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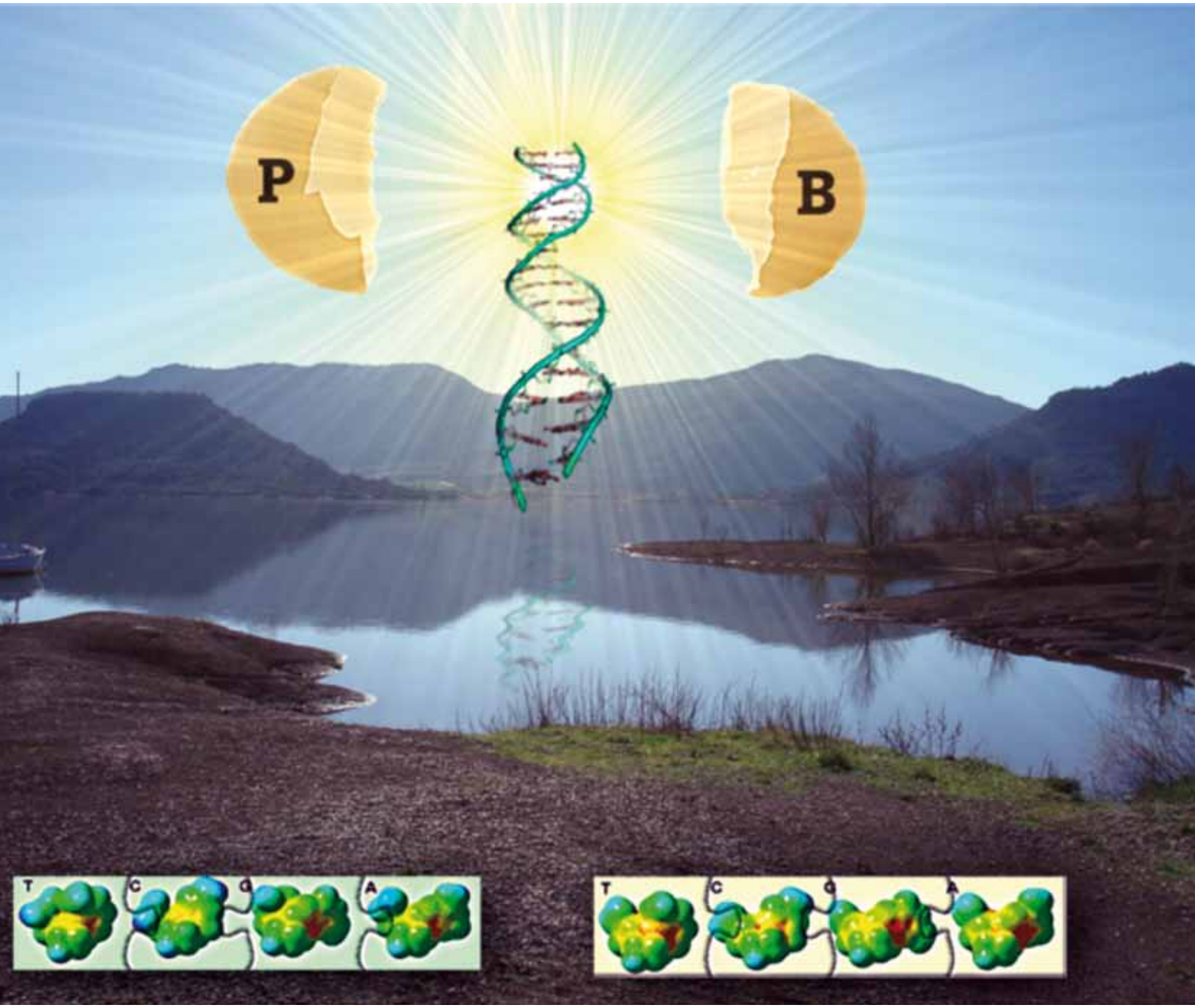

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Expanding the bononucleotide family: synthesis of borono-analogues of dCMP, dGMP and dAMP†

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We previously reported the synthesis of a bononucleotide analogue of thymidine monophosphate and its association towards the formation of a new borono-linked dinucleotide. Here we describe the completion of the set of four 2′-deoxybononucleotide analogues of natural nucleotide monophosphates, namely the previously unknown dCbn, dGbn and dAbn. These analogues were all prepared from the respective 5′-aldehydic nucleosides through a homologation/reduction sequence. The bononucleotides were subsequently obtained by either borylation (dCbn and dGbn) or cross-metathesis (CM) in the presence of the Hoveyda–Grubbs catalyst (dAbn). The reversible formation of the corresponding dinucleotides between these new analogues and uridine was studied by ^{1}H NMR, and semi-empirical calculations were carried out to provide bond length and electrostatic information that assess the structural similarities existing between these bioisosteres and their natural counterparts.

Introduction

The absence of a viable explanation for the prebiotic synthesis of RNA has led most researchers to conclude that RNA was preceded by one or more proto-RNA assembled from simple precursor molecules.[1,2] If the chemical structure of RNA has been modified over the course of evolution, the problem remains of how these ancestral RNA-like polymers came into existence and under which reaction medium. In this context, the recent discovery of the stabilization of ribose by borate rehabilitated the hypothesis that life might have originated under highly alkaline conditions.[3–7] These findings provide a justification for the stabilization and selection of ribose in prebiotic conditions. The abundance of boron and its presence in deep-ocean hydrothermal fluids further emphasized the plausibility of its role in the RNA-world theory.[8] Additionally, these results pave the way for the stabilization of more complex structures such as nucleosides and nucleotides but the subsequent stages of nucleotide assembly, such as the phosphorylation of the pentose C5 hydroxyl group, still need to be addressed.[6] Indeed, without enzymatic control, phosphodiester bond formation requires chemical activation usually giving rise to complex mixtures of compounds.[9] In this context, several laboratories have reported alternative nucleic acid monomers to link small molecules to self-replicating RNA-like polymers.[10–15]

Recently, we reported the synthesis of a 5′-boronoisosteric analogue of 5′- thymidine monophosphate (termed here Tbn for Thymidine bononucleotide). Although this compound might not be a plausible ancestor of early life due to its 5′-linked C–B bond, we designed it as a way to probe the formation of a new boronate-based DNA backbone. Indeed, in the presence of a ribonucleotide partner, this bioisostere allowed the formation in a concentration-dependent manner of a new type of internucleosidic linkage in which the natural phosphodiester backbone has been replaced by a boronate one.[16] We demonstrated that this novel reversible boronate backbone was particularly stable with the *cis*-diol functions of nucleotides compared to other diols. Moreover, the stability of these dinucleotides appeared to be mainly dependent on a preorganized north-like sugar conformation of the diol moiety, and stacking interactions. The long-term motivation behind our work has been multifold: (1) the exploration of possible primordial precursors of early life; (2) the creation of an artificial genetic system; (3) the investigation of the biological properties of these analogues[17] and (4) the incorporation of these analogues into oligonucleotides and the study of their assembly. Thus, this manuscript describes the design and preparation of the 2′-deoxy-5′-bononucleotides of cytidine, guanosine and adenosine, namely, dCbn, dGbn and dAbn, along with their association with uridine.

Results

1. Design

In designing the bononucleotides we tried to deviate as little as possible from the structural and electronic shapes of the natural nucleotides. Calculations were performed using the AM1 semi-empirical force fields as implemented in the Gaussian software. For each natural nucleotide, the obtained optimized structure was converted into a bononucleotide one and optimized again. Surface models of the bononucleotides **1–4** with mapped electrostatic potentials showed that the optimized molecules are expected to have similar electrostatic charges (Fig. 1). Fig. 2 illustrates the optimized structures obtained for the neutral bononucleotides (yellow) compared to their monophosphate counterparts (green).

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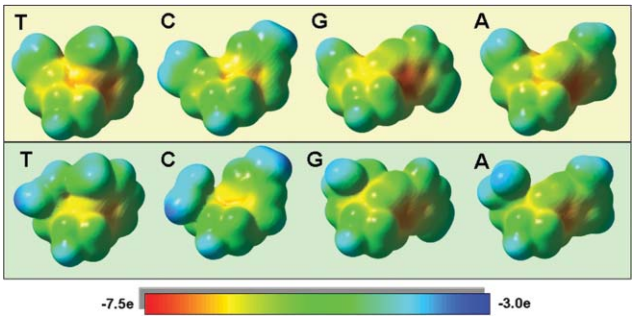


Fig. 1 Electrostatic potentials of the bononucleotides **1–4** (top) compared to the corresponding neutral nucleotide monophosphates (bottom) showing a closely related distribution of charges among analogues as compared to the natural molecules.

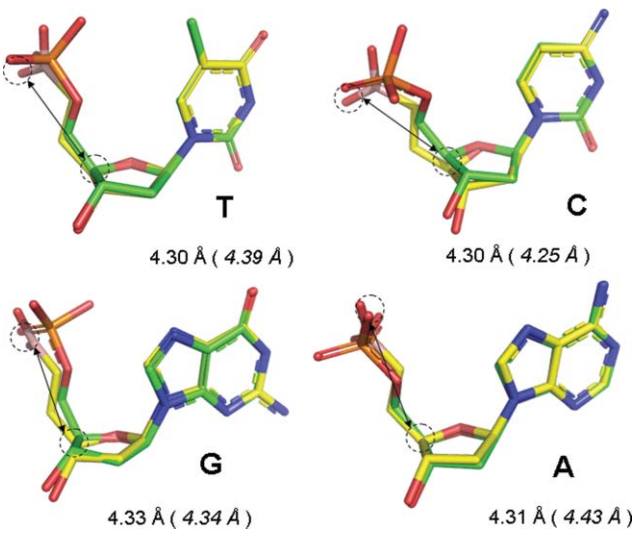
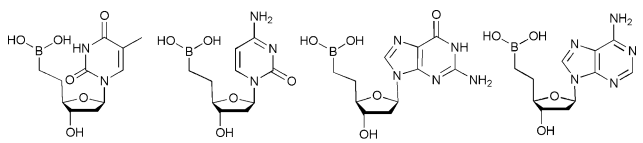


Fig. 2 Comparison of the optimized structures obtained for monophosphates (green) and the newly synthesized bononucleotides (yellow). The distances between the C4′ and one of the oxygen of the acidic groups are given in brackets for the bononucleotides and compared to the natural monophosphate parents.

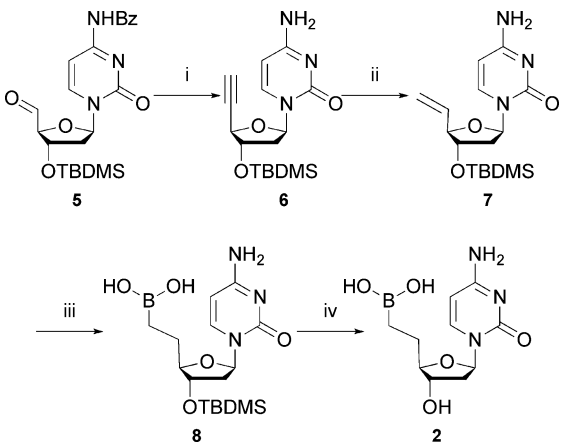
Structural fit and bond measurements were performed with the Pymol software (http://pymol.sourceforge.net/) and indicated no strong structural variation, especially for the C4′-oxygen of the acid function distance (max variation ~0.1 Å). The structures of the analogues fitted well with the natural molecules. These preliminary structural studies argue for a nearly perfect mimic of the natural structures.



2. Synthesis

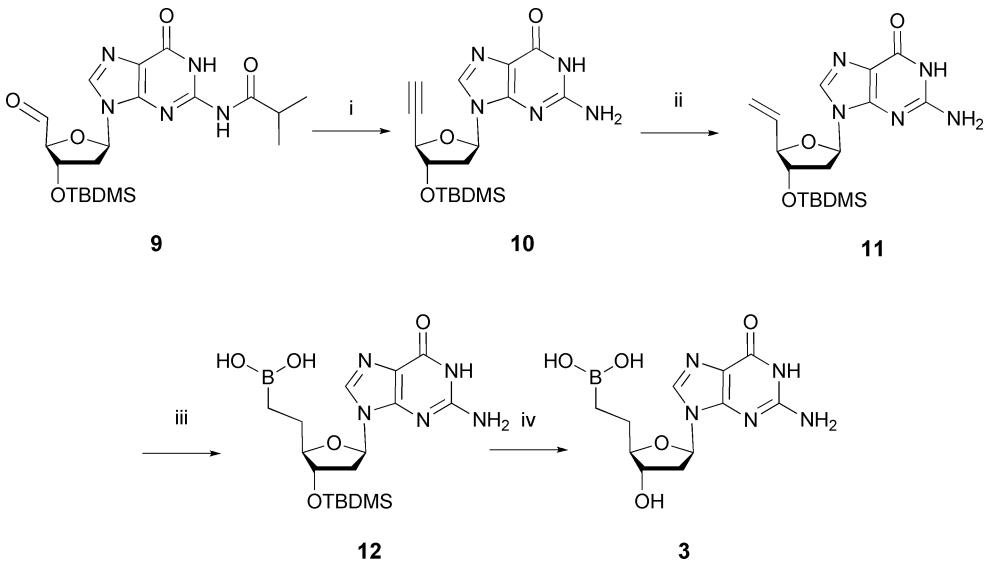
We considered that the most convenient combination of protecting groups would consist of a fluoro-labile *t*-butyldimethyl silyl group to protect the 3′-OH function and base-labile acyl groups to protect the amino functions of the heterocyclic bases. The general synthetic scheme for the preparation of dCbn, dGbn and dAbn followed the one previously developed in the group for the thymidine unit, which involved the use of easily accessible 5′-aldehyde nucleosides as the starting materials.[16] These compounds were synthesized from 5′-*O*-dimethoxytrityl nucleosides in three steps using a modification of the procedure developed by Moffatt *et al*.[18,19] Our strategy for the synthesis of the borono-analogues relied on the homologation of the corresponding 5′-aldehydic nucleosides using the Bestmann–Ohira reagent (dimethyl-1-diazo-2-oxopropylphosphonate).[20] This reagent is readily prepared from commercially available precursors and allows the conversion of aldehydes into the corresponding terminal alkynes under mild reaction conditions ($MeOH/K_2CO_3$) and with high yields.[21,22] Catalytic hydrogenation of the alkyne to the corresponding terminal alkene generally proceeds quantitatively and represents an attractive alternative to the Wittig reaction.

Synthesis of 2′-deoxycytidine bononucleotide. The synthesis of dCbn **2** proved to be quite straightforward starting from 2′-deoxycytidin-5′-al **5** (Scheme 1). The homologation/reduction sequence gave alkene **7** in 90% yield. ^{1}H NMR and TLC of the crude product showed that the N^4-benzoyl group was also lost during the homologation. The hydroboration of **7** using diisopinocampheylborane was followed by acetaldehyde promoted oxidative dealkylation while a hydrolysis afforded 3′-*O*-TBDMS boronic acid **8**.[23] Subsequent desilylation of the latter with 4 M HCl at rt gave the corresponding 2′-deoxycytidine bononucleotide **2**. The overall preparation of **2** was accomplished in 4 steps and 38.4% overall yield starting from **5**.



Scheme 1 *Reagents and conditions*: i. dimethyl-1-diazo-2-oxopropylphosphonate, K_2CO_3, MeOH, rt, 92%; ii. H_2, Lindlar catalyst 15%, MeOH, rt, 98%; iii. (a) diisopinocampheylborane, THF, rt; (b) acetaldehyde, rt, 43%; iv. 4 M HCl, rt, 99%.

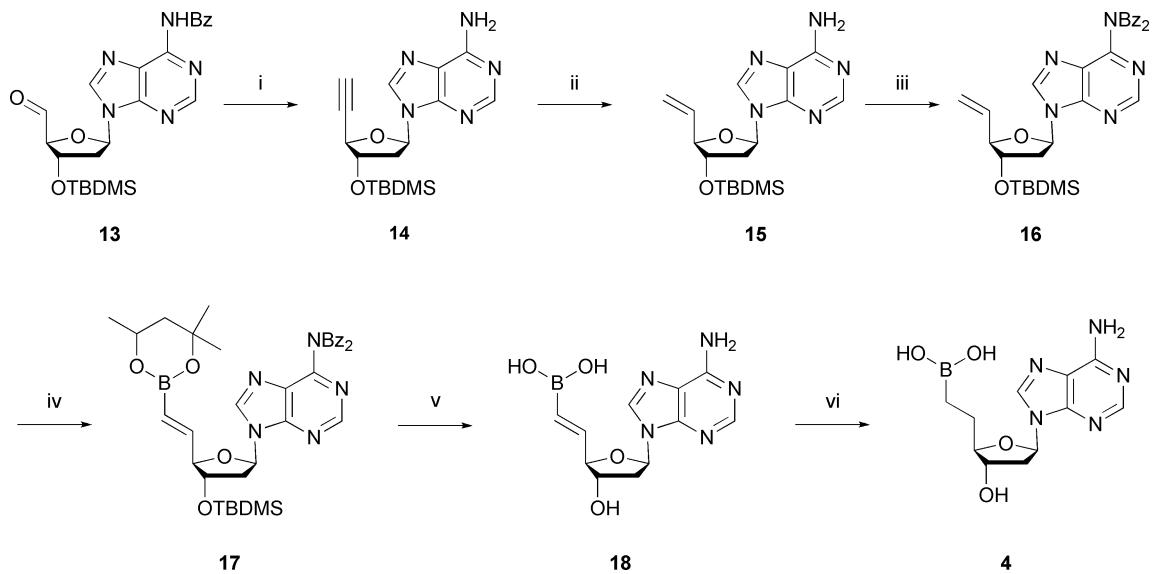
Synthesis of 2′-deoxyguanosine bononucleotide. The synthesis of dGbn **3** followed the same procedure as the one used for **2** and is depicted in Scheme 2. Hence, when 5′-carboaldehyde **9** was allowed to react in the presence of dimethyl-1-diazo-2-oxopropylphosphonate and potassium carbonate in methanol, both the homologation reaction and the loss of the N^4-isobutyryl group were observed to give alkyne **10** in 95% yield. Selective hydrogenation with Lindlar catalyst then provided the 5′-methylidene derivative **11** quantitatively. In the key step of the



Scheme 2 *Reagents and conditions*: i. dimethyl-1-diazo-2-oxopropylphosphonate, K_2CO_3, MeOH, rt, 95%; ii. H_2, Lindlar catalyst 15%, MeOH, rt, quant.; iii. diisopinocampheylborane, THF, rt, 33%; iv. Bu_4NF, rt, 90%.

synthesis, addition of diisopinocampheylborane in THF at 35 °C provided, after aqueous workup, the boronic acid **12** in 33% yield. However, it is worth noting that the reaction was never left to go to completion as prolonged reaction times increased decomposition and base release. To optimize the reaction conditions, we attempted several variations and found that better yields were obtained by avoiding treatment with acetaldehyde. To our surprise TLC monitoring showed that oxidative dealkylation had already taken place, however at this stage we cannot rule out a possible silica-promoted process. Nevertheless, this key intermediate was isolated after purification through column chromatography without any major loss of material. Desilylation of **12** using Bu_4NF afforded **3** in 90% yield. Compound **3** was thus prepared in 4 steps and 28.2 % overall yield starting from **9**.

Synthesis of 2′-deoxyadenosine bononucleotide. The adenosine bononucleotide dAbn was prepared following the same strategy (Scheme 3). Thus, the homologation/reduction sequence described above was performed on 2′-deoxyadenosin-5′-al **13** and yielded the deprotected 5′-methylideneadenosine **15** in 87% yield. This two step sequence compares favourably with the already reported synthesis of the *N*-benzoyl analogue of **15**, obtained in 70% yield by reaction of **13** with methyltriphenylphosphonium ylide.[24] To our surprise, the hydroboration conditions that were



Scheme 3 *Reagents and conditions*: i. dimethyl-1-diazo-2-oxopropylphosphonate, K_2CO_3, MeOH, rt, 90%; ii. H_2, Lindlar catalyst 15%, MeOH, rt, 98%; iii. BzCl, pyridine, 76%; iv. vinyl 2-methyl-2,4-pentanediol boronate, Grubbs–Hoveyda II catalyst 10 mol%, CH_2Cl_2, rt, 44%; v. (a) K_2CO_3, MeOH; (b) $Et_3N{\cdot}3HF$, rt, 24h, 93%; vi. H_2, Pd/C 10%, MeOH, rt, 90%.

successfully applied to the methylidene derived from T, C and G were found to be inefficient on compound **15**. Indeed, reactions were very sluggish, difficult to interpret and all the attempts to optimize the reaction conditions failed. We therefore decided to target the 2′-deoxyadenosine bononucleotide *via* a CM reaction with vinyl boron coupling partners.[25,26] Unfortunately, the attempted CM between 5′-deoxy-2′-*O*-*t*-butyldimethylsilyl-5′-methylideneadenosine **15** and vinyl boronic acid, vinyl pinacol boronate, vinyl 2-methyl-2,4-pentanediol boronate or vinyl MIDA boronate[27] in the presence of first and second generation Grubbs catalysts failed to give the desired product. Actually, similar observations were recently made by Wnuk and Andrei *et al.* who demonstrated that a 6-*N*,*N*-diprotection of the adenine ring was necessary for a metathesis between the 2′,3′-*O*-isopropylidene analogue of **15** and homoallylglycine to occur. In addition, coupling approaches aiming at the syntheses of pyrimidine and purine analogues functionalized with an alkenyl chain at C5′ led them to conclude that the 2nd generation Grubbs catalyst was more compatible with pyridines, while the Hoveyda–Grubbs 2nd generation catalyst gave better results with purine nucleosides.[28,29] Therefore, the dibenzoylation of the exocyclic 6-amino function was completed upon treatment of **15** with 2 equiv. of benzoyl chloride in pyridine to give **16** in 76% yield. Subsequent metathesis of the latter with vinyl 2-methyl-2,4-pentanediol boronate in the presence of the 2nd generation Hoveyda–Grubbs catalyst gave the expected CM product **17** in 44% yield as a single stereoisomer along with 20% of starting material which was eventually recycled.

By-products of the self-metathesis substrates were also formed during the reaction. ^{1}H NMR analysis of the crude reaction mixture showed the presence of the 5′E isomer. The 5′ proton in **17** appears at δ 6.56 ppm (ddd, $J_{H5'\text{-}H4'} = 5.9$ Hz, $J_{H5'\text{-}H6'} = 18.1$ Hz and $J_{H3'\text{-}H5'} = 2.8$ Hz) and the 6′ proton resonates at δ 5.75 ppm (d, $J_{H5'\text{-}H6'} = 17.7$ Hz). In an attempt to improve the yield, the reaction was run for a longer amount of time, however, this did not lead to complete or increased conversion of **16** into **17** as indicated by ^{1}H NMR.

Removal of the 6-*N*-benzoyl groups was conducted using K_2CO_3 in methanol for 12 h. Treatment of the crude product with $Et_3N{\cdot}3HF$ in THF effected the removal of both the 3′-*O*-*t*-butyldimethylsilyl and the 2-methyl-2,4-pentanediol protecting groups probably through an unstable organofluoroborate intermediate[30] to give boronic acid **18** in 93% yield over three steps. Hydrogenation of **18** in the presence of catalytic amounts of Pd/C (10%) in methanol occurred smoothly in excellent yield leading to the expected 2′-deoxyadenosine bononucleotide **4**. Thus, the synthesis of dAbn **4** was achieved in 6 steps and 25.2% overall yield starting from **13**.

3. Spectroscopic analysis

These new boronic acids were designed with the aim of binding with compounds containing diol moieties and especially ribonucleosides. We have already demonstrated the capacity of dTbn to complex ribonucleotides with high affinity and defined some factors that may govern this reversible process.[16] The ability of the newly synthesized bononucleotides **2–4** to bind with the 2′,3′-diol moiety of uridine was evaluated by ^{1}H NMR in DMSO-d6. When dissolved in anhydrous DMSO, the ^{1}H NMR spectrum of all compounds displayed an overlapping of at least 2 sharp signals sets, characteristic of 2 species in equilibrium in a slow exchange regime. However, upon addition of a few drops of water a drastic simplification of the spectra was observed leading to a single sharp signal set. Although boroxines are known to exist in anhydrous conditions, a change in the H1′ pattern along with the loss of the broad 3′-OH signal suggests the formation of an intramolecular cyclization between the boronic acid and the 3′-hydroxyl group. Addition of the bononucleotides **2–4** to uridine affected its signals in quite a similar manner. As already observed for dTbn, the presence of a boronic acid induced a narrowing effect on the labile proton signals. This clearly indicates a slowing down of the exchange kinetics of the labile protons. Moreover, when the amount of boronic acid is increased, the intensity of the 2′-OH and 3′-OH signals decreases, showing that the diol function is progressively replaced by a boronate one (data not shown).

Another indication of the formation of the internucleosidic linkage is given by a particular resonance of the boronic acids. As exemplified in Fig. 3 with dAbn, in an aprotic solvent such as DMSO, we detect a singlet signal at 7.43 ppm corresponding to the free boron-carried hydroxyl groups. Upon addition of uridine, this signal progressively decreases in intensity while the exocyclic amine protons at 7.25 ppm are unchanged.

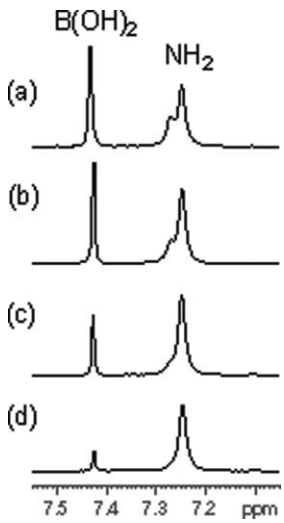


Fig. 3 Selected area of the ^{1}H NMR spectra in DMSO-d_6 of **4** (a) free (10 mM) and in the presence of (b) 5 mM, (c) 15 mM and (d) 45 mM of uridine.

Looking at the chemical shifts, the formation of the internucleosidic linkage was shown to be a slow dynamic process at the ^{1}H NMR timescale, giving rise to the emergence of new signals assigned to the bound forms of uridine and the boronic acids. Table 1 and Fig. 4 exhibit the noteworthy chemical shifts of uridine, free and bound to each of the bononucleotides. The amine function of uridine was shifted downfield (about +0.10 ppm), except with **3**, (–0.20 ppm) (Fig. 4A). The H5 proton was generally not influenced by the complexation, excepted with dCbn where a second doublet assigned to the bound uridine appeared at a slightly higher field (+0.04 ppm), as seen on Fig. 4B. These chemical shifts of the base protons are characteristic of π-stacking interactions.

Finally, the sugar conformations of the two partners were studied. It is well established that the nucleotides and their analogues exist in solution as an equilibrium between the North and

Table 1 Chemical shifts (in ppm) of free and bound uridine in DMSO-d6

	Free U	U–**1**[a]	U–**2**	U–**3**	U–**4**
NH	11.31	11.40	11.31	11.39	11.39
H6	7.88	7.71	7.70	7.69	7.68
H1′	5.77	5.78	nd[b]	5.70	5.69
H5	5.64	5.64	5.60	5.64	5.64

[a] Data from reference 16. [b] Not determined, due to the overlapping with dCbn resonances.

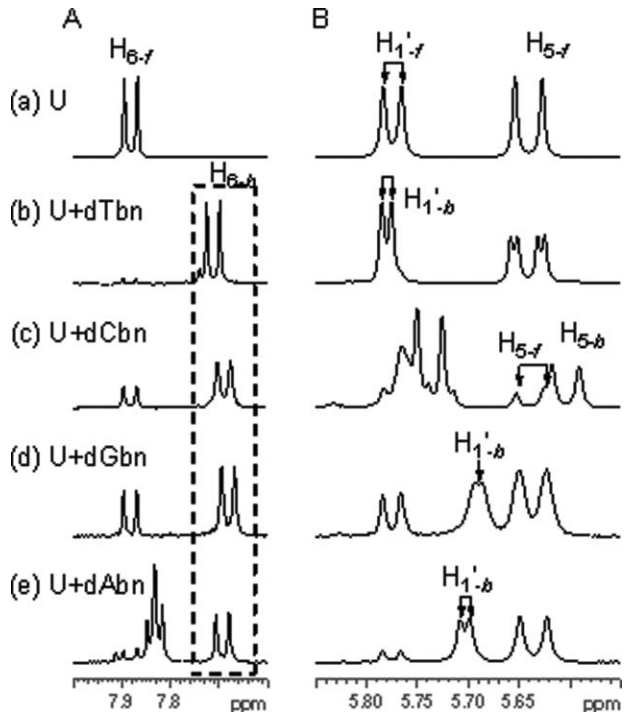
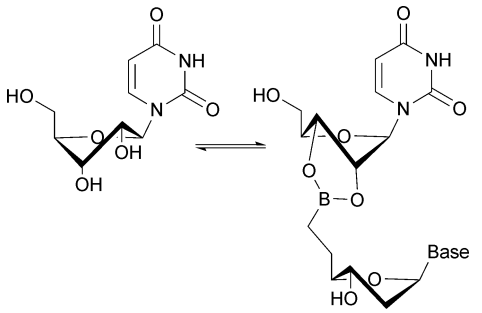


Fig. 4 Selected areas of the ^{1}H NMR spectra of uridine (a) free and in the presence of an excess of (b) **1** (2.5 equiv.), (c) **2** (1.5 equiv.), (d) **3** (1.6 equiv.) and (e) **4** (2 equiv.). [A] region showing the H6 resonances of uridine. [B] region showing the H1′ and H5 resonances of uridine.

South conformations. According to Altona and Sundaralingam the percentage of S-type conformer can reliably be estimated as $10\times{}^3J_{1'2'}$, the $^3J_{1'2}$ coupling constants being directly determined from the 1D ^{1}H spectra by a first order analysis.[31] Despite the fact that this relationship was given for compounds in aqueous solution, this method can be applied to give a good estimation of the uridine pucker modification induced by the boronate formation.

Although the chemical shift of the uridine anomeric proton was only slightly shifted, a change in the coupling was clearly observed upon addition of the boronic acids (Fig. 4B). The values of $^3J_{1'2'}$ as well as the estimated percentages of N conformers are summarized in Table 2. From these results, it appears that the North conformation is clearly favoured by the formation of the dinucleotide, confirming therefore our earlier analysis.[16] Boronic acids **1** and **3** have the same impact on the host sugar conformation, shifting the conformational equilibrium until about 70% of the North form, while **4** appears as the most influencing partner inducing about 80% of the North form. Unfortunately, no information could be obtained for **2** because of an overlapping of the uridine H1′ signal with the bononucleotide resonances.

Table 2 Conformation of the uridine sugar ring in DMSO, measured using ^{1}H NMR



	$^3J_{1'2'}$ (Hz)	%N[a]
U free	5.3	47
U + **1**[b]	2.8	72
U + **3**	2.8	72
U + **4**	<2.0	>80

[a] Calculated according to $\%N = 100 - 10\times{}^3J_{1'2'}$. [b] Data from reference 16.

In the naturally occurring nucleic acids, the furanose rings essentially adopt the S-conformation in B-DNA and the N-conformation in RNA. These newly synthesized boronucleotides induce therefore an RNA-like conformation on the ribonucleoside partner through the formation of the internucleosidic linkage.

Conclusions

We have developed a reliable protocol for the preparation of borono-analogues of all four nucleotide monophosphates. Semi-empirical calculations of these new bioisosteres indicate that they are close mimics of their natural counterparts. The successful preparation of this bnDNA nucleotide set should make possible a number of future experiments in nucleic acid recognition. Controlling the boronic acid-diol equilibrium, for instance could be relevant for the design of dynamic "smart" DNA- or RNA-like polymers. Moreover, this interaction is directional and its reversibility allows the formation of the thermodynamically most stable architectures.[32] The incorporation of these analogues in DNA strands and the study of their binding abilities will help our understanding of the encoding of genetic information. The availability of boron in the prebiotic era and its importance for the stabilization of ribose make the boronate ester backbone an ideal candidate for ensuring both the selection and proof-reading steps needed for early life evolution. Additionally, work will be needed to investigate whether other properties of the genetic system, such as transcription or replication can be affected by such artificial bononucleotides.

Experimental

Unless otherwise stated, materials were purchased from commercial suppliers and used without further purification. TLC was performed on Merck silica coated plates 60F254. Compounds were revealed by UV light (254 nm) after spraying with 5% sulfuric acid ethanol solution and heating. ^{1}H NMR and ^{13}C NMR spectra

were recorded at 20 °C on a Bruker AM spectrometer at 300 MHz (1H), 75 MHz (^{13}C) and 128 MHz (^{11}B). Chemical shifts are given in ppm referenced to the solvent residual peak. Coupling constants are given in Hertz (Hz). The ^{1}H NMR spectra for Fig. 2 and 3 were acquired at 20 °C on a Bruker AM300 MHz spectrometer. A solution of 10 mM for each compound was prepared by dissolution of the lyophilized product into DMSO-d_6 (99.8 %, Eurisotop). A stock solution was then prepared containing 10 mM of the bononucleotide and 100 mM of uridine. Aliquots of this solution were successively added to the bononucleotide alone solution in order to get several [bononucleotide]/[uridine] ratios. The exact ratios were determined on the spectra by referring to the integrations of the low-field resonances of each partner. All compounds were further characterized by Mass Spectrometry and High Resolution Mass Spectrometry using an ESI/Q-TOF Micromass spectrometer. All the solvents were freshly distilled before use. Dichloromethane was dried over calcium hydride. All the reactions were conducted under an argon atmosphere unless otherwise stated. All the glassware used was oven-dried.

2′,5′-Dideoxy-5′-ethynyl-3′-*O*-*tert*-butyldimethylsilyl cytidine (6)

5′-Aldehyde-3′-*O*-*tert*-butyldimethylsilyl-*N*-benzoyl-cytidine **5**[33] (180 mg, 0.40 mmol) was first dissolved in anhydrous MeOH (20 mL), then Bestmann–Ohira reagent (160 mg, 0.80 mmol) and anhydrous K_2CO_3 (280 mg, 2 mmol) were added to the solution and stirred under argon at room temperature for 12 h. After removal of the solvent under reduced pressure, the residue was dissolved in ethyl acetate (50 mL) and washed with saturated NH_4Cl (3 × 10 mL). The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (100% CH_2Cl_2–5% MeOH) to give 127 mg (92%) of **6** as a colourless solid. Mp: 136–138 °C. δ_H ($CDCl_3$) 0.09 (s, 6H, Si-(CH_3)$_2$), 0.89 (s, 9H, ^{t}Bu-Si), 2.04–2.14 (m, 1H, $H_{2'}$), 2.54–2.68 (m, 1H, $H_{2'}$), 2.68 (s, 1H, $H_{6'}$), 4.44–4.46 (m, 1H, $H_{3'}$), 4.56–4.59 (m, 1H, $H_{4'}$), 5.84 (d, *J* 7.2 Hz, 1H, H_5), 6.24 (t, *J* 6.3 Hz, 1H, $H_{1'}$), 7.69 (d, *J* 7.2 Hz, 1H, H_6); δ_C ($CDCl_3$) –4.8 (Si-(*C*H$_3$)$_2$), 17.9 (Si-C_{IV}), 25.7 (Si-^{t}Bu), 41.7 ($C_{2'}$), 76.0 ($C_{4'}$), 77.0 ($C_{3'}$), 77.1 ($C_{6'}$), 80.7 ($C_{5'\,IV}$), 88.2 ($C_{1'}$), 94.6 (C_5), 140.8 (C_6), 155.8 (C_2), 165.8 (C_4); MS: (ESI$^+$) *m*/*z*: 336.2 ([M+H]$^+$ 100%); HRMS-ESI$^+$ *m*/*z* calcd for $C_{16}H_{26}O_3N_3Si$ [M+H]$^+$ 336.1743 Found 336.1721.

2′,5′-Dideoxy-5′-vinyl-3′-*O*-*tert*-butyldimethylsilyl cytidine (7)

Alkyne **6** (150 mg, 0.448 mmol) dissolved in anhydrous methanol (5 mL) was reduced under hydrogen using Lindlar catalyst (23 mg, 15%) to yield the desired alkene. The reaction was monitored by ^{1}H NMR. The mixture was filtered through a bed of celite, and the solvent was removed under reduced pressure to give 143 mg (98%) of **7** as a colourless solid. Mp: 159–161 °C. δ_H ($CDCl_3$) 0.0 (s, 6H, Si-(CH_3)$_2$), 0.89 (s, 9H, ^{t}Bu-Si), 2.07–2.11 (m, 1H, $H_{2'}$), 2.45–2.50 (m, 1H, $H_{2''}$), 4.05–4.11 (m, 1H, $H_{3'}$), 4.25–4.29 (m, 1H, $H_{4'}$), 5.26–5.43 (2d, *J* 17.1, 10.5 Hz, 2H, $H_{6'}$, $H_{6''}$), 5.76 (d, *J* 7.0 Hz, 1H, H_5), 5.82–5.93 (m, 1H, $H_{5'}$ 6.20 (t, *J* 6.0 Hz, 1H, $H_{1'}$), 7.56 (d, *J* 7.2 Hz, 1H, H_6); δ_C ($CDCl_3$) –4.8 (Si-(*C*H$_3$)$_2$), 17.9 (Si-C_{IV}), 25.7 (Si-^{t}Bu), 41.6 ($C_{2'}$), 75.0 ($C_{3'}$), 86.3 ($C_{1'}$), 87.4 ($C_{4'}$), 94.3 (C_5), 118.1 ($C_{6'}$), 135.2 ($C_{5'}$), 140.4 (C_6), 155.6 (C_2), 165.6 (C_4); MS: (ESI$^+$) *m*/*z*: 338.2 ([M+H]$^+$ 100%); HRMS-ESI$^+$ *m*/*z* calcd for $C_{16}H_{28}O_3N_3Si$ [M+H]$^+$ 338.1900 Found 338.1873.

1-(2′,5′-Dideoxy-3′-*O*-*tert*-butyldimethylsilyl cytidin-5′-yl)methyl boronic acid (8)

A 10 mL round bottom flask was charged with borane dimethylsulfide (85 μL, 0.89 mmol) and dry THF freshly distilled (3 mL) under argon. The solution was warmed to 35 °C and α-pinene (330 μL, 2.07 mmol) was added dropwise. The mixture was stirred for 3 h and subsequently cooled to –30 °C. A solution of the alkene **7** (100 mg, 0.29 mmol) in THF (0.5 mL) was then added dropwise to the reaction mixture. The resulting mixture was stirred at –30 °C for 30 minutes and allowed to warm to room temperature. After an additional hour at room temperature, freshly distilled acetaldehyde (100 μL) was added and the mixture was stirred for 12–16 h to reach completion (TLC monitoring). HCl (0.1M, 1 mL) was added and all volatiles were removed under reduced pressure to give a residue, which was dissolved in ethyl acetate (20 mL) and washed with brine (3 × 10 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was eliminated under reduced pressure. The crude product was purified by column chromatography on silica gel (CH_2Cl_2/ethyl acetate 0–50% then ethyl acetate/MeOH (0–4%) to give 47 mg (43%) of **8** as a white foam. Mp: 101–103 °C. δ_H (DMSO-d_6) 0.06 (s, 6H, Si-(CH_3)$_2$), 0.53–0.62 (m, 2H, $H_{6'}$), 0.83 (s, 9H, ^{t}Bu-Si), 1.46–1.53 (m, 2H, $H_{5'}$), 1.99–2.08 (m, 1H, $H_{2'}$), 2.26–2.32 (m, 1H, $H_{2''}$), 3.51–3.57 (m, 1H, $H_{4'}$), 4.04–4.08 (m, 1H, $H_{3'}$), 5.67 (d, *J* 7.5 Hz, 1H, H_5), 6.03 (t, *J* 6.6 Hz, 1H, $H_{1'}$), 7.03–7.11 (m, -NH_2), 7.45 (d, *J* 7.5 Hz, 1H, H_6), δ_C (DMSO-d_6) –5.06, –4.8, (Si-*C*H$_3$), 18.2 ($C_{IV\,tBu}$), 25.6 (Si-^{t}Bu), 28.3 ($C_{5'}$), 40.3 ($C_{2'}$), 74.5 ($C_{3'}$), 84.3 ($C_{1'}$), 88.2 ($C_{4'}$), 94.2 (C_5), 140.6 (C_6), 155.0 (C_2), 165.5 (C_4); MS: (ESI$^+$) *m*/*z*: 384.2 ([M+H]$^+$ 100%), 356.2 (26); HRMS-ESI$^+$ *m*/*z* calcd for $C_{16}H_{31}N_3O_5SiB$ [M+H]$^+$ 384.2126 Found 384.2114.

1-(2′,5′-Dideoxy cytidin-5′-yl)-ethylboronic acid (2)

A 10 mM solution of 3′-*O*-*tert*-butyldimethylsilyl cytidine boronic acid derivative **8** (20 mg, 52.2 μmol) in aqueous HCl (4M) was stirred for 1 h at room temperature. Volatiles were removed *in vacuo* and the residue obtained was dissolved in butanol (10 mL) and washed with water. The organic layer was concentrated *in vacuo* to provide the crude product which was further purified by column chromatography (MeOH–CH_2Cl_2 20%) to afford **2** (14 mg, 99%) as a colourless solid. Mp: 208–210 °C. δ_H (D_2O) 0.90 (t, *J* 7.9 Hz, 2H, $H_{6'}$), 1.71–1.83 (m, 2H, $H_{5'}$), 2.35–2.48 (m, 2H, $H_{2'}$, $H_{2''}$), 3.95 (m, 1H, $H_{4'}$), 4.32 (m, 1H, $H_{3'}$), 6.20 (t, *J* 6.5 Hz, 1H, $H_{1'}$), 6.25 (d, *J* 7.9 Hz, 1H, H_5), 7.95 (d, *J* 7.9 Hz, 1H, H_6); δ_C (D_2O) 27.6 ($C_{5'}$), 38.8 ($C_{2'}$), 73.2 ($C_{3'}$), 85.7 ($C_{1'}$), 88.2 ($C_{4'}$), 96.2 (C_5), 141.3 (C_6), 157.5 (C_2), 166.1 (C_4); δ_B (D_2O) 33.9; MS: (ESI$^+$) *m*/*z*: 270.1 ([M+H]$^+$ 100%); HRMS-ESI$^+$ *m*/*z* calcd for $C_{10}H_{17}BN_3O_5$ [M+H]$^+$ 270.1261 Found 270.1260.

2′-Deoxy-5′-ethynyl -3′-*O*-*tert*-butyldimethylsilyl guanosine (10)

The synthesis of the alkyne **10** was conducted adopting the strategy used for the synthesis of **6**. The crude product was subjected to column chromatography on silica gel (100% AcOEt–5% MeOH) to give 628 mg (95%) of **10** as a colourless solid. Mp: 193–195 °C. δ_H (DMSO-d_6) 0.00 (s, 6H, Si-(CH_3)$_2$), 0.80 (s, 9H, ^{t}Bu-Si), 2.35 (s, 1H, $H_{6'}$), 2.51–2.74 (m, 2H, $H_{2'}$, $H_{2''}$), 4.35 (m, 1H, $H_{4'}$), 4.55 (m, 1H, $H_{3'}$), 6.03 (t, *J* 7.0 Hz, 1H, $H_{1'}$), 7.93 (s, 1H, H_8), 10.55 (s, 1H, N*H*); δ_C (DMSO-d_6) –5.0 (Si-(*C*H$_3$)$_2$), 17.7 (Si-C_{IV}), 25.6

(Si-^{t}Bu), 40.0 ($C_{2'}$), 75.4 ($C_{4'}$), 77.1 ($C_{3'}$), 78.7 ($C_{6'}$), 80.9 ($C_{5'}$), 82.4 ($C_{1'}$), 116.5 (C_5), 134.8 (C_8), 151.1 (C_2), 153.8 (C_6), 156.7 (C_4); MS: (ESI$^+$) *m/z*: 376.2 ([M+H]$^+$ 100%); HRMS-ESI$^+$ *m/z* calcd for $C_{17}H_{26}O_3N_5Si$ [M+H]$^+$ 376.1805 Found 376.1809.

2′,5′-Dideoxy-5′-vinyl-3′-*O*-*tert*-butyldimethylsilyl guanosine (11)

The reduction of **10** was conducted in an identical manner to that described for the synthesis of **7**. The mixture was filtered through a bed of celite to remove the catalyst, and concentrated to dryness to give 198 mg (99%) of **11** as a colourless solid. Mp: 148–150 °C. δ_H (DMSO-d_6) 0.00 (s, 6H, Si-(CH_3)$_2$), 0.82 (s, 9H, ^{t}Bu-Si), 2.11–2.18 (m, 1H, $H_{2'}$), 2.56–2.65 (m, 1H, , $H_{2''}$), 4.07–4.10 (m, 1H, $H_{4'}$), 4.27–4.32 (m, 1H, $H_{3'}$), 5.07–5.17 (m, 2H, $H_{6'}$, $H_{6''}$), 5.84–5.95 (m, 1H, $H_{5'}$), 6.03 (t, *J* 6.8 Hz, 1H, $H_{1'}$), 7.81 (s, 1H, H_8); δ_C (DMSO-d_6) –4.8 (Si-(*C*H$_3$)$_2$), 17.7 (Si-*C*$_{IV}$), 25.7 (Si-^{t}Bu), 40.3 ($C_{2'}$), 75.5 ($C_{3'}$), 81.9 ($C_{1'}$), 87.8 ($C_{4'}$), 117.2 ($C_{6'}$), 135.1 ($C_{5'}$), 136.6 (C_8), 151.0 (C_5 et C_6), 154.3 (C_2), 157.6 (C_4); MS: (ESI$^+$) *m/z*: 378.2 ([M+H]$^+$ 100%); HRMS-ESI$^+$ *m/z* calcd for $C_{17}H_{28}O_3N_5Si$ [M+H]$^+$ 378.1944 Found 378.1961.

1-(2′,5′-Dideoxy-3′-*O*-*tert*-butyldimethylsilyl guanosin-5′-yl)-methyl boronic acid (12)

A 10 mL round bottom flask was charged with borane dimethylsulfide (151 µL, 1.59 mmol) and dry THF freshly distilled (3 mL) under argon. The mixture was warmed to 35 °C and α-pinene (505 µL, 3.18 mmol) was added dropwise. This mixture was stirred for 3 h and then was cooled to –30 °C. A solution of the alkene **11** (100 mg, 0.26 mmol) in THF (500 µL) was added dropwise and the resulting mixture was stirred at –30 °C for 1 h, allowed to warm to room temperature slowly, and further stirred at room temperature for 12 h. All the volatiles were removed under reduced pressure and the crude residue was directly subjected to a column chromatography purification (methanol–dichloromethane 0–10%) to give 36 mg (33%) of the boronic acid **12** as a colourless solid. Mp: 134–136 °C. δ_H (DMSO-d_6) 0.00 (s, 6H, Si-(CH_3)$_2$), 0.79 (m, 2H, $H_{6'}$), 0.84 (s, 9H, ^{t}Bu-Si), 1.55–1.60 (m, 2H, $H_{5'}$), 2.11–2.21 (m, 1H, $H_{2'}$), 2.41–2.53 (m, 1H, , $H_{2''}$), 3.70 (m, 1H, $H_{4'}$), 4.21–4.23 (m, 1H, $H_{3'}$), 6.07 (t, *J* 6.9 Hz, 1H, $H_{1'}$), 7.70 (s, 1H, H_8); δ_C (DMSO-d_6) –4.8, –4.9 (Si-(*C*H$_3$)$_2$), 17.6 (Si-*C*$_{IV}$), 25.7 (Si-^{t}Bu), 28.4 ($C_{5'}$), 40.3 ($C_{2'}$), 74.6 ($C_{3'}$), 81.6 ($C_{1'}$), 88.7 ($C_{4'}$), 135.1 (C_8), 151.0 (C_5), 153.7 (C_6), 156.7 (C_2), 172.1 (C_4); MS: (ESI$^+$) *m/z*: 424.3 ([M+H]$^+$ 100%), 396.3 (24); HRMS -ESI$^-$ *m/z* calcd for [M+TFA]$^-$ 536.3631 Found 536.3621.

1-(2′,5′-Dideoxy-guanosin-5′-yl)-ethyl boronic acid (3)

To a solution of the 3′-*O*-*tert*-butyldimethylsilyl guanosine boronic acid derivative **12** (30 mg, 69.7 µmol) in THF, was added 0.35 mL of tetrabutylammonium fluoride (1.0 M in THF, 0.35 mmol) and the resulting solution was stirred at 50 °C for 12 h. After completion of the reaction (TLC monitoring), all the volatiles were removed under reduced pressure and the residue was directly subjected to column chromatography purification on silica gel to give 19 mg (90%) of boronic acid **3** as a colourless solid. Mp: 228–229 °C. δ_H (D_2O) 0.69 (t, *J* 12 Hz, 2H, $C_{6'}$), 1.58–1.65 (m, 2H, $C_{5'}$), 2.39–2.44 (m, 1H, $H_{2'}$), 2.60–2.70 (m, 1H, , $H_{2''}$), 3.82–3.85 (m, 1H, $H_{4'}$), 4.33–4.37 (m, 1H, $H_{3'}$), 6.11 (t, *J* 9.0 Hz, 1H, $H_{1'}$), 7.84 (s, 1H, H_8); δ_C (D_2O) –27.6 ($C_{5'}$), 37.9 ($C_{2'}$), 73.4 ($C_{3'}$), 83.0 ($C_{1'}$), 88.5 ($C_{4'}$), 137.0(C_8), 151.3 (C_5), 153.7 (C_6), 158.7 (C_2); δ_B (D_2O) δ 34.5 ; MS: (ESI$^-$) *m/z*: 308.1 ([M–H]$^-$ 100%); HRMS-ESI$^-$ *m/z* calcd for [M–H]$^-$ 308.1162 Found 308.1166.

2′-Deoxy-5′-ethynyl-3′-*O*-*tert*-butyldimethylsilyl adenosine (14)

Homologation of 5′-aldehyde-2′-deoxy-6-*N*-benzoyl-3′-*O*-*tert*-butyldimethylsilyl adenosine **13** (2 g, 4.26 mmol) was performed in an identical manner to that described for the synthesis of **6**. The crude product was purified by column chromatography on silica gel (Hexane/AcOEt 80–100%) to give 1.22 g (90%) of **14** as a colourless solid. Mp: 187–191 °C. δ_H ($CDCl_3$) 0.14 (s, 6H, Si-(CH_3)$_2$), 0.92 (s, 9H, ^{t}Bu-Si), 2.55–2.74 (m, 3H, $H_{2'}$, $H_{2''}$, $H_{6'}$), 4.65–4.68 (m, 2H, $H_{4'}$, $H_{3'}$), 5.93 (br s, 2H, NH_2), 6.56 (t, *J* 6.6 Hz, 1H, $H_{1'}$), 8.19 (s, 1H, H_8), 8.36 (s, 1H, H_2); δ_C ($CDCl_3$) –4.7 (Si-(*C*H$_3$)$_2$), 18.1 (Si-*C*$_{IV}$), 25.8 (Si-^{t}Bu), 41.8 ($C_{2'}$), 77.0 ($C_{3'}$), 77.4 ($C_{6'}$), 77.9 ($C_{4'}$), 80.8 ($C_{5'}$), 85.3 ($C_{1'}$), 120.0 (C_5), 139.3 (C_8), 149.8 (C_4), 152.2 (C_2), 155.2 (C_6) ; MS: (ESI$^+$) *m/z*: 360.2 ([M+H]$^+$ 100%); HRMS-ESI$^+$ *m/z* calcd for $C_{17}H_{26}O_2N_5Si$ [M+H]$^+$ 360.1856 Found 360.1866.

2′,5′-Dideoxy-5′-vinyl-3′-*O*-*tert*-butyldimethylsilyl adenosine (15)

Terminal alkyne **14** (1.96 g, 5.45 mmol) was converted into the corresponding alkene in an identical manner to that described for the synthesis of compound **7** to yield 1.93 g (98%) of **15** as a colourless solid. Mp: 153–155 °C. δ_H ($CDCl_3$) 0.08 (s, 6H, Si-(CH_3)$_2$), 0.81 (s, 9H, ^{t}Bu-Si), 2.35 (ddd, *J* 4.6, 6.3 and 13.2 Hz, 1H, $H_{2'}$), 2.70 (td, *J* 6.1 and 12.9 Hz, 1H, , $H_{2''}$), 4.24–4.31 (m, 1H, $H_{4'}$), 4.32–4.41 (m, 1H, $H_{3'}$), 5.25 (td, *J* 0.6 and 10.5 Hz, 1H, $H_{6'}$), 5.36 (td, *J* 0.6 and 17.1 Hz, 1H, $H_{6''}$), 5.77 (br s, 2H, NH_2), 5.97 (ddd, *J* 6.6, 10.5 and 17.1 Hz, 1H, $H_{5'}$), 6.40 (t, *J* 6.3 Hz, 1H, $H_{1'}$), 7.87 (s, 1H, H_8), 8.27 (s, 1H, H_2) ; δ_C ($CDCl_3$) –4.6 (Si-(*C*H$_3$)$_2$), 18.0 (Si-*C*$_{IV}$), 25.7 (Si-^{t}Bu), 40.1 ($C_{2'}$), 75.7 ($C_{3'}$), 84.4 ($C_{1'}$), 88.2 ($C_{4'}$), 117.9 ($C_{6'}$), 120.3 (C_5), 135.6 ($C_{5'}$), 139.1 (C_8), 149.6 (C_4), 152.9 (C_2), 155.4 (C_6); MS: (ESI$^+$) *m/z*: 362.3 ([M+H]$^+$ 100%); HRMS-ESI$^+$ *m/z* calcd for $C_{17}H_{28}O_2N_5Si$ [M+H]$^+$ 362.2012 Found 362.2029.

6-*N*,*N*-Dibenzoyl-2′,5′-dideoxy-5′-vinyl-3′-*O*-*tert*-butyldimethylsilyl adenosine (16)

2′,5′-Dideoxy-5′-vinyl-3′-*O*-tert-butyldimethylsilyl adenosine **15** (2.76 g, 6.30 mmol) was co-evaporated with anhydrous pyridine and then dissolved in the same solvent (100 mL). Benzoyl chloride (1.63 mL, 18.89 mmol) was then added dropwise at room temperature and stirring continued for 16 h. Saturated $NaHCO_3$ (3 mL) was then added and the resulting mixture was diluted with water (200 mL) and extracted using ethyl acetate (3 × 100 mL). The organic layer was washed with brine (70 mL) and dried on anhydrous Na_2SO_4. Solvent removal under reduced pressure and column chromatography on silica gel (Hexane/AcOEt 20–40%) gave 2.73 g (76%) of **16** as a white foam. Mp: 51–53 °C. δ_H ($CDCl_3$) δ 0.10 (s, 6H, Si-(CH_3)$_2$), 0.91 (s, 9H, ^{t}Bu-Si), 2.47 (ddd, *J* 4.6, 6.3 and 13.3 Hz, 1H, $H_{2'}$), 2.81 (td, *J* 6.2 and 13.2 Hz, 1H, , $H_{2''}$), 4.38–4.50 (m, 2H, $H_{3'}$ and $H_{4'}$), 5.25 (d, *J* 10.5 Hz, 1H, $H_{6'}$), 5.35 (d, *J* 17.3 Hz, 1H, $H_{6''}$), 6.45 (t, *J* 6.5 Hz, 1H, $H_{1'}$), 7.32–7.50 (m, 6H, H_{Bz}) 7.84–7.87 (m, 4H, H_{Bz}), 8.24 (s, 1H, H_8), 8.66 (s, 1H, H_2); δ_C ($CDCl_3$) δ –4.7 (Si-(*C*H$_3$)$_2$), 18.0 (Si-*C*$_{IV}$), 25.7 (Si-^{t}Bu), 40.0 ($C_{2'}$), 75.5 ($C_{3'}$), 84.7 ($C_{4'}$), 88.4 ($C_{1'}$), 118.0 ($C_{6'}$), 127.8 (C_5), 128.7-129.4-132.9-133.9 (C_{Bz}), 135.2 ($C_{5'}$), 143.5 (C_8),

151.7 (C_4), 152.0 (C_2), 152.4 (C_6), 172.2 (C=O); MS: (ESI$^+$) *m/z*: 570.3 ([M+H]$^+$ 100%); HRMS-ESI$^+$ *m/z* calcd for $C_{31}H_{36}O_4N_5Si$ [M+H]$^+$ 570.2537 Found 570.2537.

(*E*) 6-*N,N*-Dibenzoyl-2′,5′-dideoxy-6′-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)-5′-vinyl-3′-*O*-*tert*-butyldimethylsilyl adenosine (17)

Terminal alkene **16** (50 mg, 0.088 mmol) and Hoveyda–Grubbs II catalyst (3 mg, 0.044×10^{-5} mol) were dissolved in dry deoxygenated CH_2Cl_2 (3 mL) and poured into a sealed tube under argon. The mixture was heated at 40 °C and the cross partner 4,4,6-trimethyl-2-vinyl-1,3,2-dioxaborinane (45 µL, 0.264 mmol) was added in five portions over a period of 5 h. Stirring was continued for an additional 36 h then the reaction mixture was diluted with water (10 mL) and CH_2Cl_2 (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were collected, dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (CH_2Cl_2/Acetone 0–5%) to give 27 mg (44%) of **17** as a white foam. Mp: 50–52 °C. δ_H ($CDCl_3$) 0.10 (s, 6H, Si-(CH_3)$_2$), 0.91 (s, 9H, ^{t}Bu-Si), 1.22–1.30 (m, 9H, dioxaborinan-3×CH_3), 1.48 (dd, *J* 11.7 and 13.8 Hz, 1H, dioxaborinan-CH_2), 1.78 (dd, *J* 2.9 and 13.9 Hz, 1H, dioxaborinan-$CH_{2'}$), 2.46 (ddd, *J* 3.6, 5.8 and 13.0 Hz, $H_{2'}$), 2.64–2.73 (m, 1H, $H_{2''}$), 4.17–4.24 (m, 1H, dioxaborinan-C*H*), 4.43–4.49 (m, 2H, $H_{3'}$ and $H_{4'}$), 5.65 (d, *J* 17.7 Hz, 1H, $H_{6'}$), 6.51 (t, *J* 6.5 Hz, 1H, $H_{1'}$), 6.56 (ddd, *J* 2.8, 5.9 and 18.1 Hz, 1H, $H_{5'}$), 7.33–7.51 (m, 6H, H_{Bz}), 7.84–7.87 (m, 4H, H_{Bz}), 8.29 (s, 1H, H_8), 8.65 (s, 1H, H_2); δ_C ($CDCl_3$) –4.7 (Si-(CH_3)$_2$), 18.0 (Si-C_{IV}), 25.7 (Si-^{t}Bu), 23.0-28.0-31.1 (dioxaborinan-3×CH_3), 40.3 ($C_{2'}$), 45.9 (dioxaborinan-CH_2), 64.8 ($C_{3'}$), 70.9 (dioxaborinan-C_{IV}), 75.7 (dioxaborinan-CH), 85.0 ($C_{1'}$), 89.4 ($C_{4'}$), 127.8 (C_5), 128.7-129.4-132.9-133.9 (C_{Bz}), 143.4 (C_8), 145.2 ($C_{5'}$), 151.6 (C_4), 152.0 (C_2), 152.6 (C_6), 172.2 (C=O); MS: (ESI$^+$) *m/z*: 696.4 ([M+H]$^+$ 8%), 614.3 (100); HRMS-ESI$^+$ *m/z* calcd for $C_{37}H_{47}O_6N_5SiB$ [M+H]$^+$ 696.3389 Found 696.3381.

(*E*) 2-(2′,5′-Dideoxy-adenosin-5′-yl)-vinyl boronic acid (18)

Boronate ester **17** (100 mg, 0.143 mmol) was dissolved in methanol (5 mL) and potassium carbonate (99 mg, 0.715 mmol) was then added to the solution which was stirred at room temperature for 24 h. After removal of the solvent, the residue was dissolved in ethyl acetate (50 mL) and washed with saturated $NaHCO_3$ (25 mL). The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The crude product was used for the next reaction without further purification and directly dissolved in THF. Triethylamine trihydrofluoride (58 µL, 0.715 mmol) was added at room temperature and the solution was stirred for 24 h at room temperature. All volatiles were removed under reduced pressure and the crude product was purified on column chromatography using reverse phase (Lichroprep C_2) silica gel (water/acetonitrile 0–15%) to afford 38 mg (93%) of **18** as a white foam. Mp (decomp. temp.): 153–158 °C. δ_H (D_2O) 2.49–2.58 (m, 1H, $H_{2'}$), 2.68–2.76 (m, 1H, $H_{2''}$), 4.40–4.48 (m, 2H, $H_{3'}$ and $H_{4'}$), 5.78 (d, *J* 17.9 Hz, 1H, $H_{6'}$), 5.78 (dd, *J* 5.6 and 17.9 Hz, 1H, $H_{5'}$), 6.29 (t, *J* 6.4 Hz, 1H, $H_{1'}$), 8.02 (s, 1H, H_8), 8.18 (s, 1H, H_2); δ_C (D_2O) 40.0 ($C_{2'}$), 74.0 ($C_{3'}$), 83.0 ($C_{1'}$), 89.6 ($C_{4'}$), 118.3 (C_5), 133.9 ($C_{5'}$), 139.5 (C_2), 148.2 (C_4), 152.4 (C_8), 155.1 (C_6) ; MS: (ESI$^+$) *m/z*: 292.2 ([M+H]$^+$ 100%); HRMS-ESI$^+$ *m/z* calcd for $C_{11}H_{15}O_4N_5B$ [M+H]$^+$ 292.1221 Found 292.1217.

2-(2′,5′-Dideoxy-adenosin-5′-yl)-ethyl boronic acid (4)

2-(2′,5′-Dideoxy-adenosin-5′-yl)-vinyl boronic acid **18** (50 mg, 0.17 mmol) was dissolved in anhydrous methanol (5 mL). Palladium on charcoal (1.4 mg, 10%) was added to the mixture, which was kept under a hydrogen atmosphere and stirred for 6 h. The reaction mixture was then filtrated through a bed of celite and concentrated to dryness. The crude product was purified on column chromatography using reverse phase (Lichroprep C2) silica gel (water/acetonitrile 0–15%) to give 40 mg (90%) of **4** as a colourless solid after lyophilisation in water. Mp (decomp. temp.): 211–216 °C. δ_H (D_2O) 0.80 (t, *J* 8.0 Hz, 2H, $H_{6'}$), 1.62–1.78 (m, 2H, $H_{5'}$), 2.51–2.58 (m, 1H, $H_{2'}$), 2.73–2.82 (m, 1H, $H_{2''}$), 3.94–4.01 (m, 1H, $H_{4'}$), 4.42–4.46 (m, 1H, $H_{3'}$), 6.33 (t, *J* 6.7 Hz, 1H, $H_{1'}$), 8.12 (s, 1H, H_8), 8.22 (s, 1H, H_2); δ_C (D_2O) 27.6 ($C_{5'}$), 38.3 ($C_{2'}$), 73.4 ($C_{3'}$), 83.2 ($C_{1'}$), 88.6 ($C_{4'}$), 118.5 (C_5), 139.5 (C_2), 148.5 (C_4), 152.5 (C_8), 155.3 (C_6); δ_B (128 MHz, D_2O) 34.4; MS: (ESI$^+$) *m/z*: 294.2 ([M+H]$^+$ 31%), 266.2 (100); HRMS-ESI$^+$ *m/z* calcd for $C_{11}H_{17}O_4N_5B$ [M+H]$^+$ 294.1373 Found 294.1366.

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