Synthesis of 2'-Allyl-2'-Deoxynucleosides by Radical Reactions

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2'-α-Allyl-2'-deoxynucleosides derived from uridine, cytidine, adenosine and guanosine have been synthesized in high overall yields by photolysis of appropriately protected 2'-O-phenoxythiocarbonyl derivatives in the presence of allyltributylstannane.

The 2'-allyl-2'-deoxynucleosides were 5'-O-DMT-protected and converted into 2'-deoxynucleoside 3'-O-phosphoramidites to serve as monomers for oligonucleotides.

'Antisense' oligonucleotides are designed to interfere specifically with an mRNA for the control of cellular and viral gene expression.[1] Cleavage by cellular nucleases in modified oligonucleotides can be avoided by replacement of the phosphodiester linkage by a functionalized carbon bridge or an amide-type bridge.[2-4] Modifications in the sugar moiety is an alternative approach, whereas the nucleoside base has to be left untouched in order not to impair the essential hydrogen bonding between base pairs. When our work started, 2'-O-alkylated (up to C₄) ribonucleosides had been established as promising monomers for antisense oligonucleotides. The thermodynamic stability of the duplex between a 2'-OMe modified oligonucleotide and its complementary oligonucleotide strand was higher than for the unmodified DNA/RNA duplex, combined with increased resistance to nucleases and high specific binding.[5] Because the binding specificity is usually higher for unsaturated than for saturated alkyl derivatives,[6] work was initiated on 2'-deoxy derivatives with an unsaturated alkyl group in the C-2' position of the nucleosides uridine, cytidine, adenosine and guanosine. The target molecules were 2'-allyl-2'-deoxynucleosides appropriately protected and activated for

coupling as 3'-phosphoramidites for assembly into 2'-allyl-2'-oligodeoxynucleotides. Side-chain unsaturation directly onto the sugar in the 2'-position is available by Wittig reactions with 2'-oxonucleosides as reported for 2'-methylene derivatives.[7] Saturated or unsaturated alkyl groups can be introduced into 2'-deoxy-2'-oxonucleosides by organometallic reagents. The subsequent removal of the β-hydroxy group formed in the reaction, however, is known to cause problems.[8] A recent alternative is the intramolecular stereocontrolled free-radical cyclisation reaction using a silicon-bearing allyl group tethered to a 3'-hydroxy group. The allyl group adds onto a radical at the vicinal 2'-center which is generated from the corresponding phenyl selenide.[9] We wanted to allylate the nucleoside directly by a simple intermolecular process. Initially a bromine in the 2'-position in 2'-deoxyuridine was tried, in part because the 2'-bromo intermediate (2) is readily available from a reaction between uridine and acetyl bromide.[10]

Azoisobutyronitrile (AIBN) was used as a radical initiator in the reaction between the bromide (2) and allyltributylstannane. The reaction was slow, and was terminated after reflux in toluene for 5 days; the allylated
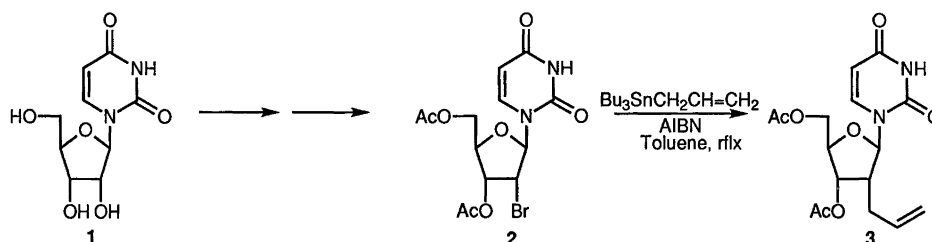
Scheme 1.

product **3** was isolated in 28% yield. The coupling constant between H-1' and H-2' in the ¹H NMR spectrum was 2.2. Hz as expected for an α-configuration at C-2'.[11]

In the search for a more efficient method for 2'-allylation, the 2'-phenoxythiocarbonyl derivatives **5** were prepared and photolyzed in the presence of allyltributylstannane. Free radical allylation reactions using allylstannanes have the advantages of tolerating quite complex functionalities in the substrate and being stoichiometric in reagents.[12] This methodology had been applied successfully to the synthesis 3'-deoxy-3'-allylthymidine and the 2'-deoxyuridine analogue.[13] Very recently the same methodology has become popular for the preparation of allyl intermediates for bridging pyrimidine nucleosides units after various chemical manipulations of the allyl group.[2,14]

On completion of our experimental work, a synthesis of 2'-allyl-2'-deoxyuridine (**7a**) was reported essentially by the same methodology which we had used for the preparation of both pyrimidine and purine derivatives.[15]

The synthetic sequence was started with protection of the 3'-OH and the 5'-OH as silyl derivatives (**4**) by reaction with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane in pyridine. For the allylation reaction, no protection of the functional groups in the pyrimidine or purine bases was used, except for the 2-amino group in guanosine which was converted into the N,N-dimethylaminomethylene derivative **1d** to improve solubility. The amidination reaction was effected by DMF dimethyl acetal.[16]

Several thiono derivatives have been used in radical-initiated deoxygenation reactions in carbohydrate derivatives.[17] Phenylthioxo-derivatives are well suited because of good reactivity of phenylthionylcarbonyl chloride with secondary alcohols, and because the resulting thionocar-

bonate undergoes clean photolytic cleavage.[18] The thiocarbonylation using excess 4-dimethylaminopyridine (DMAP) as a base proceeded chemoselectively; no acylation of the amino groups in cytidine or adenosine was observed. Yield of isolated products **5** were ca. 80%.

Photolysis of the thiono derivatives **5** was effected using a 125 W medium-pressure Hg lamp with the main emission band at 365–366 nm. For the illumination, a quartz tube of inner diameter 5 mm was used as the reaction vessel. Stirring was effected by bubbling N₂ gas through the tube. Under these conditions the reaction was slow (4 days) except for the uridine derivative (6 h). The allylated product **6**, however, was isolated in 71–78%. A clean stereochemical course gave the 2'-α-allyl derivative. The assignment was based on a weak coupling between H-1' and H-2' in the ¹H NMR spectrum;[11] in the uridine **6a** and the adenosine **6c** the coupling constants were 2.2 and 4.0 Hz, respectively, whereas H-1' appeared as a singlet in the spectra of the cytidine **6b** and the guanosine **6d**. The stereochemical assignment is tentative because the endocyclic $^3J_{HH}$ of the pentose sugar is also expected to be affected to some extent by preferential conformation. Desilylation of **6** by tetrabutylammonium fluoride (TBAF) in dry THF produced nucleosides **7** in 90–96% yield. We thus have a reaction sequence from ribonucleosides to 2'-allyl-2'-deoxyribonucleosides with high overall yields.

The allylated deoxynucleosides **7**, except for the uridine analogue **7a**, carry protection on an amino group because these compounds were designed as intermediates in projected oligonucleotide syntheses. Benzoylation of the amino group in cytosine or adenosine is compatible with the methodology for automated oligonucleotide synthesis. The benzoylation was carried out on the silyl-protected

Scheme 2.

B =   **a** Uracil   **b** Cytosine   **c** Adenine   **d** N²-Dimethyl-aminomethylideneguanine
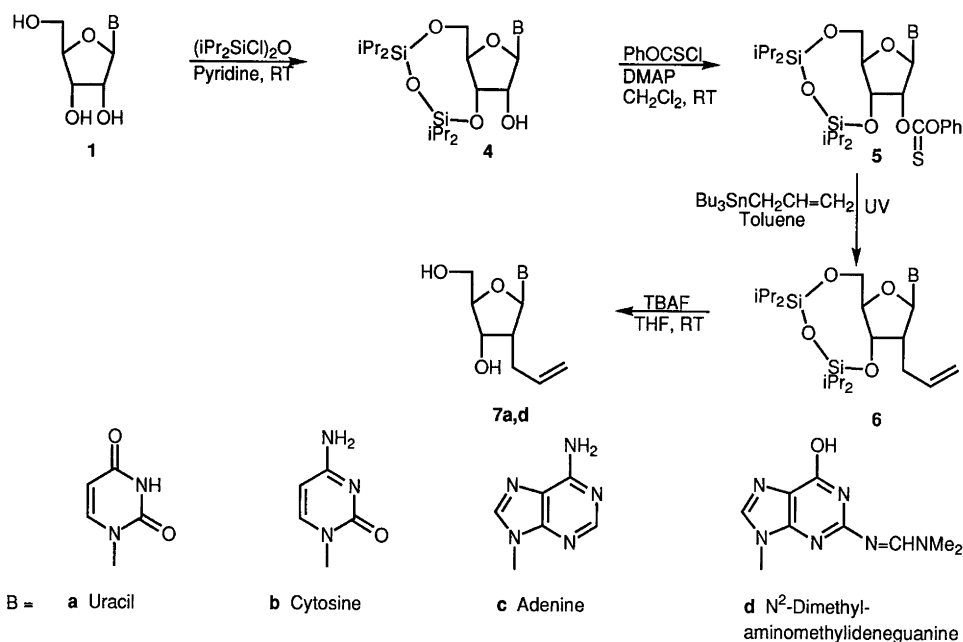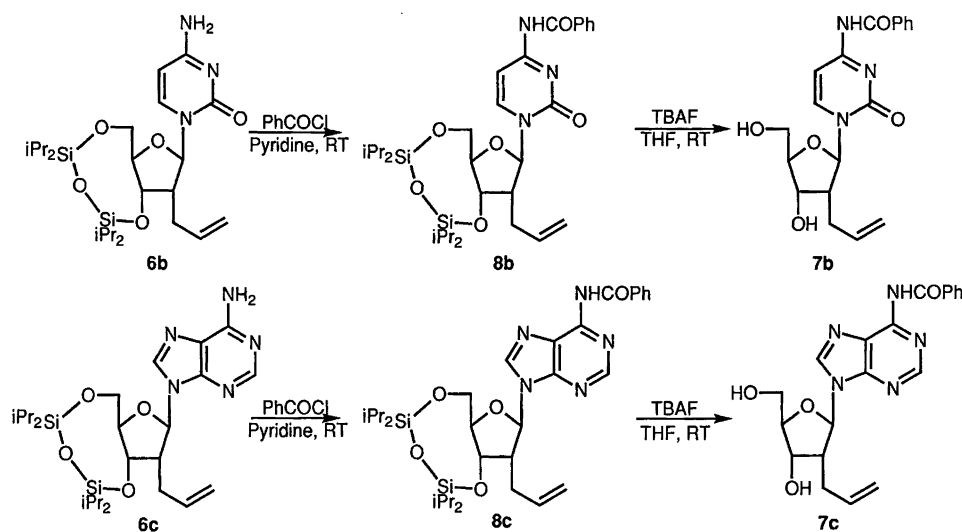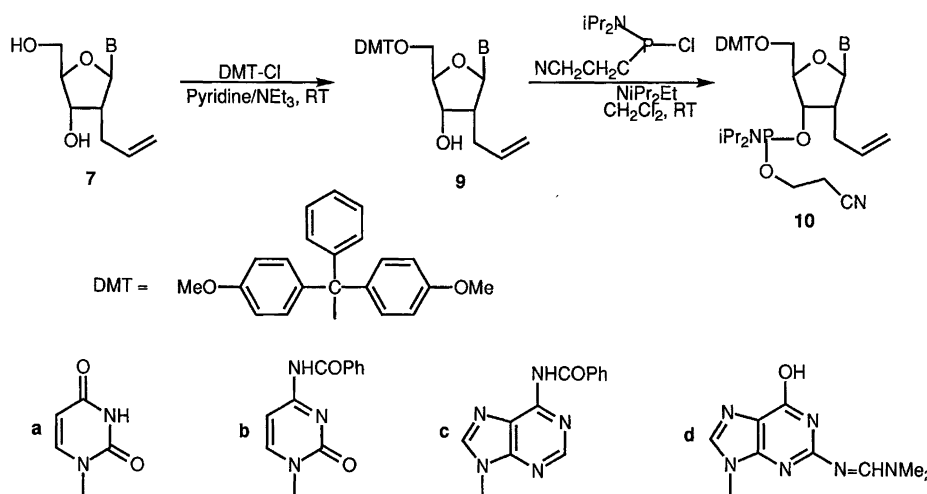
Scheme 3.

compounds **6b** and **6c** to avoid *O*-acylation. The benz-amides **8b** and **8c** were desilylated by TBAF (*vide supra*). The 2-amino group of guanosine was amidinated before any further manipulation of the monomer (*vide supra*). Amidination rather than amidation was used for protection of guanosine because the amidine groups stabilized 2'-deoxypurine nucleosides against the acid-catalyzed depurination.[16,19]

The 5'-OH group in the nucleosides **7** was protected as the 4,4'-dimethoxytrityl (DMT) derivatives which have optimal acid sensitivity for the use in oligonucleotide synthesis.[20] The trityl derivatives **9** were isolated in 81–83% yields from **7**. Subsequently, the 3'-hydroxy group in **9** was phosphitylated to produce the 2-cyanoethyl phosphoramidites **10** for subsequent use in automated oligonucleotide synthesis.[21] The products **10** are acid sensitive, and were isolated and purified by chromatography on silica by including 2% triethylamine in the eluent; yields were in the range 79–89%.

Experimental

The ¹H and ¹³C NMR spectra were recorded on a Varian XL-300 or a Varian Gemini-200 instrument. The ³¹P NMR spectra were recorded on a Bruker AM250 spectrometer. APT, DEPT and HECTOR have been used in the assignment of the signals.

2'-Allyl-2'-deoxy-3',5'-di-O-acetyluridine (3). Allyltributyl-stannane (0.4 ml, 1.29 mmol) was added to a solution of 2'-bromo-2'-deoxy-3',5'-di-*O*-diacetyluridine[10] (0.253 g, 0.65 mmol) and AIBN (0.011 g, 0.07 mmol) under N₂ in degassed, dry toluene (3 ml), and the reaction mixture was heated under reflux for 5 days. Fresh AIBN (0.07 mmol) was added in three portions in one-day intervals. The solvent was distilled off after 5 days, the residue extracted with dichloromethane (25 ml), the solution shaken with 1 M NaHCO₃ (50 ml) and the dried (Na₂SO₄) solution evaporated. The product was purified

Scheme 4.

by chromatography on silica gel (75 g) using light petroleum–EtOAc (3:1) yield 0.065 g (28%) of a non-crystalline solid. Anal.: C, H. ^{1}NMR (CDCl$_3$): δ 2.17 and 2.19 (6 H, s, 2 × Ac), 2.2 (2 H, m, CH$_2$-all), 2.6 (1 H, m, H-2′), 4.02 (1 H, m, H-4′), 4.09 (1 H, dd, $J_{4',5'}$ 2.9 Hz, $J_{5',5'}$ 13.1 Hz, H-5′), 4.21 (1 H, dd, $J_{4',5'}$ 2.7 Hz, H-5′), 5.09 (2 H, t, CH$_2$-all), 5.67 (1 H, $J_{5,6}$ 8.1 Hz, H-5), 5.78 (1 H, d, $J_{1',2'}$ 2.2 Hz, H-1′), 5.92 (1 H, m, CH =), 7.73 (1 H, d, J 8.1 Hz, H-6), 9.41 (1 H, NH). ^{13}C NMR (CDCl$_3$): δ 20.68 and 20.80 (2 × COCH_3), 29.92 (C-2′), 31.29 (CH$_2$-all), 62.58 (C-5′), 70.77 (C-3′), 83.52 (C-4′), 90.96 (C-1′), 103.31 (C-5), 117.16 (CH$_2$ =), 136.05 (CH =), 138.93 (C-6), 150.03 (C-2), 162.68 (C-4), 169.71 (CO), 170.07 (CO).

General procedure for the preparation of 3′,5′-O-(1,1,3,3-tretraisopropyldisiloxane-1,3-diyl)nucleosides **(4)**. 1,3-Dichloro-1,1,3,3-tetraisopropyldisiloxane (5.25 mmol) was added to a solution of the nucleoside (5 mmol) in dry pyridine (8 ml) at ambient temperature under N$_2$. TLC monitoring showed the reaction to be complete after ca. 3 h. Excess of the reagent was then decomposed by addition of MeOH (1 ml) and the solvents evaporated off at reduced pressure. The residue was extracted with ethyl acetate (40 ml), the solution shaken with 1 M NaHCO$_3$ (2 × 75 ml) and the dried (NaSO$_4$) organic phase evaporated. The product was isolated and purified by column chromatography on silica gel as described below.

3′,5′-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)uridine **(4a)**. Light petroleum–EtOH (1:1) was used as the eluent in chromatography; yield 90% of a non-crystalline solid.

^{1}H NMR (CDCl$_3$): δ 0.9–1.15 (4 × Pr^i), 3.2 (2′-OH), 3.95 (1 H, dd, $J_{4',5'}$ 2.3 Hz, $J_{5',5'}$ 13.0 Hz, H-5′), 4.1–4.2 (2 H, m, H-2′,4′), 4.19 (1 H, dd, $J_{4',5'}$ 1.75 Hz, H-5′), 4.31 (1 H, dd, J 4.6 Hz, J 8.6 Hz, H-3′), 5.69 (1 H, J 5,6 8.1 Hz, H-5), 5.73 (1 H, s, H-1′), 7.74 (1 H, d, J 8.1 Hz, H-6), 9.98 (NH). ^{13}C NMR (CDCl$_3$): δ 14.2–15.05 and 18.4–19.05 (Pr^i), 29.49 (C-5′), 70.01 (C-3′), 76.09 (C-2′), 82.81 (C-4′), 91.77 (C-1′), 102.56 (C-5), 140.14 (C-6), 150.02 (C-2), 163.08 (C-4).

3′,5′-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)cytidine **(4b)**. EtOH–CHCl$_3$ (12:88) was used as the eluent in chromatography; yield 87% of a non-crystalline solid. Anal.: C$_{21}$H$_{39}$N$_3$O$_6$Si$_2$: C, H. ^{1}H NMR (CDCl$_3$): δ 1.0–1.15 (m, 4 × Pr^i), 4.04 (1 H, dd, $J_{4',5'}$ 2.4 Hz, $J_{5',5'}$ 13.3 Hz, H-5′), 4.1 (1 H, m, H-2′), 4.2 (3 H, m, H-3′,4′,5), 5.68 (1 H, s, H-1′), 5.78 (1 H, d, $J_{5,6}$ 7.5 Hz, H-5), 7.94 (1 H, d, J 7.5 Hz, H-6). ^{13}C NMR (CDCl$_3$): δ 12.2–13.3 and 16.6–117.3 (4 × Pr^i), 59.71 (C-5′), 67.88 (C-3′), 74.76 (C-2′), 81.44 (C-4′), 91.33 (C-1′), 94.08 (C-5), 140.76 (C-6), 155.95 (C-2), 165.66 (C-4).

3′,5′-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-adenosine **(4c)**. EtOH–CH$_2$Cl$_2$ (5:95) was used as the eluent in chromatography; yield 91% of non-crystalline

product. Anal.: C$_{22}$H$_{39}$N$_5$O$_5$Si$_2$: C, H. ^{1}H NMR (CDCl$_3$): δ 1.1 (m, 4 × Pr^i), 3.52 (1 H, br s, 2′-OH), 4.03 (3 H, m, H-4′,5′), 4.26 (2 H, dd, J 5.5 Hz, J 5.4 Hz, H-2′), 5.1 (1 H, m, H-3′), 5.91 (2 H, NH$_2$), 5.99 (1 H, s, H-1′), 7.99 (1 H, s, H-2), 8.30 (1 H, s, H-8). ^{13}C NMR (CDCl$_3$): δ 12.6–13.3 and 16.8–17.7 (Pr^i), 61.68 (C-5′), 70.71 (C-3′), 75.08 (C-2′), 82.81 (C-4′), 89.68 (C-1′), 102.30 (C-5), 120.53 (C-5), 139.58 (C-8), 149.14 (C-4), 152.76 (C-6), 155.35 (C-2).

3′,5′-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-N^2-dimethylaminomethyleneguanosine **(4d)**. N^2-Dimethylaminomethyleneguanosine was prepared from guanosine and N,N-dimethylformamide dimethylacetal in methanol.[16]

After protection, the product was silylated as described above and the product was isolated and purified by column chromatography on silica gel using a gradient of MeOH (1–5%) in CH$_2$Cl$_2$; yield 87% of a non-crystalline material. Anal.: C$_{25}$H$_{44}$N$_6$O$_6$Si$_2$: C, H. ^{1}H NMR (CDCl$_3$): δ 1.1 (m, 4 × Pr^i), 3.07 and 3.17 (Me$_2$N), 4.03 (3 H, m, H-4′,5′), 4.38 (1 H, d, J 5.2 Hz, H-2′), 4.56 (1 H, m, H-3′), 6.03 (1 H, d, J 1.4 Hz, H-1′), 7.78 (1 H, s, H-8), 8.59 (1 H, s, CH-N), 9.83 (NH). ^{13}C NMR (CDCl$_3$): δ 12.5–13.3 and 16.8–17.4 (4 × Pr^i), 35.10 and 41.32 (Me$_2$N), 61.14 (C-5′), 70.19 (C-3′), 75.33 (C-2′), 81.75 (C-4′), 87.90 (C-1′), 120.45 (C-5), 135.38 (C-8), 149.14 (C-4), 156.89 (C-2), 158.12 (C-6).

General procedure for the preparation of 3′,5′-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2′-O-(phenoxy-thiocarbonyl)nucleosides **(5)**. A solution of 3′,5′-O-(tetraisopropyldisiloxane-1,3-diyl)nucleoside **(4)** (2 mmol) and DMAP (13 mmol) in dichloromethane (15 ml) under N$_2$ was cooled to 0°C and chlorothioformate (2.2 mmol) added. The reaction mixture was stirred at ambient temperature for 6 h before the reaction was stopped by addition of water (25 ml). The mixture was shaken with dichloromethane (2 × 25 ml), the dried (MgSO$_4$) dichloromethane solution evaporated and the residue was subjected to column chromatography on silica gel (*vide infra*).

3′,5′-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-2′-O-(phenoxythiocarbonyl)uridine **(5a)**. Stepwise gradient of MeOH–CH$_2$Cl$_2$ (2:98 v/v, then 5:95 v/v) was used as the eluent in chromatography; yield 90% of a non-crystalline solid. Anal.: C$_{28}$H$_{42}$N$_2$O$_8$SSi$_2$: C, H. ^{1}H NMR (CDCl$_3$): δ 1.05 (m, 4 × Pr^i), 4.05 (1 H, dd, $J_{5',5'}$ 13.4 Hz, H-5′), 4.1 (1 H, m, H-4′), 4.26 (1 H, dd, $J_{4',5'}$ 2.45 Hz, $J_{5',5'}$ 13.4 Hz, H-5′), 4.5 (1 H, m, H-3′), 5.74 (1 H, J 5,6 8.0 Hz, H-5), 5.95 (1 H, s, H-1′), 6.01 (1 H, d, J 4.6 Hz, H-2′), 7.1/7.3/7.4 (Ph), 7.74 (1 H, d, J 8.1 Hz, H-6), 8.87 (NH). ^{13}C NMR (CDCl$_3$): δ 12.8–13.4 and 16.9–17.4 (Pr^i), 59.48 (C-5′), 68.15 (C-3′), 82.24 (C-2′), 83.76 (C-4′), 88.58 (C-1′), 102.30 (C-5), 121.75/126.67/129.55/153.44 (Ph), 139.47 (C-6), 149.52 (C-2), 162.90 (C-4), 196.72 (CS).

3',5'-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-2'-O-(phenoxythiocarbonyl)cytidine (5b). EtOAc was used as the eluent in chromatography; yield 82% of a non-crystalline yellowish solid. Anal.: $C_{28}H_{43}N_3O_7SSi_2$: C, H. ^{1}H NMR (CDCl$_3$): δ 1.05 (4 × Pr^i), 4.02 (1 H, dd, $J_{5',5'}$ 13.4 Hz, H-5'), 4.08 (1 H, m, H-4'), 4.24 (1 H, dd, $J_{4',5'}$ 2.50, $J_{5',5'}$ 13.4 Hz, H-5'), 4.49 (1 H, m, H-3'), 5.79 (1 H, $J_{5,6}$ 7.5 Hz, H-5), 5.98 (1 H, s, H-1'), 6.01 (1 H, d, J 4.6 Hz, H-2'), 7.1/7.3/7.4 (Ph), 7.77 (1 H, d, J 7.5 Hz, H-6). ^{13}C NMR (CDCl$_3$): δ 12.8–13.4 and 16.9–17.5 (Pr^i), 59.75 (C-5'), 68.36 (C-3'), 82.04 (C-2'), 84.17 (C-4'), 88.85 (C-1'), 94.78 (C-5), 121.85/126.53/129.50/153.51 (Ph), 140.52 (C-6), 155.23 (C-2), 165.92 (C-4), 193.64 (CS).

3',5'-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-2'-O-(phenoxythiocarbonyl)adenosine (5c). Light petroleum–EtOAc (1:2) was used as the eluent in chromatography; yield 93% of a non-crystalline yellowish solid. Anal.: $C_{28}H_{43}N_3O_7SSi_2$: C, H. ^{1}H NMR (CDCl$_3$): δ 1.09 (m, 4 × Pr^i), 4.1 (3 H, m, H-4',5'), 5.3 (1 H, m, H-3'), 6.07 (1 H, s, H-1'), 6.36 (1 H, d, J 5.4 Hz, H-2'), 7.1/7.3/7.4 (Ph), 8.03 (1 H, s, H-2), 8.31 (1 H, s, H-8). ^{13}C NMR (CDCl$_3$): δ 12.8–13.3 and 16.9–17.4 (Pr^i), 60.32 (C-5'), 69.31 (C-3'), 82.11 (C-2'), 84.02 (C-4'), 87.33 (C-1'), 120.40 (C-5), 121.72/126.77/129.61/153.35 (Ph), 139.90 (C-8), 149.70 (C-4), 152.15 (C-6), 155.03 (C-2), 193.96 (CS).

3',5'-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-N^2-dimethylaminomethylene-2'-O-(phenoxythiocarbonyl)guanosine (5d). Gradient of MeOH (1–3%) in CH$_2$Cl$_2$ was used as the eluent in chromatography; yield 87% of a non-crystalline yellowish product. Anal.: $C_{32}H_{48}N_6O_8SSi_2$: C, H. ^{1}H NMR (CDCl$_3$): δ 1.07 (m, 4 × Pr^i), 3.09 (Me$_2$N). 4.2 (3 H, m, H-4',5'), 4.65 (1 H, m, H-3'), 6.10 (1 H, s, H-1'), 6.45 (1 H, d, J 4.6 Hz, H-2'), 7.1/7.3/7.4 (Ph), 7.89 (1 H, s, H-8), 8.64 (CHN), 9.35 (NH). ^{13}C NMR (CDCl$_3$): δ 12.5–13.5 and 16.7–17.5 (Pr^i), 35.16 and 41.27 (NMe$_2$), 60.31 (C-5'), 68.99 (C-3'), 82.32 (C-2'), 84.20 (C-4'), 86.71 (C-1'), 121.19 (C-5), 121.69/126.77/129.56/153.37 (Ph), 135.33 (C-8), 149.20 (C-4), 157.02 (C-2), 157.79 (C–N), 158.60 (C-6), 194.01 (CS).

General procedure for the preparation of 2'-allyl-2'-deoxy-3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-nucleosides (6). The apparatus consisted of a quartz tube of 5 mm inner diameter. Stirring was effected by bubbling dry N$_2$ through the toluene solution in the glass tube. The solvent level was kept constant in the reaction tube by allowing the gas to become solvent saturated by passing it through dry and degassed toluene immediately before entering the reaction tube. The light source was 125 W 'medium-pressure Hg lamp' (Applied Photophysics, max. emission at 365–366 nm, less intense bands at 265, 297, 303, 313 and 334 nm).

Allyltributylstannane (3 mmol) was added to a solution of the 3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-

2'-O-(phenoxythiocarbonyl)nucleoside (5) (1.5 mmol) in dry and degassed toluene (2 ml). N$_2$ was slowly bubbled through the tube to effect stirring. Some precipitate may gradually deposit on the wall side facing the light source in which case the tube should be partly rotated. The progress of the illuminated reacting was monitored by TLC. The reaction required ca. 4 days for completion, except for the uridine where the reaction time was 6 h. The solvent was then removed at reduced pressure, the residue extracted into dichloromethane (50 ml), the solution was shaken with 1 M NaHCO$_3$, dried (Na$_2$SO$_4$) and evaporated. The product was isolated and purified by column chromatography on silica gel (*vide infra*).

2'-Allyl-2'-deoxy-3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)uridine (6a). Stepwise gradient of light petroleum–EtOAc (3:1 v/v, then 2:1 v/v) was used as the eluent in chromatography; yield 72% of a non-crystalline, white solid. Anal.: $C_{24}H_{42}N_2O_6Si_2$: C, H. ^{1}H NMR (CDCl$_3$): δ 1.0 (4 × Pr^i), 2.3 (2 H, m, CH$_2$ =), 2.6 (1 H, m, H-2'), 3.90 (1 H, m, H-4'), 3.96 (1 H, dd, $J_{4',5'}$ 2.8 Hz, $J_{5',5'}$ 13.1 Hz, H-5'), 4.09 (1 H, dd, $J_{4',5'}$ 2.8 Hz, H-5'), 4.47 (1 H, m, H-3'), 5.09 (2 H, t, CH$_2$ =), 5.67 (1 H, d, $J_{5,6}$ 8.1 Hz, H-5), 5.73 (1 H, d, J 2.2 Hz, H-1'), 6.92 (1 H, m, CH =), 7.71 (1 H, d, J 8.1 Hz, H-6), 9.40 (NH). ^{13}C NMR (CDCl$_3$): δ 12.5–13.4 and 16.9–17.5 (4 × Pr^i), 28.21 (C-2'), 30.60 (CH$_2$-all), 60.70 (C-5'), 68.88 (C-3'), 83.36 (C-4'), 88.64 (C-1'), 101.74 (C-5), 117.13 (CH$_2$ =), 135.75 (CH =), 139.75 (C-6), 150.04 (C-2), 163.55 (C-4).

2'-Allyl-2'-deoxy-3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)cytidine (6b). Gradient of EtOH (2–7%) in CH$_2$Cl$_2$ was used in chromatography; yield 71% of non-crystalline white solid. Anal.: $C_{28}H_{43}N_3O_5Si_2$: C, H. ^{1}H NMR (CDCl$_3$): δ 1.05 (m, 4 × Pr^i), 2.44 (2 H, m, CH$_2$-all), 2.69 (1 H, m, H-2'), 4.04 (2 H, m, H-4',5'), 4.22 (1 H, dd, $J_{4',5'}$ 2.7 Hz, $J_{5',5'}$ 13.0 Hz, H-5'), 4.49 (1 H, m, H-3'), 5.13 (2 H, m, CH$_2$ =), 5.87 (1 H, $J_{5',6'}$ 7.5 Hz, H-5), 6.01 (1 H, m, CH =), 7.79 (1 H, d, J 7.5 Hz, H-6). ^{13}C NMR (CDCl$_3$): δ 12.8–13.4 and 16.9–17.5 (4 × Pr^i), 31.11 (C-2'), 48.01 (CH$_2$-all), 60.33 (C-5'), 68.25 (C-3'), 83.51 (C-4'), 90.28 (C-1'), 96.08 (C-5), 117.10 (CH$_2$ =), 126.09 (CH =), 144.78 (C-6), 154.32 (C-2), 162.07 (C-4).

2'-Allyl-2'-deoxy-3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)adenosine (6c). Gradient of EtOH (1–5%) in CH$_3$Cl was used in chromatography; yield 78% of non-crystalline white solid. Anal.: $C_{25}H_{43}N_5O_4Si_2$: C, H. ^{1}H NMR (CDCl$_3$): δ 1.05 (4 × Pr^i), 2.27 (1 H, m, H-2'), 2.68 (2 H, m, CH$_2$-all), 4.03 (3 H, m, H-4',5'), 5.06 (3 H, m, H-3', CH$_2$ =), 5.82 (1 H, m, CH =), 5.96 (1 H, d, J 4.0 Hz, H-1'), 6.08 (NH$_2$), 7.97 (1 H, s, H-2), 8.32 (1 H, s, H-8). ^{13}C NMR (CDCl$_3$): δ 12.7–13.4 and 17.0–17.5 (Pr^i), 30.64 (C-2'), 47.16 (CH$_2$-all), 62.53 (C-5'), 71.50 (C-3'), 84.12 (C-4'), 87.62 (C-1'), 117.29 (CH$_2$ =), 120.23 (C-5), 135.54 (CH =), 139.22 (C-8), 149.40 (C-4), 152.71 (C-6), 155.39 (C-2).

2'-Allyl-2'-deoxy-3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-N²-dimethylaminomethyleneguanosine **(6d)**. Gradient of MeOH (1–3%) in CH₂Cl₂ was used in chromatography; yield 71% of non-crystalline yellowish solid. Anal.: $C_{28}H_{48}N_6O_5Si_2$: C, H. ¹H NMR (CDCl₃): δ 1.05 (m, 4 × Prⁱ), 2.40 (2 H, m, CH₂-all), 2.67 (1 H, m, H-2'), 3.09 (6 H, s, Me₂N), 3.92 (1 H, m, H-4'), 3.98 (1 H, dd, $J_{5',5'}$ 13.0 Hz, H-5'), 4.13 (1 H, dd, $J_{4',5'}$ 2.3 Hz, $J_{5',5'}$ 13.0 Hz), 4.53 (1 H, t, H-3'), 5.17 (2 H, m, CH₂ =), 5.89 (1 H, s, H-1'), 6.10 (CH =), 7.89 (1 H, s, H-8), 8.66 (1 H, CH-N), 9.37 (NH). ¹³C NMR (CDCl₃): δ 12.5–13.5 and 16.7–17.7 (Prⁱ), 30.67 (C-2'), 35.21 and 41.21 (NMe₂), 46.92 (CH₂-all), 60.39 (C-5'), 69.11 (C-3'), 86.02 (C-4'), 90.51 (C-1'), 117.21 (CH₂ =), 121.15 (C-5), 135.27 (C-8), 136.03 (CH =), 149.18 (C-4), 157.19 (C-2), 157.87 (CH-N), 158.65 (C-6).

General procedure for the preparation of 2'-allyl-2'-deoxy-nucleosides **(7)**. 1 M TBAF in dry THF (1.8 ml) was added to a solution of the 2'-allyl-2'-deoxy-3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)nucleoside **(6a,d** or **8b,c)** (0.8 mmol) in dry THF (10 ml) at ambient temperature. TLC monitoring showed that the reaction was complete after 6–7 min. The reaction mixture was then evaporated to dryness, the residue extracted into EtOAc (30 ml), the solution shaken with 1 M NaHCO₃ (30 ml), dried (Na₂SO₄) and evaporated. The product was isolated and purified by column chromatography on silica gel (*vide infra*).

2'-Allyl-2'-deoxyuridine **(7a)**. MeOH–CH₂Cl₂ was used as the eluent in chromatography; yield 96% of a white solid. Anal.: $C_{12}H_{16}N_2O_5$: C, H. ¹H NMR (CD₃OD): δ 2.14 (1 H, m, H-2'), 2.39 (2 H, m, CH₂-all), 3.72 (2 H, d, *J* 3.6 Hz, H-5'), 3.97 (1 H, m, H-4'), 4.26 (1 H, d, *J* 5.2 Hz, H-3'), 5.00 (2 H, m, CH₂ =), 5.71 (1 H, d, $J_{5,6}$ 8.2 Hz, H-5), 5.7 (1 H, m, CH =), 6.05 (1 H, d, *J* 9.0 Hz, H-1'), 7.94 (1 H, d, *J* 8.2 Hz, H-6). ¹³C NMR (CD₃OD): δ 30.24 (C-2'), 50.12 (CH₂-all), 63.79 (C-5'), 74.35 (C-3'), 89.14 (C-4'), 89.84 (C-1'), 103.39 (C-5), 117.01 (CH₂ =), 137.11 (CH =), 142.91 (C-6), 152.91 (C-2), 166.20 (C-4).

2'-Allyl-2'-deoxy-N⁴-benzoylcytidine **(7b)**. Gradient of MeOH (1–10%) in CH₂Cl₂ was used in chromatography; yield 93% of a white solid. Anal.: $C_{19}H_{21}N_3O_5$: C, H. ¹H NMR (CD₃OD): δ 2.15 (1 H, m, H-2'), 2.39 (2 H, m, CH₂-all), 3.75 (2 H, m, H-5'), 4.0 (1 H, m, H-4'), 4.3 (1 H, m, H-3'), 4.9 (2 H, m, CH₂ =), 5.7 (1 H, m, CH =), 6.11 (1 H, d, *J* 7.9 Hz, H-1'), 7.5 (4 H, m, H-5 and Ph), 7.9 (2 H, Ph), 8.39 (1 H, d, *J* 7.6 Hz, H-6). ¹³C NMR (CD₃OD): δ 29.67 (C-2'), 49.98 (CH₂-all), 61.16 (C-5'), 72.34 (C-3'), 87.32 (C-4'), 91.03 (C-1'), 97.80 (C-5), 118.02 (CH₂ =), 127.7/128.8/132.9 (Ph), 135.05 (CH =), 145.46 (C-6), 155.24 (C-2), 162.11 (C-4), 166.57 (CO).

2'-Allyl-2'-deoxy-N⁶-benzoyladenosine **(7c)**. Gradient of EtOH (1–10%) in CH₂Cl₂ was used in chromatography; yield 95% of a white solid. Anal.: $C_{20}H_{21}N_5O_4$: C, H. ¹H NMR (CDCl₃): δ 2.26 (1 H, m, H-2'), 2.7/2.9 (2 H, m, CH₂-all), 4.11 (2 H, m, H-4',5'), 4.29 (1 H, dd, $J_{4',5'}$ 2.4 Hz, $J_{5',5'}$ 13.2 Hz, H-5'), 4.54 (1 H, m, H-3'), 5.1 (2 H, m, CH₂ =), 5.8 (1 H, m, CH =), 5.97 (1 H, d, *J* 4.0 Hz, H-1'), 7.4/7.5/7.9 (Ph), 8.16 (1 H, s, H-2), 8.62 (1 H, s, H-8). ¹³C NMR (CDCl₃): δ 30.85 (C-2'), 46.80 (CH₂-all), 63.45 (C-5'), 73.05 (C-3'), 85.01 (C-4'), 90.34 (C-1'), 117.70 (CH₂ =), 123.11 (C-5), 128.1/128.7/129.5/132.9/134.1 (Ph), 135.57 (CH =), 143.65 (C-8), 150.87 (C-4), 152.11 (C-6), 152.44 (C-2), 165.95 (CO).

2'-Allyl-2'-deoxy-N²-dimethylaminomethyleneguanosine **(7d)**. Gradient of MeOH (1–10%) in CH₂Cl₂ was used in chromatography; yield 90% of a white solid. Anal.: $C_{16}H_{22}N_6O_4$: C, H. ¹H NMR (CD₃OD): δ 2.41 (2 H, m, CH₂-all), 2.69 (1 H, m, H-2'), 3.10 (6 H, s, Me₂N), 3.77 (2 H, d, *J* 3.5 Hz, H-5'), 3.94 (1 H, m, H-4'), 4.39 (1 H, t, H-3'), 5.01 (2 H, m, CH₂ =), 5.76 (CH =), 6.13 (1 H, s, H-1'), 7.93 (1 H, s, H-8), 8.72 (1 H, CH-N), 9.36 (NH). ¹³C NMR (CD₃OD): δ 31.02 (C-2'), 35.19 and 41.24 (NMe₂), 49.40 (CH₂-all), 63.08 (C-5'), 73.11 (C-3'), 84.67 (C-4'), 90.21 (C-1'), 117.09 (CH₂ =), 123.90 (C-5), 133.12 (C-8), 135.58 (CH =), 149.15 (C-4), 156.42 (C-2), 157.16 (CH-N), 158.26 (C-6).

2'-Allyl-2'-deoxy-N⁴-benzoyl-3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)cytidine **(8b)**. Benzoyl chloride (0.20 ml, 1.54 mmol) was added to a solution of 2'-allyl-2'-deoxy-3',5'-O-(1,1,3,3,-tetraisopropyldisiloxane-1,3-diyl)cytidine (360 mg, 0.71 mmol) in dry pyridine (4 ml) under N₂. The reaction mixture was stirred at ambient temperature for 8 h. The mixture was cooled in ice, water (3 ml) and 25% ammonia (aq., 2 ml) were added and the mixture was left to stir for 20 min. The solvents were then removed at reduced pressure, the residue was extracted with dichloromethane (40 ml), and the solution was shaken with 1 M NaHCO₃, dried (Na₂SO₄) and evaporated. The residue was subjected to column chromatography on silica gel (100 g) using hexane–EtOAc (initially 2:1 v/v, then 1:1 v/v) as the eluent; yield 0.396 (91%) as a white solid. Anal.: $C_{31}H_{45}N_3O_6Si_2$: C, H. ¹H NMR (CDCl₃): δ 1.07 (4 × Prⁱ), 2.4 (2 H, m, CH₂-all), 2.7 (1 H, m, H-2'), 4.0 (2 H, m, H-4',5'), 4.22 (1 H, dd, $J_{4',5'}$ 2.7 Hz, $J_{5',5'}$ 13.0 Hz, H-5'), 4.49 (1 H, m, H-3'), 5.13 (2 H, m, CH₂ =), 5.86 (1 H, s, H-1'), 6.11 (1 H, m, CH =), 7.51 (4 H, m, H-5 and Ph), 7.3/7.6 (3 H, Ph), 8.32 (1 H, d, *J* 7.4 Hz, H-6). ¹³C NMR (CDCl₃): δ 12.5–13.4 and 16.9–17.5 (Prⁱ), 30.97 (C-2'), 48.08 (CH₂-all), 60.27 (C-5'), 68.09 (C-3'), 83.31 (C-4'), 90.09 (C-1'), 96.00 (C-5), 116.91 (CH₂ =), 128.08/128.94/133.09 (Ph), 136.00 (CH =), 144.61 (C-6), 154.24 (C-2), 162.04 (C-4), 166.70 (CO).

2'-Allyl-2'-deoxy-N⁶-benzoyl-3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)adenosine **(8c)**. Benzoyl chloride (0.25 ml, 1.93 mmol) was added to a solution of 2'-allyl-

2'-deoxy-3',5'-O-(1,1,3,3,-tetraisopropyldisiloxane-1,3-diyl)adenosine (505 mg, 0.95 mmol) in dry pyridine (8 ml) under N₂. The reaction mixture was stirred at ambient temperature for 4 h. The mixture was cooled in ice, water (3 ml) and 25% ammonia (aq., 2 ml) added and the mixture was stirred for 20 min. The solvents were removed at reduced pressure, the residue extracted with dichloromethane (20 ml), and the solution was shaken with 1 M NaHCO₃, dried (Na₂SO₄) and evaporated. The residue was subjected to column chromatography on silica gel (100 g) using a gradient of EtOH (0–3%) in CHCl₃; yield 0.396 g (89%) as a white solid. Anal.: $C_{32}H_{47}N_5O_5Si_2$: C, H. ¹H NMR (CDCl₃): δ 1.05 (4 × Prⁱ), 2.3 (1 H, m, H-2'), 2.7/2.9 (2 H, m, CH₂-all), 4.0 (3 H, m, H-4',5'), 5.09 (3 H, m, H-3', CH₂ =), 5.78 (1 H, m, CH =), 5.98 (1 H, d, J 4.0 Hz, H-1'), 7.39/7.52/7.86 (Ph), 8.17 (1 H, s, H-2), 8.63 (1 H, s, H-8). ¹³C NMR (CDCl₃): δ 12.7–13.4 and 17.0–17.5 (Prⁱ), 30.87 (C-2'), 46.85 (CH₂-all), 62.20 (C-5'), 71.32 (C-3'), 84.04 (C-4'), 87.87 (C-1'), 117.67 (CH₂ =), 123.34 (C-5), 128.7/129.4/132.92/134.04 (Ph), 135.54 (CH =), 143.66 (C-8), 151.75 (C-4), 152.09 (C-6), 152.42 (C-2), 165.95 (CO).

General procedure for the preparation of 2'-allyl-2'-deoxy-5'-O-(4,4'-dimethoxytrityl)nucleosides (9). 4,4'-Dimethoxytrityl chloride (0.77 mmol) and triethylamine (1.6 mmol) were added to a solution of the 2'-allyl-2'-deoxynucleoside (7) (0.70 mmol) in dry pyridine (8 ml) under N₂. The reaction mixture was stirred at ambient temperature for 1 h. The reaction was quenched by addition of methanol (1 ml) and the mixture evaporated to dryness at reduced pressure. The residue was extracted with EtOAc (20 ml) and the solution was shaken with 1 M NaHCO₃(20 ml), dried (Na₂SO₄) and evaporated. The product was isolated and purified by column chromatography on silica gel (*vide infra*).

2'-Allyl-2'-deoxy-5'-O-(4',4'-dimethoxytrityl)uridine (9a). Light petroleum–EtOAc (1:1) containing 1% NEt₃ was used as the eluent in chromatography; yield 81% of a white solid. Anal.: $C_{33}H_{34}N_2O_7$: C, H. ¹H NMR (CDCl₃): δ 2.2 (1 H, m, H-2'), 2.46 (2 H, m, CH₂-all), 3.42 (2 H, m, H-5'), 3.78 (6 H, 2 × OMe) 4.11 (1 H, m, H-4'), 4.4 (1 H, m, H-3'), 5.14 (2 H, m, CH₂ =), 5.40 (1 H, d, J 1.2 Hz, H-1'), 5.75 (1 H, m, CH =), 6.12 (1 H, d, $J_{5,6}$ 8.2 Hz, H-5), 6.8–7.4 (13 H, Ar), 7.66 (1 H, d, J 8.2 Hz, H-6), 8.81 (NH). ¹³C NMR (CDCl₃): δ 28.34 (CPh₃), 28.50 (C-2'), 48.99 (CH₂-all), 63.89 (C-5'), 73.51 (C-3'), 85.74 (C-4'), 87.90 (C-1'), 102.67 (C-5), 113.31/127.78/128.35/129.14/130.08/135.28/144.25/158.79 (DMTr), 117.15 (CH₂ =), 135.14 (CH =), 140.29 (C-6), 150.53 (C-2), 163.11 (C-4).

2'-Allyl-2'-deoxy-N⁴-benzoyl-5'-O-(4,4'-dimethoxytrityl)-cytidine (9b). Light petroleum–EtOAc (1:1) containing 1% NEt₃ was used as the eluent in chromatography; yield 80% of a white solid. Anal.: $C_{40}H_{39}N_3O_7$: C, H. ¹H NMR (CDCl₃): δ 2.41 (2 H, m, CH₂-all), 2.68 (1 H, m,

H-2'), 3.80 (6 H, 2 × MeO), 4.05 (2 H, m, H-4',5'), 4.22 (1 H, dd, $J_{4',5'}$ 2.4 Hz, $J_{5',5'}$ 13.1 Hz, H-5'), 4.47 (1 H, m, H-3'), 5.12 (2 H, m, CH₂ =), 5.87 (1 H, s, H-1'), 6.1 (1 H, m, CH = all), 6.75–7.3 (13 H, DMTr), 7.5–7.9 (6 H, m, H-5 and Ph), 8.34 (1 H, d, J 7.6 Hz, H-6). ¹³C NMR (CDCl₃): δ 28.40 (CPh₃), 30.94 (C-2'), 48.05 (CH₂-all), 55.20 (MeO), 60.28 (C-5'), 68.11 (C-3'), 83.67 (C-4'), 90.10 (C-1'), 96.00 (C-5), 117.04 (CH₂ =), 113.04 / 127.03 / 127.60 / 127.89 / 128.23 / 128.94 / 129.96 / 133.09/135.10/144.36/158.07 (Ar), 136.00 (CH =), 144.61 (C-6), 154.24 (C-2), 162.07 (C-4), 166.72 (CO).

2'-Allyl-2'-deoxy-N⁶-benzoyl-5'-O-(4,4'-dimethoxytrityl)-adenosine (9c). Light petroleum–EtOAc (1:1) containing 1% NEt₃ was used as the eluent in chromatography; yield 83% of a white solid. Anal.: $C_{41}H_{39}N_5O_6$: C, H. ¹H NMR (CDCl₃): δ 2.27 (1 H, m, H-2'), 2.7/2.9 (2 H, m, (2 H, m, CH₂-all), 3.78 (6 H, 2 × OMe), 4.01 (3 H, m, H-4',5'), 4.30 (1 H, dd, $J_{4',5'}$ 2.4 Hz, $J_{5',5'}$ 13.2 Hz, H-5'), 4.55 (1 H, m, H-3'), 5.08 (2 H, m, CH₂ =), 5.78 (1 H, m, CH =), 5.98 (1 H, d, J 4.0 Hz, H-1'), 6.7–7.2 (13 H, DMTr), 7.4/7.5/7.9 (Ph), 8.17 (1 H, s, H-2), 8.64 (1 H, s, H-8). ¹³C NMR (CDCl₃): δ 29.70 (CPh₃), 30.61 (C-2'), 46.52 (CH₂-all), 55.43 (MeO), 59.20 (C-5'), 71.87 (C-3'), 85.21 (C-4'), 90.42 (C-1'), 113.84/125.59/127.21/ 128.06/130.45/135.59/145.27/158.11 (DMTr), 117.73 (CH₂ =), 122.13 (C-5), 128.8/129.5/132.9/134.1 (Ph), 136.05 (CH =), 144.05 (C-8), 151.45 (C-4), 152.15 (C-6), 153.12 (C-2), 166.20 (CO).

2'-Allyl-2'-deoxy-N²-dimethylaminomethylene-5'-O-(4,4'-dimethoxytrityl)guanosine (9d). Stepwise gradient of light petroleum–EtAOc (2:1 v/v, then 1:1 v/v) containing 1% NEt₃ was used as the eluent in chromatography; yield 81% of a white solid. Anal.: $C_{37}H_{60}N_6O_6$: C, H. ¹H NMR (CDCl₃): δ 2.40 (2 H, m, CH₂-all), 2.69 (1 H, m, H-2'), 3.09 (6 H, s, Me₂N), 3.39 (2 H, m, H-5'), 3.78 (2 × MeO), 4.17 (1 H, m, H-4'), 4.57 (1 H, t, H-3'), 5.15 (2 H, m, CH₂ =), 5.89 (H, s, H-1'), 6.10 (CH =), 6.7–7.4 (13 H, DMTr), 7.88 (1 H, s, H-8), 8.65 (1 H, CH-N), 9.35 (NH). ¹³C NMR (CDCl₃): δ 28.45 (C-2'), 35.23 and 41.27 (NMe₂), 45.86 (CH₂-all), 55.11 (MeO), 61.03 (C-5'), 73.11 (C-3'), 85.88 (C-4'), 89.37 (C-1'), 113.41/ 127.33/128.09/129.12/129.91/135.07/144.19/158.70 (DMTr), 117.06 (CH₂ =), 123.42 (C-5), 133.19 (C-8), 135.58 (CH =), 149.157 (C-4), 155.40 (C-2), 157.09 (CH-N), 158.22 (C-6).

General procedure for the preparation of 2'-allyl-2'-deoxy-3'-O-[(2-cyanoethoxy)diisopropylaminophosphanyl]-5'-O-(4,4'-dimethoxytrityl)nucleoside (10). The 2'-allyl-2'-deoxy-5'-O-(4',4'-dimethoxytrityl)nucleoside (9) (0.50 mmol) was dried by dissolution in dry acetonitrile (30 ml) followed by reevaporation. The residual nucleoside was dissolved in dry dichloromethane (20 ml), ethyldiisopropylamine (0.9 mmol) added and the solution cooled to 0°C. At this temperature, a solution of 2-cyanoethyl diisopropylphosphoramidochloridite (0.76 mmol) in dry dichloro-

methane (10 ml) was added dropwise with stirring over 3 min. TLC monitoring showed the reaction to be compete after ca. 1 h at ambient temperature. The reaction was then quenched by addition of EtOH (5 ml), diluted with dichloromethane (30 ml) and the solution shaken with 1 M NaHCO₃, dried (NaSO₄), and evaporated to dryness. The product was isolated and purified by column chromatography on silica gel (vide infra).

2'-Allyl-2'-deoxy-3'-O-[(2-cyanoethoxy)diisopropyl-aminophosphanyl]-5'-O-(4,4'-dimethoxytrityl)nucleoside (10a). Gradient of EtOH (1–2%) in CH₂Cl₂ containing 2% NEt₃ in chromatography; yield 85% of a white solid. Anal.: $C_{42}H_{51}N_4O_8P$: C, H. ³¹P NMR (CH₂Cl₂; coaxial inner tube for D₂O lock): δ 144.76 and 146.35.

2'-Allyl-2'-deoxy-N⁴-benzoyl-3'-O-[(2-cyanoethoxy)-diisopropylaminophosphanyl]-5'-O-(4,4'-dimethoxy-trityl)cytidine (10b). Gradient of EtOH (0–3%) in CH₂Cl₂ containing 2% NEt₃ was used in chromatography; yield 82% of a white solid. Anal.: $C_{49}H_{56}N_5O_8P$: C, H. ³¹P NMR (CH₂Cl₂; coaxial inner tube for D₂O lock): δ 147.25 and 148.01.

2'-Allyl-2'-deoxy-N⁶-benzoyl-3'-O-[(2-cyanoethoxy)-diisopropylaminophosphanyl]-5'-O-(4,4'-dimethoxy-trityl)adenosine (10c). Gradient of EtOH (0–3%) in CH₂Cl₂ containing 2% NEt₃ was used in chromatography; yield 89% of a white solid. Anal.: $C_{50}H_{56}N_7O_7P$: C, H. ³¹P NMR (CH₂Cl₂; coaxial inner tube for D₂O lock): δ 148.14 and 149.21.

2'-Allyl-2'-deoxy-3'-O-[(2-cyanoethoxy)diisopropyl-aminophosphanyl]-N²-dimethylaminomethylene-5'-O-(4,4'-dimethoxytrityl)guanosine (10c). Gradient of EtOH (0–3%) in CH₂Cl₂ containing 2% NEt₃ was used in chromatography; yield 79% of a white solid. Anal.: $C_{46}H_{78}N_8O_7P$: C, H. ³¹P NMR (CH₂Cl₂; coaxial inner tube for D₂O lock): δ 147.76 and 148.35.

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