H, H-3′), 6.46 (m, 1H, H-1′), 8.11 (s, 1H, H-8), 8.35 (s, 1H, H-2), 8.62 (m, 5H, Ar-H), 9.01 (br, s, NH); ^{13}C NMR (DMSO, relative to Me_4Si): δ 14.40 (CH_3), 17.30 (CH_2), 60.40 (OCH_2), 58.10, 56.30 (OCH), 129.00 (C-Ar), 170.70 (C=O); ^{31}P NMR (DMSO, relative to H_3PO_4): δ 89.70 (q, $J_{PB} = 161.20$ Hz); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −41.80 (d, $^1J_{BP} = 169.4$ Hz); IR (cm^{-1}, KBr pellet) 2408, 2359 ν(BH); 2200 ν(CN). Anal. Calcd. for $C_{29}H_{32}O_7N_6BP$: C, 56.09; H, 5.16; N, 13.54. Found: C, 55.89; H, 5.09; N, 13.01.

3′-O-Acetyl-5′-diethylphosphitecyanoborano-2′-deoxythymidine (6b). The reaction between 0.35 g (1.24 mmol) of 3′-acetylthymidine, 0.24 g (1.24 mmol) of diethylchlorophosphitecyanoborane (**5a**) and 0.5 mg of Et_3N produced 0.26 g (0.58 mmol, 46.5% yield) of 3′-O-acetyl-5′-diethylphosphitecyanoborano-2′-deoxythymidine (**6b**). Spectroscopic and Analytical Data: ^{1}H NMR (DMSO, relative to Me_4Si): δ 1.41, 1.44 (t, 6H, CH_3), 1.00–1.80 (br, 2H, BH_2), 1.95 (s, 3H, CH_3), 2.30–2.41 (m, 2H, H-2′), 2.12 (s, 3H, $COCH_3$), 4.18–4.24 (m, 2H, H-5′), 4.13–4.15 (m, 1H, H-4′), 4.28 (m, 4H, OCH_2), 5.26 (m, 1H, H-3′), 6.41 (m, 1H, H-1′), 7.36 (d, 1H, H-6), 9.21 (br, s, NH); ^{13}C NMR (DMSO, relative to Me_4Si): δ 14.20 (CH_3), 18.40 (CH_2), 60.90 (OCH_2), 57.90, 56.10 (OCH), 41.00 ($COCH_3$), 169.70 (C=O); ^{31}P NMR (DMSO, relative to H_3PO_4): δ 91.40 (q, $J_{PB} = 161.25$ Hz); ^{11}B NMR (DMSO relative to $BF_3{\cdot}OEt_2$) δ −40.58 (d, $^1J_{BP} = 168.5$ Hz); IR (cm^{-1}, KBr pellet) 2412, 2361 ν(BH); 2224 ν(CN). Anal. Calcd. for $C_{17}H_{27}O_8N_3BP$: C, 45.82; H, 6.06; N, 9.43. Found: C, 45.74; H, 5.98; N, 9.01.

N^2-Isobutyryl-3′-O-acetyl-5′-diethylphosphitecyanoborano-2′-deoxyguanosine (6c). The reaction between 0.05 g (0.13 mmol) of N^2-isobutyryl-3′-acetyl-2′-deoxyguanosine, 0.026 g (0.13 mmol) of diethylchlorophosphitecyanoborane (**5a**) and 13.0 mg (0.13 mmol) of Et_3N produced 0.035 g (0.06 mmol, 45.8% yield) of N^2-isobutyryl-3′-O-acetyl-5′-diethylphosphitecyanoborano-2′-deoxyguanosine (**6c**). Spectroscopic and Analytical Data: ^{1}H NMR (DMSO, relative to Me_4Si): δ 1.20,1.30 (d, 6H, CH_3), 1.00–1.30 (br, 2H, BH_2), 2.39–2.40 (m, 2H, H-2′), 3.20 (s, 3H, OCH_3), 3.91–4.21 (m, 2H, H-5′), 4.06–4.13 (m, 1H, H-4′), 4.22 (m, 4H, OCH_2), 4.72–4.95 (m, 1H, H-3′), 6.01 (br, s, NH), 6.53 (m, 1H, H-1′), 8.01 (s, 1H, H-8); ^{13}C NMR (DMSO, relative to Me_4Si): δ 14.10, 16.50 (CH_3), 17.90 (CH_2), 34.10 (CH attached to C=O), 59.2 (OCH_2), 57.10, 56.50 (OCH), 42.35 ($COCH_3$), 172.10 (C=O); ^{31}P NMR (DMSO, relative to H_3PO_4): δ 90.80 (q, $J_{PB} = 160.80$ Hz); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −41.28 (d, $^1J_{BP} = 166.4$ Hz); IR (cm^{-1}, KBr pellet) 2421, 2361 ν(BH); 2209 ν(CN). Anal. Calcd. for $C_{21}H_{32}O_8N_6BP$: C, 46.64; H, 5.92; N, 15.55. Found: C, 46.02; H, 5.81; N, 15.12.

N^4-3′-O-dibenzoyl-5′-diethylphosphitecyanoborano-2′-deoxycytidine (6d). The reaction between 0.025 g (0.06 mmol) of N^4-3′-O-dibenzoyl-2′-deoxycytidine, 0.012 g (0.06 mmol) of diethylchlorophosphitecyanoborane (**5a**) and 6.0 mg (0.06 mmol) of Et_3N produced 0.028 g (0.053 mmol, 87.7% yield) of N^4-3′-O-dibenzoyl-5′-diethylphosphitecyanoborano-2′-deoxycytidine (**6d**). Spectroscopic and Analytical Data: ^{1}H NMR (DMSO, relative to Me_4Si): δ 1.37, 1.39 (t, 6H, CH_3), 1.00–1.40 (br, 2H, BH_2), 2.30–2.38 (m, 2H, H-2′), 3.72 (m, 2H, H-5′), 3.91–4.11 (m, 1H, H-4′), 4.24 (m, 4H, OCH_2), 4.58–4.71 (m, 1H, H-3′), 6.01 (d, 1H, H-5), 6.46 (m, 1H, H-1′), 7.91 (d, 1H, H-6), 8.47 (m, 5H, Ar-H), 9.21 (br, s, NH); ^{13}C NMR (DMSO, relative to Me_4Si): δ 14.60 (CH_3), 16.70 (CH_2), 61.40 (OCH_2), 57.10, 57.10 (OCH), 127.70 (C-Ar), 130.10, 128.70 (CH=CH), 168.90 (C=O); ^{31}P NMR (DMSO, relative to H_3PO_4): δ 91.40 (q, $J_{PB} = 161.89$ Hz); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −42.02 (d, $^1J_{BP} = 167.4$ Hz); IR (cm^{-1}, KBr pellet) 2398, 2349 ν(BH); 2219 ν(CN). Anal. Calcd. for $C_{28}H_{32}O_8N_4BP$: C, 56.35; H, 5.37; N, 9.39. Found: C, 55.99; H, 5.24; N, 10.01.

N^6-3′-O-dibenzoyl-5′-diethylphosphitecarbomethoxyborano-2′-deoxyadenosine (7a). The reaction between 0.027 g (0.06 mmol) of N^6, 3′-O-dibenzoyl-2′-deoxyadenosine, 0.0136 g (0.06 mmol) of diethylchlorophosphite-carbomethoxyborane and 6.0 mg (0.06 mmol) of triethylamine produced 0.033 g (0.05 mmol, 83.3% yield) of N^6-3′-O-dibenzoyl-5′-diethyl-phosphitecarbomethoxyborano-2′-deoxyadenosine (**7a**). Spectroscopic and Analytical Data: ^{1}H NMR (DMSO, relative to Me_4Si): δ 1.38, 1.40 (t, 6H, CH_3), 1.00–1.50 (br, 2H, BH_2), 2.42–2.60 (m, 2H, H-2′), 3.40 (s, 3H, OCH_3), 3.91–4.11 (m, 2H, H-5′), 4.12–4.14 (m, 1H, H-4′), 4.25 (m, 4H, OCH_2), 4.81–5.00 (m, 1H, H-3′), 6.44 (m, 1H, H-1′), 8.12 (s, 1H, H-8), 8.35 (s, 1H, H-2), 8.62 (m, 5H, Ar-H), 9.04 (br, s, NH); ^{13}C NMR (DMSO, relative to Me_4Si): δ 14.20 (CH_3), 17.00 (CH_2), 61.00 (OCH_2), 58.10, 55.00 (OCH), 58.00 (OCH_3), 129.00 (C-Ar), 169.00 (C=O); ^{31}P NMR (DMSO, relative to H_3PO_4): δ 98.20 (q, $J_{PB} = 163.12$ Hz); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −36.21 (d, $^1J_{BP} = 168.2$ Hz); IR (cm^{-1}, KBr pellet) 2411, 2352 ν(BH); 1656 ν(C=O). Anal. Calcd. for $C_{30}H_{35}O_9N_5BP$: C, 55.30; H, 5.40; N, 10.75. Found: C, 55.35; H, 5.37; N, 10.72.

3′-O-Acetyl-5′-diethylphosphitecarbomethoxyborano-2′-deoxythymidine (7b). The reaction between 0.35 g (1.24 mmol) of 3′-acetylthymidine, 0.28 g (1.24 mmol) of diethylchlorophosphitecarbomethoxyborane and triethylamine (0.001 g, 0.01 mmol) produced 0.266 g (0.56 mmol, 45.2% yield) of 3′-O-acetyl-5′-diethylphosphitecarbomethoxyborano-2′-deoxythymidine (**7b**). Spectroscopic and Analytical Data: ^{1}H NMR (DMSO, relative to Me_4Si): δ 1.41, 1.42 (t, 6H, CH_3), 1.00–1.60 (br, 2H, BH_2), 1.93 (s, 3H, CH_3), 2.30–2.41 (m, 2H, H-2′), 3.20, 3.90 (s, 3H, OCH_3), 4.18–4.21 (m, 2H, H-5′), 4.12–4.15 (m, 1H, H-4′), 4.28 (m, 4H, OCH_2), 5.26 (m, 1H, H-3′), 6.41 (m, 1H, H-1′),

7.36 (d, 1H, H-6), 9.22 (br, s, NH); ^{13}C NMR (DMSO, relative to TMS): δ 14.40 (CH_3), 17.00 (CH_2), 58.00 (OCH_2), 57.90, 56.10 (OCH), 53.00 (OCH_3), 168.00 (C=O); ^{31}P NMR (DMSO, relative to H_3PO_4) δ 99.40 (q, $J_{PB} = 160.2$ Hz); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −34.82 (d, $^1J_{BP} = 167.1$ Hz); IR (cm^{-1}, KBr pellet) 2409, 2368 ν(BH); 1649 ν(C=O). Anal. Calcd. for $C_{18}H_{30}O_{10}N_2BP$: C, 45.37; H, 6.30; N, 5.88. Found: C, 45.31; H, 6.29; N, 5.92.

N^2-Isobutyryl-3′-O-acetyl-5′-diethylphosphitecarbomethoxyborano-2′-deoxyguanosine (7c). The reaction between 0.050 g (0.13 mmol) of N^2-isobutyryl-3′-acetyl-2′-deoxyguanosine, 0.030 g (0.13 mmol) of diethylchlorophosphitecarbomethoxyborane and 0.0133 g (0.13 mmol) of triethylamine produced 0.032 g (0.06 mmol, 46.2% yield) of N^2-isobutyryl-3′-O-acetyl-5′-diethylphosphitecarbomethoxyborano-2′-deoxyguanosine (**7c**). Spectroscopic and Analytical Data: ^{1}H NMR (DMSO, relative to Me_4Si): δ 1.20–1.30 (d, 6H, CH_3), 1.00–1.30 (br, 2H, BH_2), 2.39–2.40 (m, 2H, H-2′), 3.12 (m, 1H, CH), 3.30 (s, 3H, OCH_3), 3.91–4.20 (m, 2H, H-5′), 4.06–4.13 (m, 1H, H-4′), 4.22 (m, 4H, OCH_2), 4.72–4.95 (m, 1H, H-3′), 6.01 (br, s, NH), 6.51 (m, 1H, H-1′), 7.99 (s, 1H, H-8), ^{13}C NMR (DMSO, relative to Me_4Si): δ 14.10, 16.20 (CH_3), 17.40 (CH_2), 33.00 (CH attached to C=O), 59.20 (OCH_2), 57.10, 56.10 (OCH), 54.00 (OCH_3), 171.00 (C=O); ^{31}P NMR (DMSO, relative to H_3PO_4): δ 98.80 (q, $J_{PB} = 161.98$ Hz); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −35.01 (d, $^1J_{BP} = 164.9$ Hz); IR (cm^{-1}, KBr pellet) 2426, 2363 ν(BH); 1651 ν(C=O). Anal. Calcd. for $C_{22}H_{35}O_{10}N_5BP$: C, 46.23; H, 6.13; N, 12.25. Found: C, 46.20; H, 6.15; N, 12.22.

N^4-3′-O-Dibenzoyl-5′-diethylphosphitecarbomethoxyborano-2′-deoxycytidine (7d). The reaction between 0.025 g (0.06 mmol) of N^4, 3′-O-dibenzoyl-2′-deoxycytidine, 0.0139 g (0.06 mmol) of diethylchlorophosphitecarbomethoxyborane and 0.006 g (0.06 mmol) of triethylamine gave 0.032 g (0.028 mmol, 46.6% yield) of N^4-3′-O-dibenzoyl-5′-diethylphosphitecarbomethoxyborano-2′-deoxycytidine (**7d**). Spectroscopic and Analytical Data: ^{1}H NMR (DMSO, relative to Me_4Si): δ 1.36, 1.39 (t, 6H, CH_3), 1.00-1.40 (br, 2H, BH_2), 2.32–2.38 (m, 2H, H-2′), 3.37 (s, 3H, OCH_3), 3.71 (m, 2H, H-5′), 3.91–4.06 (m, 1H, H-4′), 4.17 (m, 4H, OCH_2), 4.58–4.71 (m, 1H, H-3′), 6.04 (d, 1H, H-5), 6.46 (m, 1H, H-1′), 7.91 (d, 1H, H-6), 8.51 (m, 5H, Ar-H), 9.20 (br, s, NH); ^{13}C NMR (DMSO, relative to Me_4Si): δ 15.00 (CH_3), 18.00 (CH_2), 62.00 (OCH_2), 57.90 (OCH), 52.80 (OCH_3), 128.00 (C-Ar), 130.10, 128.70 (CH=CH), 168.90 (C=O); ^{31}P NMR (DMSO, relative to H_3PO_4): δ 99.60 (q, $J_{PB} = 162.87$ Hz); ^{11}B NMR (DMSO, relative to $BF_3{\cdot}OEt_2$) δ −36.82 (d, $^1J_{BP} = 168.1$ Hz); IR (cm^{-1}, KBr pellet) 2391, 2342 ν(BH); 1661 ν(C=O). Anal. Calcd. for $C_{29}H_{35}O_{10}N_3BP$: C, 55.50; H, 5.58; N, 6.70. Found: C, 55.53; H, 5.61; N, 6.67.

Alternative synthesis for N-protected-3′-O-protected-5′-[diethylphosphite (cyano or carbomethoxy)borano]deoxynucleosides (6a–7d). An alternative method for the syntheses of compounds **6a–7d** involved the condensation of the diethylphosphite(cyano or carbomethoxy)borane (**8a, b**) with the N- and O-protected deoxynucleosides in the presence of the coupling agent dicyclohexylcarbodiimide (DCC), following the general method described by Hall and coworkers[10] (see Sch. 3). N^6, 3′-O-dibenzoyl-2′-deoxyadenosine (0.027 g, 0.06 mmol), 3′-acetylthymidine (0.35 g, 1.24 mmol), N^2-isobutyryl-3′-acetyl-2′-deoxyguanosine (50.0 mg, 0.13 mmol), or N^4, 3′-O-dibenzoyl-2′-deoxycytidine (25.0 mg, 0.06 mmol) respectively, diethylphosphitecyanoborane[23] (10.6 mg, 0.06 mmol), (0.22 g, 1.24 mmol), (23.0 mg, 0.13 mmol) and (10.6 mg, 0.06 mmol) respectively and dicyclohexylcarbodiimide (25 mg, 0.12 mmol), (0.51 g, 2.48 mmol), (53.64 mg, 0.26 mmol), (25 mg, 0.12 mmol) respectively were dissolved in anhydrous acetonitrile and the mixture was stirred at room temperature for 48 h. After this period of time another equivalent of DCC was added to the reaction mixture and the stirring continued for additional 24 h. The reaction mixture was then filtered and the solvent was removed under reduced pressure. The resulting residue was redissolved in *ca*. 40 mL of dichloromethane and washed repeatedly with water (3×30 mL). The organic layer in the extract was then dried with $MgSO_4$, filtered and the solvent removed under reduced pressure. The resulting oily product was purified by flash chromatography on silica gel using a solvent mixture of ethyl acetate:hexane (9:1). The product amounts and percent yields are: N^6-3′-O-dibenzoyl-5′-diethylphosphitecyanoboranodeoxyadenosine (**6a**), 33 mg, 96.5% yield; 3′-O-acetyl-5′-diethylphosphitecyanoborano-2′-deoxythymidine (**6b**), 0.264 g, 47.2% yield; N^2-isobutyryl-3′-O-acetyl-5′-diethylphosphite-cyanoborano-2′-deoxyguanosine (**6c**), 38 mg, 49.7% yield; N^4-3′-O-dibenzoyl-5′-diethylphosphite-cyanoborano-2′-deoxycytidine (**6d**), 30 mg, 93.9% yield; N^6-3′-O-dibenzoyl-5′-diethylphosphitecarbomethoxyboranodeoxyadenosine (**7a**), 31.5 mg, 80.0% yield; 3′-O-acetyl-5′-diethylphosphite-carbomethoxyborano-2′-deoxythymidine (**7b**), 0.261 g, 43.5% yield; N^2-isobutyryl-3′-O-acetyl-5′-diethylphosphitecarbomethoxyborano-2′-deoxyguanosine (**7c**), 29.5 mg, 38.4% yield; N^4-3′-O-dibenzoyl-5′-diethylphosphite-carbomethoxyborano-2′-deoxycytidine (**7d**), 30 mg, 43.3% yield. The spectral and analytical data for these products were essentially identical to those of the compounds produced in Sch. 1.

CONCLUSIONS

This report describes the syntheses of new boranopyrophosphates and nucleic acids containing P-BH_2X bonds. Use of substituted boranes, which are less reducing and should prove to be less toxic than analogous compounds containing BH_3 groups, greatly increases the scope and applications

of this class of boronated biomolecules. Several pyrophosphate analogues have been shown to possess antiviral activity against the growth of Herpes virus as well as other viruses.[24] Hence, in addition to being versatile synthons, the boranopyrophosphates reported herein could prove to be important therapeutic agents. Since several of the reaction sequences in Schs. 1–3 are general ones, they should provide the rationale for the syntheses of as yet unknown nucleic acid derivatives. The pharmacological properties of the compounds described in this report are currently under investigation and will be reported elsewhere.

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