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Synthesis of nucleic-acid base containing norbornene derivatives as monomers for ring-opening-metathesis–polymerization

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Received (in Cambridge, UK) 7th August 2001, Accepted 19th October 2001
First published as an Advance Article on the web 21st November 2001

A series of norbornene derivatives containing nucleic-acid bases (thymine, adenine, cytosine, guanine, or uracil) have been prepared as monomers for ring-opening-metathesis–polymerization (ROMP). Many of the initially prepared monomers had poor solubility but this could be overcome by appropriate choice of a linker between the norbornene and base units. Some of the monomers were successfully polymerised to give homopolymers derived from nucleic-acid bases.

Introduction

Synthetic polymers which are capable of mimicking and/or interacting with biopolymers would have a number of potential applications including pharmaceuticals, stationary phases for chromatography, and tools for understanding the factors that determine the structure–activity relationships of biopolymers. However, most polymerization methods produce polymers with very broad molecular weight distributions, which are hence poor models of monodisperse biopolymers. A living polymerization[1] has the potential to produce polymers with much narrower molecular weight distributions, and allows the preparation of a variety of polymer architectures including block copolymers. In recent years there have been significant advances in living Ring-Opening-Metathesis–Polymerization[2] (ROMP) using well-defined catalysts such as the well-known ruthenium based catalysts developed by Grubbs.[3] One of the most attractive classes of monomer for ROMP is norbornene† derivatives since these are readily prepared by Diels–Alder reactions and contain a strained alkene[4] which undergoes ROMP rapidly and irreversibly. We have previously shown that the ROMP of suitable norbornene derivatives can lead to synthetic polymers containing bio-relevant amino-acids[5,6] and peptides.[7] Arimoto[8] has also reported the ROMP of a derivative of the cyclic peptide vancomycin, and the ROMP of carbohydrate containing norbornenes has also been reported.[9]

Based on this precedent, and attracted by the potential biological applications of the polymers, we initiated a project aimed at investigating the compatibility of ROMP with monomers containing a nucleic-acid base. Previous work on synthetic polymers derived from nucleic-acid bases has relied on free radical initiated polymerization of acrylate derivatives,[10] or the step by step synthesis of polymers derived from peptide nucleic acids.[11] The monomers (Fig. 1) were designed to have a modular structure consisting of three parts: the base, a linker and a norbornene unit. The norbornene unit is susceptible to ROMP, is easily prepared, and its stereochemistry can be controlled.

† The IUPAC name for norbornene is bicyclo[2.2.1]heptene.

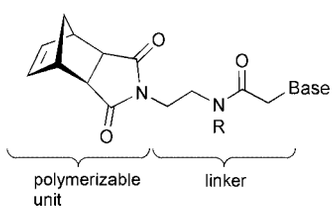


Fig. 1 General structure of the monomers.

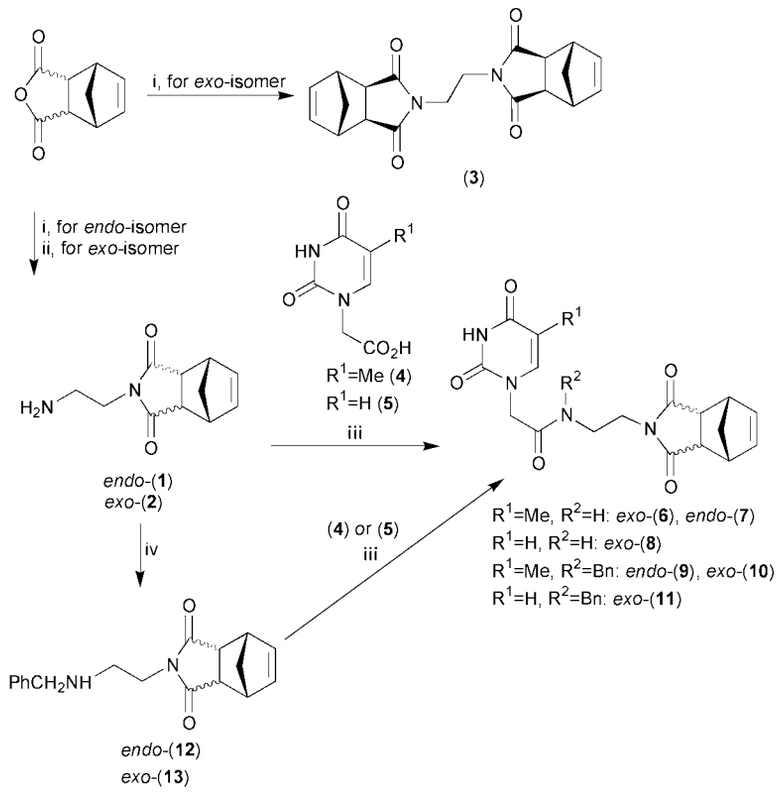
The linker was designed to be of flexible length, to facilitate the synthesis of the monomers, and to allow the solubility of the monomers to be controlled (by varying R). The base unit is attached to the linker using the same nitrogen atom as is used in nucleic acids.

In a previous communication,[12] we have reported the synthesis of two of the simplest monomers represented by Fig. 1: thymine derivatives **6** and **7**. Compounds **6** and **7** were found to undergo ROMP when treated with Grubbs' catalyst to give living polymers with narrow molecular weight distributions. In this manuscript, the synthesis of monomers derived from other nucleic-acid bases is reported, along with modifications to the monomer structure to improve the solubility of the compounds.

Results and discussion

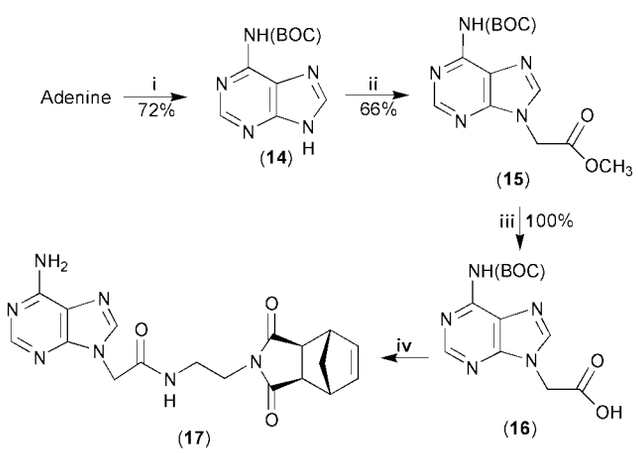
endo-Norborn-5-ene-2,3-dicarboxylic anhydride reacted with ethylenediamine to give amine **1** (Scheme 1). Interestingly, attempts to repeat this chemistry using *exo*-norborn-5-ene-2,3-dicarboxylic anhydride were unsuccessful, giving bis-imide **3** even when ethylenediamine was used in large excess. This problem was circumvented by the use of *N*-tritylethylenediamine[13] followed by acidic deprotection of the *N*-trityl group to give amine **2**. Reaction of amines **1** or **2** with thyminylacetic acid[14] **4** in the presence of water-soluble carbodiimide (EDC) gave the desired monomers **6** and **7**. Monomers **6** and **7** were found to undergo ROMP as previously reported,[12] so the synthesis of the complementary adenine monomers **17** and **22** was undertaken.

DOI: 10.1039/b107139d



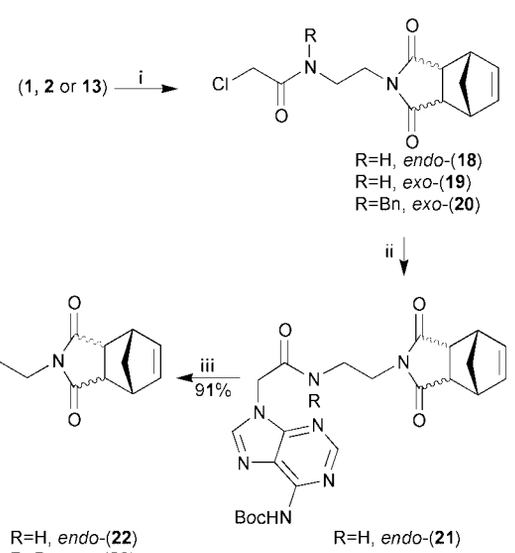
Scheme 1 *Reagents*: **i**, $H_2NCH_2CH_2NH_2$; **ii**, a, $H_2NCH_2CH_2NHCPh_3$, b, CF_3CO_2H, c, NEt_3; **iii**, EDC; **iv**, a, PhCHO, b, $NaBH_3CN$.

Protection of the exocyclic amine (N^6) of the adenine unit was necessary during the synthesis of the monomers, and an acid labile Boc-group appeared to be ideal for this purpose, though Boc-protection of adenine has not previously been reported. Despite the electron deficient nature of adenine, regioselective introduction of the Boc-protecting group to give adenine derivative **14** was achieved in 72% yield by treatment of adenine with Boc_2O and sodium hydride (Scheme 2). Compound **14** was converted into N^6-Boc-adeninyl-N^9-acetic acid derivative **16** as shown in Scheme 2 with the alkylation of compound **14** being completely regioselective to give the desired N^9-alkylated product **15** as determined by analysis of subsequent derivatives *vide infra*. Reaction of acid **16** with amine **2** followed by a trifluoroacetic acid induced removal of the Boc-protecting group gave monomer **17** as shown in Scheme 2.



Scheme 2 *Reagents*: **i**, $(^tBuOCO)_2O$, NaH; **ii**, $BrCH_2CO_2CH_3$, K_2CO_3; **iii**, NaOH; **iv**, a, (**2**), EDC, b, TFA, c, $NaHCO_3$.

However, the route shown in Scheme 2 failed for the corresponding *endo*-isomer **22**. Thus, an alternative synthesis of monomer **22** was developed (Scheme 3) in which the Boc-adenine was introduced by an alkylation reaction rather than an amide bond formation. Treatment of *endo*-norbornene derivative **1** with chloroacetyl chloride gave chloride **18** which when treated with Boc-adenine **14** and sodium hydride in the presence of 18-crown-6 gave protected monomer **21** in moderate yield. Subsequent removal of the Boc-protecting group was accomplished with trifluoroacetic acid, giving the desired monomer **22**. The *exo*-monomer **17** was also prepared by this route, but the reaction between the chloride **19** and Boc-adenine **14** proceeded in only 7% yield, illustrating that the chemistry needed to prepare these compounds is very sensitive to the stereochemistry of the reactants.



Scheme 3 *Reagents*: **i**, $ClCOCH_2Cl$, NEt_3; **ii**, (**14**), NaH, 18-crown-6; **iii**, a, CF_3CO_2H, b, $NaHCO_3$.

The regiochemistry of monomers **17** and **22** was not immediately obvious, as the reaction between Boc-adenine **14** and chloro-norbornene derivative **18** or methyl bromoacetate could have occurred on N^7 or N^9 of the adenine ring. An X-ray structure of the Boc-protected intermediate **21** (Fig. 2) confirmed

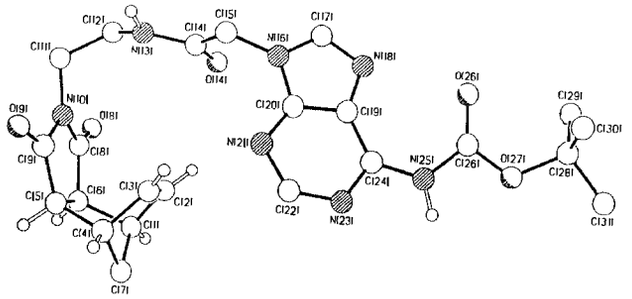
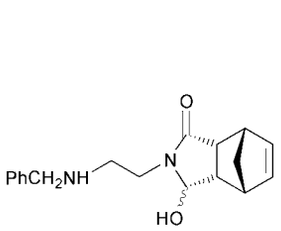


Fig. 2 The molecular structure of adenine derivative **21**.

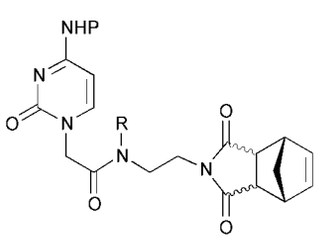
that for the *endo*-monomer, the alkylation had occurred on N^9 as desired. *exo*-Isomer **17** was also deduced to be the desired N^9-alkylated compound based on comparison of the ^{13}C-NMR shifts of the adenine ring with those of compound **22**. ^{13}C-NMR shifts are known to be sensitive to the position of alkylation of adenine derivatives.[15]

Whereas thymine derivatives **6** and **7** had been found to be sufficiently soluble in organic solvents, adenine derived monomers **17** and **22** were found to be only soluble in methanol and DMSO and as such were not suitable for ROMP studies. It was also anticipated that monomers derived from cytosine and guanine would be even less soluble than the adenine derivatives. The X-ray crystal structure of compound **21** showed that the amide-NH within the linker was involved in intermolecular hydrogen bonds. It was reasoned that use of either a tertiary amide or an ester in the linker would prevent the formation of these hydrogen bonds and hence increase the solubility of the monomers. In order to keep a common monomer structure, these versions of the thymine monomers were also prepared. Since it is well known that *exo*-isomers of norbornene derivatives undergo ROMP more readily than the *endo*-isomers, only the *exo*-isomers of the monomers were prepared, except that both isomers of the thymine monomers were synthesized to prove that the methodology was compatible with *endo*-norbornene derivatives, should these be required.

Thus, amines **1** and **2** were both reacted with benzaldehyde followed by imine reduction with sodium cyanoborohydride to give *N*-benzyl-amines **12** and **13** (Scheme 1). Attempts to carry out this reduction with sodium borohydride resulted in over-reduction, and aminol **24** was isolated from the reduction of the imine derived from amine **1**. Amines **12** and **13** both reacted with acid **4** and EDC to give the desired thymine monomers **9** and **10**. Amine **13** also reacted with chloroacetyl chloride to give chloride **20**, which, when treated with Boc-adenine **14** followed by TFA deprotection gave adenine derived monomer **23** (Scheme 3). Monomers **9**, **10** and **23** were all considerably more soluble in organic solvents such as dichloromethane than the corresponding monomers **6**, **7** and **17**. At room temperature, the NMR spectra of monomers **9**, **10** and **23** were complicated by the presence of rotamers about the tertiary amide bond. The regiochemistry of compound **23** was deduced to be the desired N^9-alkylated compound based on comparison of the ^{13}C-NMR shifts of the adenine ring with those of compounds **17** and **22**.[15]



(**24**)



P=H, R=H: *endo*-(**25**), *exo*-(**26**)
P=H, R=Bn: *exo*-(**27**)
P=Boc, R=H: *endo*-(**28**), *exo*-(**29**)
P=H.TFA, R=H: *endo*-(**30**)

Cytosine containing monomers **25**–**27** were all prepared simply by reacting the corresponding chloride (**18**–**20** respectively) with cytosine in the presence of sodium hydride. Again, the compounds with a secondary amide linker (**25**, **26**) were found to be soluble only in polar solvents (methanol and DMSO) whilst the compound with a tertiary-amide linker (**27**) was soluble in chloroform. The solubility of monomers **25** and **26** could be improved by reacting them with di-*tert*-butyl dicarbonate in the presence of sodium hydride to give derivatives **28** and **29** in which the exocyclic amine was protected. These derivatives were soluble in chlorinated organic solvents such as dichloromethane and chloroform. However, this was not a desirable strategy for the synthesis of polymers since the complete removal of protecting groups from polymeric material is difficult to achieve.

As with the adenine monomers, the synthesis of monomers **25**–**27** could have given regio-isomers of the desired products. That the *endo*-isomer **25** had the desired structure was proven by X-ray analysis of its trifluoroacetate salt **30** (Fig. 3). The

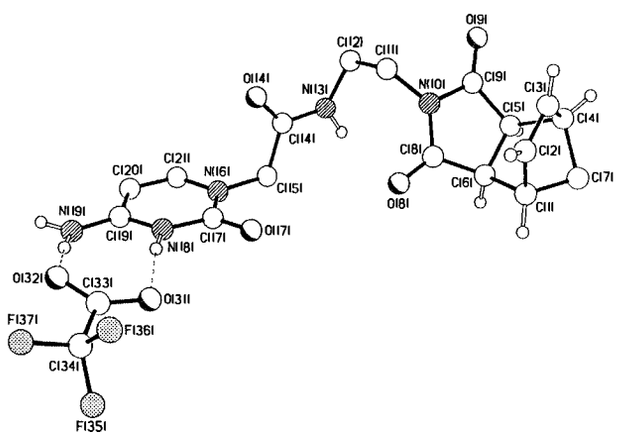
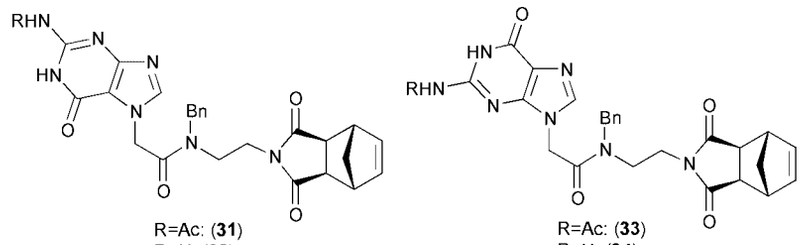


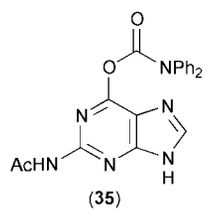
Fig. 3 The molecular structure of cytosine derivative **30**.

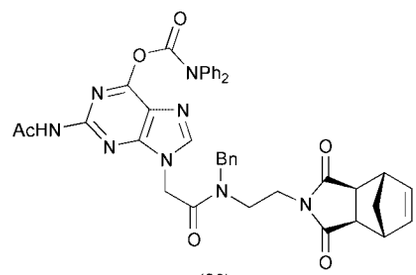
exo-isomers **26** and **27** gave essentially identical ^{13}C-NMR shifts as observed for *endo*-isomer **25**, suggesting that they have the same regiochemistry. Proof of this was obtained from NOE experiments, where for all three monomers, irradiation of the linker methylene-group directly attached to the cytosine ring resulted in enhancement of H^6 but not H^5, a result that is only consistent with attachment of the linker to N^1 as desired.

The guanine-derived monomers were initially prepared using the same route as that developed for the cytosine derivatives. However, it was necessary to protect the exocyclic amine of guanine before reaction with a chloro-norbornene derivative, and even then, reactions involving secondary amide derivatives **18** and **19** led to products which were only soluble in DMSO. Another complication of the guanine derivatives was the formation of regio-isomers due to alkylation of guanine at both N^7 and N^9. Use of chloride **20**, which contains a tertiary amide bond, was slightly more successful. Treatment of chloride **20** with N^2-acetylguanine[16] gave a 1.6 : 1 ratio of the regio-isomers **31** and **33**. Compounds **31** and **33** were soluble in organic solvents and could be readily separated by flash chromatography. Unfortunately, the major product was the undesired N^7-alkylated product as determined from the ^{13}C-NMR chemical shifts of the guanine unit.[17] Compounds **31** and **33** were however, readily deprotected by treatment with ammonium hydroxide to give monomers **32** and **34**, but this dramatically reduced the solubility of the compounds, which were only soluble in DMSO and hence not suitable for use as ROMP monomers.

The regiochemistry problem was solved by the use of N^2-acetyl-O^6-diphenylcarbamoylguanine[18] **35**. Literature precedent







indicated that this guanine derivative would alkylate preferentially on N^9 due to blocking of N^7 by the large protecting group on O^6. In practice, reaction of guanine derivative **35** with chloride **20** gave the desired N^9-alkylated product **36** in 71% yield and uncontaminated by any N^7-alkylated products. Treatment of protected derivative **36** with aqueous ammonia cleaved both protecting groups giving monomer **34** in 82% yield.

To solve the remaining problem, solubility, the use of a larger aromatic group attached to the linker amide was investigated. Hence, the synthesis of monomer **42** containing a naphthyl group within the linker was undertaken (Scheme 4). Treatment of amine **2** with 2-naphthaldehyde gave imine **37** which could be reduced with sodium cyanoborohydride to give secondary amine **38**. Acylation of amine **38** with chloroacetyl chloride gave chloride **39** which again reacted with guanine derivative **35** to give protected monomer **40** in 95% yield. Again, only a single regio-isomer was observed during this alkylation, and comparison of the ^{13}C NMR shifts of this product with those of N^7 and N^9 alkylated guanines established the regiochemistry. Deprotection of compound **40** using aqueous ammonia gave initially imine **41**, which on further treatment with water gave the desired monomer **42**, and as hoped this was found to be considerably more soluble in organic solvents than compound **34**. Whilst compound **42** was only sparingly soluble in pure dichloromethane, it was readily soluble in a 9 : 1 dichloromethane–methanol mixture, making it possibly suitable for ROMP studies.

To complete the set of monomers derived from each nucleic-acid base, uracil derivatives were also prepared. Monomer **8** with a secondary amide linker was prepared from the known uracilylacetic acid[19] **5** exactly as described for the corresponding thymine derivative (Scheme 1). The solubility properties of monomer **8** were also very similar to those of the corresponding thymine derivatives **6** and **7**. Similarly, monomer **11** with a tertiary amide linker was prepared by reaction of amine **13** with uracilylacetic acid[19] **5**. Compound **11** was found to be readily soluble in organic solvents such as chloroform.

The monomers containing an *N*-benzyl (or *N*-2-naphthyl) based linker were expected to be sufficiently soluble in organic solvents to undergo ROMP using well-defined ruthenium based initiators such as the Grubb's catalyst. However, all of these monomers were found to exist as rotamers about the tertiary amide bond which complicated their ^{1}H and ^{13}C NMR spectra. It was anticipated that the polymers derived from these monomers would also exist as rotamers about this amide bond, and this would make the characterization of the polymers very difficult or impossible. Changing the tertiary-amide to an ester was expected to overcome this problem whilst still giving monomers with appreciable solubility in organic solvents. To investigate this, *endo*- and *exo*-norborn-5-ene-2,3-dicarboxylic anhydrides[20] were reacted with ethanolamine (2-hydroxyethylamine) to give alcohols **43** and **44** (Scheme 5). Alcohols **43** and **44** were subsequently reacted with chloroacetyl chloride to give chlorides **45** and **46**. Compounds **43**–**46** were then used as the key intermediates for the synthesis of all of the monomers.

Alcohols **43** and **44** reacted with thyminylacetic acid[14] **4** to give monomers **47** and **48** respectively. As hoped, monomers **47** and **48** had similar solubilities to the corresponding tertiary amide derivatives **9** and **10**, but exhibited far simpler NMR spectra due to the absence of rotamers about the amide bond. Chloride **46** reacted with Boc-adenine **14** to give protected adenine monomer **50** which could be deprotected by treatment with trifluoroacetic acid to give monomer **51**. Compound **51** was again soluble in organic solvents such as chloroform and gave crystals suitable for X-ray analysis (Fig. 4), which confirmed that alkylation had occurred on N^9 as required. Reaction of chloride **46** with cytosine gave monomer **52**, the regiochemistry of which was assigned on the basis of the similarity of its NMR chemical shifts with those of the cytosine derivatives prepared earlier.

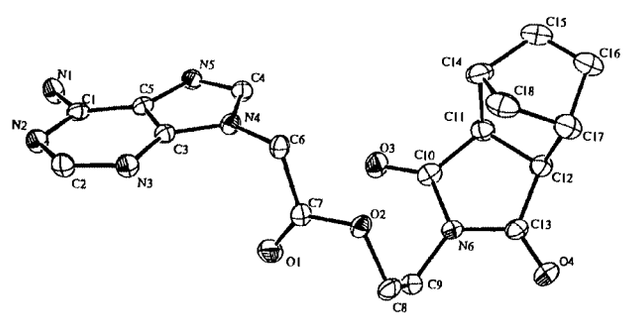
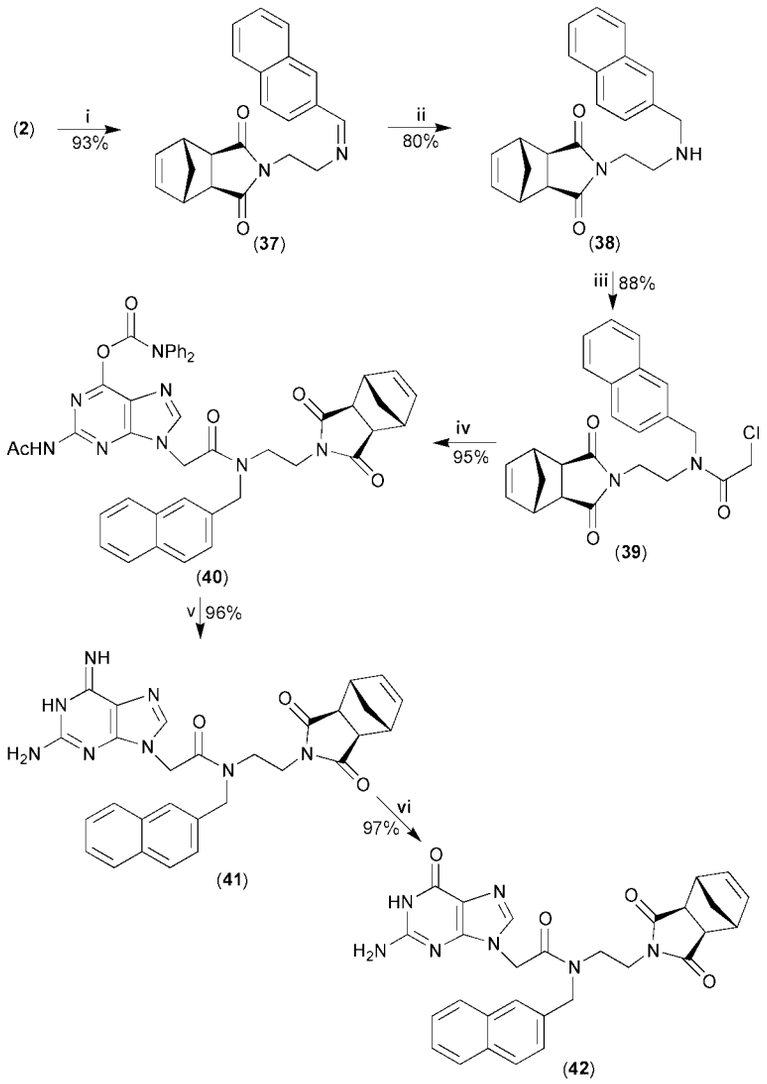
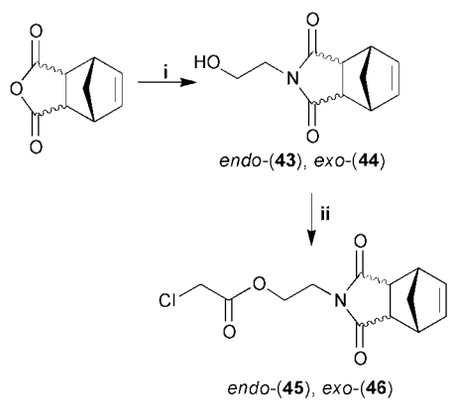


Fig. 4 The molecular structure of adenine derivative **51**.

Treatment of chloride **46** with N^2-acetylguanine[16] gave a 1 : 1 mixture of the N^7 and N^9 regio-isomers **53** and **54** respectively. These were readily separable by flash chromatography, and the regiochemistry was assigned on the basis of their ^{13}C NMR chemical shifts as discussed above. Unfortunately, it was not possible to remove the acetyl-protecting group from compound **54** since treatment with ammonia preferentially cleaved the ester bond in the linker giving amide **55** and alcohol **44**. Whilst the regiochemistry problem was potentially solvable by the use of an *O*-carbamoyl protecting group to direct alkylation to N^9



Scheme 4 *Reagents*: **i**, NEt_3, 2-naphthaldehyde; **ii**, $NaBH_3CN$; **iii**, $ClCH_2COCl$; **iv**, **35**, NaH, $N^+Bu_4I^-$; **v**, NH_4OH; **vi** H_2O.



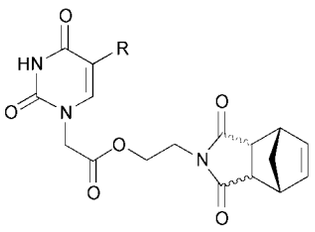
Scheme 5 *Reagents*: **i**, $H_2NCH_2CH_2OH$; **ii**, $ClCH_2COCl$, NEt_3.

as discussed above, this would still require the use of ammonia to remove the protecting group. It was also noted that compound **54** was not as soluble in organic solvents as the naphthyl amide derivative **42**, so it was decided that an ester based linker would not be appropriate for a guanine monomer. Finally, uracil monomer **49** was prepared by reaction between alcohol **44** and uracilylacetic acid[19] **5**, thus completing the synthesis of monomers from four of the five nucleic-acid bases.

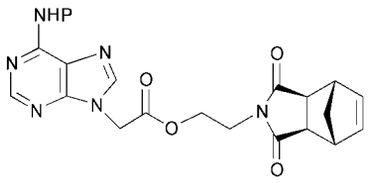
Having prepared monomers with suitable solubilities, the ROMP using ruthenium-based initiators of a representative subset of the monomers was investigated. In a previous communication[12] we demonstrated that Grubbs catalyst **56** successfully initiates the ROMP of monomers **6** and **7**. Due to the limited solubility of these monomers, these initial studies were restricted to high catalyst loadings (typically employing three equivalents of monomer). Nonetheless, ^{1}H NMR (in d_8-THF) and MALDI-TOF mass spectrometry provided good evidence that initiation occurred and that the process was well-controlled ($M_w/M_n \approx 1.1$).

Protection of the linker amide with a benzyl group gave monomer **10** which was more soluble and more amenable towards ROMP than monomers **6** or **7**. The polymerization of **10** with initiator **56** was monitored by ^{1}H NMR in CD_2Cl_2; five-equivalents of monomer were consumed in two hours at room temperature. However, under these conditions a large proportion of the initiator remained unconsumed. We have previously reported[6] that initiator **57** exhibits lower k_p/k_i ratios (rate of propagation : rate of initiation) than initiator **56**. When **57** was used to initiate the ROMP of five-equivalents of monomer **10**, a ^{1}H NMR spectrum very similar to that observed when initiator **56** was used, was obtained, but no residual initiator carbene remained.

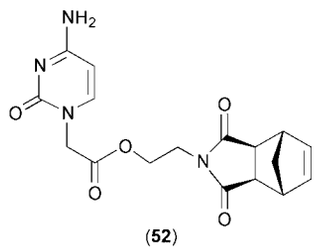
A preparative scale polymerization of **10** was then carried out in CH_2Cl_2 ([**10**] : [**57**] = 50). After 24 hours the reaction was terminated and the product isolated in 17% yield by precipitation from acetone. This product exhibits some solubility, albeit low, in chlorocarbon solvents. The ^{1}H NMR monomer olefinic resonances at δ6.26 and δ6.28 in $CDCl_3$ were absent in the product, replaced by a broad resonance at 5.75 ppm.



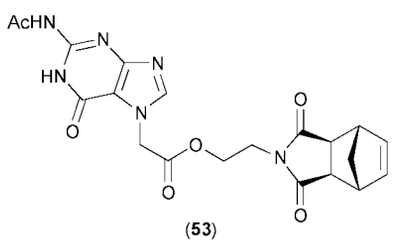
R=Me, *endo*-(**47**), *exo*-(**48**)
R=H, *exo*-(**49**)



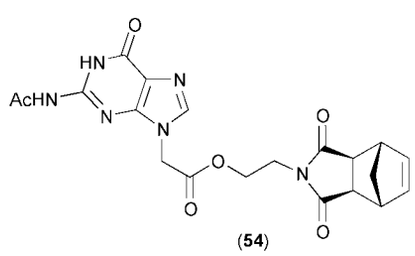
P=Boc (**50**), P=H (**51**)



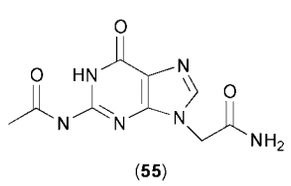
(**52**)



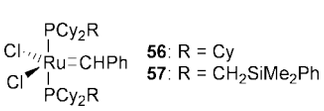
(**53**)



(**54**)



(**55**)



56: R = Cy
57: R = CH_2SiMe_2Ph

GPC analysis of the product using a differential refractometer detector gave $M_n = 2050$ ($M_w/M_n = 1.31$). The low yield and low molecular weight are consistent with a slow propagation rate (M_n calculated for 50-mer = 23130; M_n calculated for 17% conversion = 3930). The slow polymerization may be a reflection of the steric bulk of the substituent attached to the norbornene. As the propagating chain length increases so the active site becomes increasingly less accessible to successive monomer molecules.

The ROMP of the ester analogue of **10**, **48**, has also been investigated using initiators **56** and **57**. As for monomer **10**, propagating alkylidene resonances are observed when five-equivalents of monomer **48** are added to either initiator in CD_2Cl_2; again, no residual initiator carbene signal is observed when initiator **57** is employed. Poly **48** is noticeably less soluble than poly **10**. However, this does not seem to impede the ROMP of **48**. When 50-equivalents of monomer **48** were mixed with initiator **57** in chloroform, a sticky gel precipitated over a period of 24 hours. Trituration of the recovered gel with hexane afforded a white powder in 97% yield; its ^{1}H NMR spectrum in d_6-DMSO revealed signals consistent with the ring-opened poly(norbornene) product. However, all attempts to analyse the molecular weight of this product (by GPC in DMSO) were unsuccessful.

Although compounds **17** and **22** are insoluble in common organic solvents (except methanol), their Boc-protected forms are more soluble, so their polymerization was studied. The *endo*-isomer **21** did not polymerize with either initiator **56** or **57**, but the Boc-derivative of *exo*-isomer **17** has been polymerized using both initiators in $CDCl_3$. Even at high catalyst loadings (three-equivalents of monomer), the oligomers produced are only sparingly soluble and this has hampered efforts at scaling up the reaction. For example, although three-equivalents of Boc-**17** are totally consumed in just five-minutes at ambient temperature, all attempts to polymerize 20-equivalents over 24 hours have resulted in yields of less than 20%. The only characterizing data that could be obtained for the polymer is the ^{1}H NMR spectrum in d_6-DMSO. This shows two broad overlapping resonances at δ 5.71 and δ 5.59 attributable to *trans*- and *cis*-olefinic environments, respectively, of the ring-opened product. The relative intensity of the two signals implies that the polymer contains >70% *trans*-vinylene linkages.

Although the tertiary amide linker counterpart **23** is more soluble in chlorocarbons, its polymerization was only partially successful. Using ^{1}H NMR to monitor the reaction of **23** with **57** (5 : 1) showed that all of the initiator was consumed over 24 hours and the sharp monomer signals were gradually replaced by broad polymer resonances. However, all efforts to carry this reaction out on a larger scale in order to isolate and characterize poly**23** have failed. The ROMP of ester analogue **51** was also problematic. In an NMR scale experiment, three equivalents of **51** served to slowly decompose initiator **56** with no evidence for polymer formation. However, with initiator **57** a new carbene resonance was observed after 60 minutes, and additional sharp, low frequency signals, consistent with the formation of a first insertion product were observed. In the ensuing 24 hours the new carbene signal broadened, as did the other signals, suggesting that further propagation may have occurred. This process was slow, however, and after a total of 48 hours no carbene containing species were observed and most of the monomer remained unconsumed.

Cytosine derivatives **25** and **26** were insoluble in suitable solvents for studies employing initiators **56** or **57**, so their Boc-protected analogues **28** and **29** were used instead. In $CDCl_3$, three equivalents of monomer **28** require two days for complete polymerization with initiator **56**. A dramatic demonstration of the difference in reactivity of the *endo*- and *exo*-isomers was observed where, under identical conditions, monomer **29** polymerized within 10 minutes. Even at low chain lengths, the oligomers obtained from these monomers began to precipitate from the polymerization. The homopolymer of **29** (theoretically a 20-mer, but prepared in 13% yield) was only soluble in d_6-DMSO, but this allowed the ^{1}H and ^{13}C NMR spectra to be recorded. In the ^{13}C spectrum, the *cis*- and *trans*-olefin signals are well separated (134.5 and 131.5 ppm respectively) and reveal that the polymer is *trans*-biased ($\sigma_t \approx 0.75$). However, the use of

this soluble monomer failed to produce a readily soluble homopolymer, and it has therefore not proved possible to carry out GPC analyses.

The *N*-benzyl counterpart of **26**, **27**, has also proved difficult to study. In an NMR tube reaction, five-equivalents of **27** are polymerized within 2 hours, but no propagating alkylidene is observed. Furthermore, attempts to prepare a 50-mer of poly**27** yielded only unreacted monomer.

The only guanine-containing compound of sufficient solubility for ROMP studies is the *exo*-*N*-naphthyl compound **42**. In a mixture of CD_2Cl_2 and CD_3OD (9 : 1), ^1H NMR studies on the attempted ROMP of this compound with initiator **56** failed to detect any evidence for polymerization.

Conclusions

Three series of nucleic-acid base derived monomers for ROMP have been prepared. The series of compounds which contained a secondary amide linker were found, in some cases, to be too insoluble in organic solvents to be suitable for use in ROMP reactions. By changing the secondary amide linker to a tertiary amide, a series of more soluble monomers was prepared. Routes to these monomers from each of the five nucleic-acid bases have been developed, and regiochemical problems associated with guanine derivatives have been overcome by judicious choice of protecting groups. The only problem with this series of monomers is the complicated nature of their NMR spectra due to the presence of rotamers about the tertiary amide bond. This will complicate the characterization and analysis of polymers derived from these monomers. However, for polymers incorporating guanine units these are the optimal monomers. Replacement of the amide bond in the linker by an ester unit also led to a more soluble series of monomers. The ease of synthesis and simplicity of the NMR spectra make this the optimal monomer structure for all bases except guanine.

This study has revealed that the crucial factor in the ROMP of these monomers is the solubility of the propagating chain. Unfortunately, it appears that even for the more soluble monomers (typically containing the *N*-benzyl linker) at short polymer chain lengths precipitation still occurs. This may be due to hydrogen bonding between the nucleotide units (both inter- and intra-chain); this would serve to not only reduce the solubility of the living polymer, but also to encapsulate, and hence reduce access to, the active ruthenium centre. This is consistent with the results obtained when we have attempted to scale up the polymerizations to 20- or 50-monomer equivalents. Yields are typically low (10–20%) and where we have been able to obtain GPC data, the molecular weights have been well below the target figures. Further work on the polymerization of these monomers, as well as an investigation into the properties of the polymers is in progress and will be reported in due course.

Experimental

^1H NMR spectra were recorded at 250 MHz on a Bruker AM250 spectrometer fitted with a ^1H-^{13}C dual probe at ambient temperature unless otherwise stated. Spectra were referenced internally to the residual protons in the NMR solvent; signals are reported downfield of TMS. The multiplicity of signals are reported as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), broad (br) or a combination of these. ^{13}C NMR spectra were recorded on the same spectrometer at 62.5 MHz at ambient temperature unless otherwise stated. The spectra were referenced to the NMR solvent and signals are reported downfield of TMS.

Infrared spectra were recorded on a Perkin–Elmer 1600 series FTIR spectrometer, either as a KBr disc or as a thin film between NaCl plates in the reported solvent. The characteristic absorptions are reported as broad (br), strong (s), medium (m) or weak (w). Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Elemental analyses were performed on a Carlo Erba model 1106 or 1108 analyser.

Mass spectrometry was performed at the EPSRC national service at the University of Wales, Swansea. Samples were ionized by chemical ionization (CI), electron ionization (EI), electrospray (ES) or fast atom bombardment (FAB). Only molecular ion and base peaks are reported, with intensities (% of base peak) being given in parentheses. X-Ray crystallographic analyses were carried out by the EPSRC service centre at the University of Southampton, or at Imperial College of Science, Technology and Medicine, London.

Flash chromatography was performed on Matrex Silica 60 (35–70 micron) as supplied by Fischer Scientific, using the reported solvent(s). Thin-layer chromatography was carried out on polyester backed silica sheets, and visualized using ultraviolet light.

Sodium hydride was used as a 60% dispersion in mineral oil and washed with petroleum (40–60) before use. DMF and pyridine were dried over calcium hydride, distilled and stored over molecular sieves. THF was dried over sodium and distilled prior to use. Benzaldehyde was distilled immediately before use. All other solvents were used as supplied. All reagents were obtained from commercial sources and used without additional purification. All non-aqueous reactions were carried out in oven-dried glassware.

endo-Amine 1

endo-Norborn-5-ene-2,3-dicarboxylic anhydride (30 g, 0.1827 mol) was dissolved in warm toluene (250 ml). 1,2-Diaminoethane (48.9 ml, 0.7309 mol) was added and the mixture was heated to reflux temperature overnight. The cooled solution was evaporated *in vacuo* and stirred with ethyl acetate (150 ml) for five minutes. The solution was then filtered and concentrated *in vacuo* to a yellow oil which solidified under high vacuum to give the product as a pale yellow solid (22.7 g, 60%). Mp 60–62 °C (Anal. Calcd. for $C_{11}H_{14}N_2O_2 \cdot \frac{1}{4}H_2O$: C, 62.68; H, 6.94; N, 13.30. Found: C, 62.63; H, 6.76; N, 13.37%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3382 (br), 1697 (s); δ_H ($CDCl_3$) 1.2 (2H, br), 1.4 (1H, d *J* 8.7 Hz), 1.5 (1H, d *J* 8.7 Hz), 2.5 (2H, t *J* 6.4 Hz), 3.1 (2H, d, *J* 1.1 Hz), 3.15–3.25 (4H, m), 5.9 (2H, s); δ_C ($CDCl_3$) 39.5, 41.0, 44.3, 45.2, 51.7, 134.0, 177.4; *m*/*z* (CI, NH_3) 207 (MH^+, 100%) [Found: (CI, NH_3) 207.1130 (MH^+, $C_{11}H_{15}N_2O_2$ requires 207.1133)].

(*N*-Trityl-2-aminoethyl)-*exo*-norborn-5-ene-2,3-dicarboxylic imide

N-Tritylethylenediamine[13] (6.14 g, 0.0205 mol) was dissolved in toluene (60 ml). *exo*-Norborn-5-ene-2,3-dicarboxylic anhydride[20] (2.59 g, 0.0157 mol) was added and the mixture was heated to reflux temperature for sixty four hours. The cooled solution was then diluted with dichloromethane (100 ml) and washed with dilute hydrochloric acid (2 M, 3 × 40 ml), saturated aqueous sodium hydrogen carbonate (40 ml) and water (40 ml). The dried ($MgSO_4$) organic phase was then evaporated *in vacuo* to give the product as a white solid (7.2 g, 92%). Mp 164.5–165 °C (Anal. Calcd. for $C_{30}H_{28}N_2O_2$: C, 80.33; H, 6.29; N, 6.25. Found: C, 80.13; H, 6.29; N, 6.04%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3450 (br), 1695 (s); δ_H ($CDCl_3$) 1.3 (1H, d *J* 9.8 Hz), 1.4 (1H, d *J* 9.8 Hz), 1.8 (1H, s), 2.4 (2H, t *J* 5.9 Hz), 2.7 (2H, s), 3.3 (2H, s), 3.6 (2H, t *J* 5.9 Hz), 6.3 (2H, s), 7.1–7.4 (15H, m); δ_C ($CDCl_3$) 39.0, 41.8, 43.0, 45.2, 48.0, 70.6, 126.4, 127.9, 128.5, 137.9, 145.7, 178.3; *m*/*z* (CI, NH_3) 449 (MH^+, 50%), 243 (100) [Found: (FAB) 448.2159 (M^+, $C_{30}H_{28}N_2O_2$ requires 448.2151)].

exo-Amine 2 trifluoroacetate

Trifluoroacetic acid (3.77 ml, 48.9 mmol) was added drop-wise to a solution of (*N*-trityl-2-aminoethyl)-*exo*-norborn-5-ene-2,3-

dicarboxylic imide (4.39 g, 9.8 mmol) in dichloromethane (20 ml) and the mixture was stirred overnight. The excess solvent was removed *in vacuo* and the residue was suspended in diethyl ether (15 ml). The suspension was filtered to yield the product as a white crystalline solid (2.7 g, 86%). Mp 146–151 °C (Anal. Calcd. for $C_{17}H_{15}N_2O_4F_3$: C, 48.74; H, 4.72; N, 8.75. Found: C, 48.56; H, 4.73; N, 8.78%); ν_{max}(KBr)/cm^{-1} 3100–2900 (br), 1706 (s), 1682 (s); δ_H (d_6-DMSO) 1.2 (1H, d *J* 10.0 Hz), 1.3 (1H, d *J* 10.0 Hz), 2.7 (2H, s), 3.0 (2H, t *J* 6.0 Hz), 3.1 (2H, s), 3.7 (2H, t *J* 6.0 Hz), 6.3 (2H, s), 8.0 (3H, br); δ_C (d_6-DMSO) 35.8, 36.7, 42.8, 44.5, 47.7, 137.8, 177.8; *m*/*z* (CI, NH_3) 207 (M^+ cation, 100%) [Found: (CI, NH_3) 207.1134 (M^+, $C_{11}H_{15}N_2O_2$ cation requires 207.1133)].

Bis-norbornene derivative 3

exo-Norborn-5-ene-2,3-dicarboxylic anhydride (3 g, 18.3 mmol) was dissolved in warm toluene (25 ml). 1,2-Diaminoethane (5 ml, 74 mmol) was added and the mixture was heated to reflux temperature overnight. The cooled solution was evaporated *in vacuo* and stirred with ethyl acetate (25 ml) for five minutes. The solution was then filtered and concentrated *in vacuo*. The residue was purified by flash chromatography (CH_2Cl_2) to give the product as a colourless oil (3.5 g, 55%). ν_{max}($CHCl_3$)/cm^{-1} 1702 (s); δ_H ($CDCl_3$) 1.3 (1H, d *J* 8.7 Hz), 1.5 (1H, d *J* 8.7 Hz), 2.7 (2H, s), 3.3 (2H, s), 3.7 (2H, s), 6.3 (2H, s); δ_C ($CDCl_3$) 37.0, 43.0, 45.0, 48.0, 137.8, 178.1;*m*/*z* (EI) 352 (M^+, 10%), 66 (100) [Found: (EI) 352.1423 (M^+, $C_{20}H_{20}N_2O_2$ requires 352.1423)].

Thymine monomer 6

Thymine acetic acid[14] **4** (2.30 g, 12.5 mmol) and *exo*-amine **2** trifluoroacetate (2.00 g, 6.2 mmol) were suspended in a mixture of DMF (10 ml) and triethylamine (1.74 ml, 12.5 mmol). EDC (2.39 g, 12.5 mmol) was added in portions over ten minutes and the mixture was stirred overnight under an argon atmosphere. The solution was then evaporated *in vacuo* and purified by flash chromatography (10% MeOH–90% EtOAc) to yield the product as a white solid (0.69 g, 30%). R_f = 0.39 (10% MeOH–90% EtOAc); Mp 180–181 °C; ν_{max}(KBr)/cm^{-1} 3320 (s), 3060 (m), 1768 (m), 1685 (s); δ_H (d_6-DMSO) 1.2 (1H, d *J* 9.7 Hz), 1.3 (1H, d *J* 9.7 Hz), 1.7 (3H, s), 2.6 (2H, s), 3.1 (2H, s), 3.15–3.25 (2H, m), 3.35–3.45 (2H, m), 4.2 (2H, s), 6.3 (2H, s), 7.3 (1H, s), 8.2 (1H, br), 11.4 (1H, br); δ_C (d_6-DMSO) 11.6, 35.8, 37.2, 42.2, 44.0, 47.0, 48.9, 108.8, 137.3, 141.7, 150.6, 164.1, 166.8, 177.3; *m*/*z* (CI, NH_3) 390 (M + NH_4^+, 34%), 127 (100) [Found: (CI, NH_3) 373.1512 (MH^+, $C_{18}H_{21}N_4O_5$ requires 373.1512)].

Thymine monomer 7

Thymine acetic acid[14] **4** (1.92 g, 10.0 mmol) and *endo*-amine **1** (1.00 g, 4.9 mmol) were dissolved in DMF (50 ml). EDC (1.93 g, 10.0 mmol) was added in portions to the mixture and the solution was stirred overnight at room temperature under an argon atmosphere. The solvent was then evaporated *in vacuo* and the residue was dissolved in water (60 ml) and left in a refrigerator for three hours. The resultant white precipitate was collected and found to be the required product (1.37 g, 74%). Mp 124–125 °C; ν_{max}(KBr)/cm^{-1} 3510 (m), 3282 (m), 3109 (m), 2997 (m), 2946 (m), 2814 (m), 1766 (m), 1690 (s), 1576 (m); δ_H (d_6-DMSO) 1.5 (2H, s), 1.7 (3H, s), 3.0–3.3 (8H, m), 4.2 (2H, s), 6.1 (2H, s), 7.5 (1H, s); δ_C (d_6-DMSO) 11.7, 35.9, 36.6, 43.9, 45.0, 49.0, 51.4, 107.9, 134.1, 141.8, 150.7, 164.2, 166.8, 177.2; *m*/*z* (CI, NH_3) 390 (M + NH_4^+, 18%), 373 (MH^+, 58), 127 (100) [Found: (CI, NH_3) 373.1512 (MH^+, $C_{18}H_{21}N_4O_5$ requires 373.1512)].

Uracil monomer 8

exo-Amine **2** trifluoroacetate (0.50 g, 1.56 mmol) was dissolved in a solution of triethylamine (0.25 ml, 1.80 mmol) and DMF (7 ml). Uracilylacetic acid[19] **5** (0.53 g, 3.1 mmol) was added followed by EDC (0.60 g, 3.1 mmol) and the mixture was stirred overnight under an argon atmosphere. The excess solvent was evaporated *in vacuo* and the crude residue was purified by flash chromatography (10% MeOH–90% EtOAc) to afford the title compound as a white solid (0.30 g, 54%). R_f = 0.31 (10% MeOH–90% EtOAc); Mp 162–164 °C; ν_{max} (KBr)/cm^{-1} 3329 (s), 3092 (m), 3006 (m), 2888 (m), 2837 (m), 1768 (s), 1698 (s), 1553 (s); δ_H (d_6-DMSO) 1.1 (1H, d *J* 9.7 Hz), 1.3 (1H, d *J* 9.7 Hz), 2.7 (2H, s), 3.1 (2H, s), 3.15–3.25 (2H, m), 3.35–3.45 (2H, m), 4.2 (2H, s), 5.6 (1H, d *J* 7.9 Hz), 6.3 (2H, s), 7.5 (1H, d *J* 7.9 Hz), 8.2 (1H, br t *J* 5.7 Hz); δ_C (d_6-DMSO) 36.3, 37.7, 42.7, 44.5, 47.5, 49.5, 100.8, 137.8, 146.5, 151.1, 164.0, 167.2, 177.8; *m*/*z* (CI, NH_3) 376 (M + NH_4^+, 64%), 359 (MH^+, 100) [Found: (EI) 358.1273 (M^+, $C_{17}H_{18}N_4O_5$ requires 358.1277)].

endo-(Bn)-thymine monomer 9

Thymine acetic acid[14] **4** (0.94 g, 5.1 mmol) and amine **12** (0.75 g, 2.5 mmol) were suspended in DMF (2 ml). EDC (0.98 g, 5.1 mmol) was added in portions to the suspension, which was stirred overnight. The resulting clear solution was then diluted with ethyl acetate (50 ml) and washed with dilute hydrochloric acid (2 M, 3 × 15 ml), saturated aqueous sodium hydrogen carbonate solution (3 × 15 ml) and water (2 × 15 ml). The dried ($MgSO_4$) organic phase was evaporated *in vacuo* to give a white solid, which was purified by flash chromatography (EtOAc) to give the product as a white solid (0.66 g, 56%). R_f = 0.23 (EtOAc); Mp 74–78 °C; ν_{max}($CHCl_3$)/cm^{-1} 3195 (br w), 3060 (w), 2943 (w), 1692 (s); δ_H ($CDCl_3$, room temperature, rotamers present) 1.45–1.55 (1H, m), 1.65–1.75 (1H, m), 1.9 (3H, 2 × s), 3.2–3.6 (8H, m), 4.4–4.7 (4H, 3 × s), 6.0 (2H, s), 6.9 and 7.0 (1H, 2 × s), 7.1–7.5 (5H, m), 9.4 (1H, br); δ_C ($CDCl_3$, room temperature, rotamers present) 12.3, 35.3 and 35.6, 43.0 and 44.2, 44.6 and 44.8, 45.9, 48.5 and 48.9, 50.4, 52.3, 110.3 and 110.4, 126.5–129.2 (6 peaks), 134.4 and 134.5, 135.4 and 136.3, 141.1 and 141.4, 151.2, 164.7, 166.8 and 167.6, 177.9 and 178.0; *m*/*z* (CI, NH_3) 463 (MH^+, 11%), 106 (100) [Found: (CI, NH_3) 463.1976 (MH^+, $C_{25}H_{27}N_4O_5$ requires 463.1981)].

exo-(Bn)-thymine monomer 10

Thymine acetic acid[14] **4** (2.38 g, 12.9 mmol) and amine **13** (1.92 g, 6.4 mmol) were suspended in DMF (5 ml). EDC (2.48 g, 12.9 mmol) was added in portions and the mixture was stirred overnight. The resulting clear solution was then diluted with ethyl acetate (100 ml) and washed with dilute hydrochloric acid (2 M, 3 × 30 ml), saturated aqueous sodium hydrogen carbonate solution (3 × 30 ml) and water (2 × 30 ml). The ethyl acetate was evaporated *in vacuo* and the crude product was purified by flash chromatography (EtOAc) to give the title compound as a white solid (2.03 g, 68%). R_f = 0.30 (EtOAc); Mp 175–176 °C; ν_{max}($CHCl_3$) 3219 (br w), 3051 (w), 2951 (w), 1689 (s); δ_H ($CDCl_3$, room temperature, rotamers present) 1.15–1.25 (1H, m), 1.45–1.55 (1H, m), 1.9 (3H, 2 × s), 2.6 and 2.7 (2H, 2 × s), 3.2–3.7 (6H, m), 4.4–4.6 (4H, 3 × s), 6.2 and 6.3 (2H, 2 × s), 6.9 and 7.0 (1H, 2 × s), 7.2–7.5 (5H, m), 9.2 (1H, br); δ_C ($CDCl_3$, room temperature, rotamers present) 12.3, 35.9 and 36.0, 43.0, 44.3, 44.9 and 45.1, 47.9, 48.4 and 48.5, 49.0 and 50.4, 110.5, 126.5–129.4 (6 peaks), 135.3 and 136.2, 137.7, 141.0 and 141.4, 151.1, 164.4, 166.9 and 167.7, 178.1 and 178.3; *m*/*z* (CI, NH_3) 480 (M + NH_4^+, 12%), 463 (MH^+, 36) [Found: (CI, NH_3) 463.1977 (MH^+, $C_{25}H_{27}N_4O_5$ requires 463.1981)].

exo-(Bn)-uracil monomer 11

Uracilylacetic acid[19] **5** (1.5 g, 8.8 mmol) and benzylamine **13** (1.3 g, 4.4 mmol) were suspended in DMF (6 ml). EDC (1.7 g, 8.8 mmol) was added in portions and the mixture was stirred overnight under an argon atmosphere. The reaction was then diluted with ethyl acetate (70 ml) and washed with dilute hydrochloric acid (2 M, 3 × 40 ml), saturated aqueous sodium

hydrogen carbonate solution (40 ml) and water (40 ml). The dried ($MgSO_4$) organic phase was evaporated *in vacuo* to a white solid which was purified by flash chromatography (EtOAc) to give the title compound as a white solid (1.0 g, 50%). R_f = 0.17 (EtOAc); Mp 112–114.5 °C; ν_{max} (KBr)/cm^{-1} 3207 (br), 3065 (m), 2981 (m), 2949 (m), 1769 (m), 1710 (s); δ_H ($CDCl_3$, room temperature, rotamers present) 1.1–1.5 (2H, m), 2.6 and 2.7 (2H, 2 × s), 3.3 (2H, 2 × s), 3.5–3.8 (4H, m), 4.5–4.7 (4H, 4 × s), 5.7 (1H, m), 6.3 (2H, 2 × s), 7.1 (1H, d *J* 7.9 Hz), 7.1–7.4 (5H, m), 8.8 (1H, br); δ_C (d_6-DMSO, room temperature, rotamers present) 35.3 and 35.7, 42.4, 42.7, 44.5 and 44.6, 47.4 and 47.6, 47.8 and 48.3, 48.6 and 49.2, 100.7 and 100.8, 127.2, 127.4, 127.7, 128.6, 128.8, 136.5 and 137.1, 137.8, 146.6, 151.1 and 151.3, 164.0, 167.0 and 167.5, 177.6 and 177.9; *m*/*z* (CI, NH_3) 466 (M + NH_4^+, 32%), 449 (MH^+, 100) [Found: (CI, NH_3) 449.1825 (MH^+, $C_{24}H_{25}N_4O_5$ requires 449.1825)].

Benzylidene imine of amine 1

endo-Amine **1** (0.50 g, 2.4 mmol) was dissolved in dichloromethane (15 ml). An excess of magnesium sulfate was added to the stirred solution and freshly distilled benzaldehyde (0.25 ml, 2.4 mmol) was added drop-wise. The mixture was then stirred overnight under an argon atmosphere. The solution was filtered and evaporated *in vacuo* to a yellow oil which solidified under high vacuum to give the product as a pale yellow solid (0.68 g, 96%). Mp 74.5–76 °C; ν_{max} (KBr)/cm^{-1} 3052 (w), 2999 (m), 1700 (s), 1645 (s); δ_H ($CDCl_3$) 1.5 (1H, d *J* 8.8 Hz), 1.7 (1H, d *J* 8.8 Hz), 3.3 (2H, s), 3.4 (2H, s), 3.65–3.75 (4H, m), 6.0 (2H, pseudo-t *J* 1.7 Hz), 7.35–7.45 (3H, m), 7.65–7.75 (2H, m), 8.2 (1H, s); δ_C ($CDCl_3$) 39.1, 44.8, 45.8, 52.2, 58.1, 128.1, 128.6, 130.9, 134.4, 135.9, 162.7, 177.5; *m*/*z* (EI) 294 (M^+, 10%), 91 (100) [Found: (EI) 294.1371 (M^+, $C_{18}H_{18}N_2O_2$ requires 294.1368)].

endo-*N*-Benzylamine 12

The benzylidene imine of amine **1** (2.50 g, 8.0 mmol) and sodium cyanoborohydride (0.53 g, 8.0 mmol) were thoroughly mixed as solids. A solution of acetic acid (8 drops) in methanol (20 ml) was added and the mixture was stirred for four hours under an argon atmosphere. The solution was then evaporated *in vacuo* and dissolved in ethyl acetate (60 ml). The organic phase was washed with dilute hydrochloric acid (2 M, 20 ml), saturated aqueous sodium hydrogen carbonate (20 ml) and water (20 ml). The dried ($MgSO_4$) organic phase was evaporated to a pale yellow solid which was purified by flash chromatography (10% MeOH–90% EtOAc) to give the product as a white solid (1.23 g, 54%). R_f = 0.33 (10% MeOH–90% EtOAc); Mp 53–54 °C (Anal. Calcd. for $C_{18}H_{20}N_2O_2$: C, 72.94; H, 6.81; N, 9.46. Found: C, 72.90; H, 6.63; N, 9.66%); ν_{max}($CHCl_3$)/cm^{-1} 3449 (w), 3330 (w), 3064 (w), 2945 (m), 1694 (s); δ_H ($CDCl_3$) 1.5 (1H, d *J* 8.7 Hz), 1.7 (1H, d *J* 8.7 Hz), 1.9 (1H, s), 2.7 (2H, t *J* 6.2 Hz), 3.15–3.20 (2H, m), 3.25–3.35 (2H, m), 3.5 (2H, t *J* 6.2 Hz), 3.7 (2H, s), 6.0 (2H, pseudo-t *J* 1.8 Hz), 7.25–7.35 (5H, m); δ_C ($CDCl_3$) 38.0, 44.9, 45.8, 46.6, 52.2, 53.2, 127.0, 128.1, 128.4, 134.5, 140.1, 177.9; *m*/*z* (CI, NH_3) 297 (MH^+, 100%) [Found: (CI, NH_3) 297.1599 (MH^+, $C_{18}H_{21}N_2O_2$ requires 297.1603)].

Benzylidene-imine of amine 2

exo-Amine **2** trifluoroacetate (5.85 g, 18.3 mmol) and triethylamine (2.80 ml, 20.1 mmol) were dissolved in dichloromethane (50 ml). An excess of magnesium sulfate was then added. Freshly distilled benzaldehyde (2.04 ml, 20.1 mmol) was added drop-wise and the solution was stirred overnight under an argon atmosphere. The solution was then evaporated *in vacuo* to a golden yellow oil which was dissolved in diethyl ether (20 ml) and cooled in ice to precipitate the triethylammonium trifluoroacetate by-product. The solution was filtered and reduced to a yellow oil which solidified under high vacuum to yield the title compound as a white solid (5.37 g, 100%). Mp 80–86 °C; ν_{max} (KBr)/cm^{-1} 3065 (w), 1697 (s), 1647 (m); δ_H ($CDCl_3$) 1.4 (2H, s), 2.6 (2H, s), 3.2 (2H, s), 3.8 (4H, m), 6.2 (2H, pseudo-t *J* 1.8 Hz), 7.4 (3H, m), 7.6 (2H, m), 8.2 (1H, s); δ_C ($CDCl_3$) 39.3, 42.7, 45.2, 47.8, 57.6, 128.1, 128.6, 130.8, 135.9, 137.8, 162.8, 177.9; *m*/*z* (CI, NH_3) 295 (MH^+, 100%) [Found: (CI, NH_3) 295.1445 (MH^+, $C_{18}H_{19}N_2O_2$ requires 295.1446)].

exo-*N*-Benzylamine 13

The benzylidene imine of amine **2** (1.22 g, 4.1 mmol) and sodium cyanoborohydride (0.26 g, 4.1 mmol) were mixed as solids and a solution of acetic acid (5 drops) in methanol (10 ml) was added. The mixture was stirred for four hours under an argon atmosphere. The solvent was evaporated *in vacuo* and the residue was dissolved in ethyl acetate (50 ml). The organic phase was washed with saturated aqueous sodium hydrogen carbonate solution (3 × 20 ml) and water (20 ml). The dried ($MgSO_4$) solution was evaporated *in vacuo* to give the product as a white solid (0.66 g, 54%). Mp 112–113 °C (Anal. Calcd. for $C_{18}H_{20}N_2O_2$: C, 72.94; H, 6.81; N, 9.46. Found: C, 72.95; H, 6.88; N, 9.52%); ν_{max}($CHCl_3$)/cm^{-1} 3438 (br), 2992 (w), 1696 (s); δ_H ($CDCl_3$) 1.5 (2H, s), 1.6 (1H, br s), 2.7 (2H, s), 2.8 (2H, t *J* 6.1 Hz), 3.3 (2H, s), 3.6 (2H, t *J* 6.1 Hz), 3.8 (2H, s), 6.3 (2H, s), 7.2–7.3 (5H, m); δ_C ($CDCl_3$) 38.1, 42.8, 45.2, 46.4, 47.8, 53.2, 127.0, 128.1, 128.4, 137.8, 139.9, 178.3; *m*/*z* (CI, NH_3) 297 (MH^+, 100%) [Found: (CI, NH_3) 297.1593 (MH^+, $C_{18}H_{21}N_2O_2$ requires 297.1603)].

N^6-Boc-adenine 14

Adenine (3.0 g, 22.2 mmol) was suspended in DMF (100 ml) and sodium hydride (3.55 g of a 60% dispersion, 88.8 mmol) was added. After five minutes, di-*tert*-butyl dicarbonate (19.38 g, 88.8 mmol) was added in portions and the mixture was stirred overnight. The solution was then concentrated *in vacuo* to a yellow residue, which was cautiously re-dissolved in water (40 ml). The pH was adjusted to pH 6 and the solution was left to stand in an ice bath for ten minutes. The resulting creamy white precipitate was collected, and dried under vacuum to give the required product (3.76 g, 72%). Mp 280–300 °C; ν_{max}(KBr)/cm^{-1} 3336 (s), 3182 (br s), 2981 (s), 1728 (s), 1570 (s); δ_H (d_6-DMSO) 1.5 (9H, s), 8.4 (1H, s), 8.6 (1H, s), 10.7 (1H, br); δ_C (d_6-DMSO) 28.0, 81.1, 145.4, 151.3, 152.7; *m*/*z* (CI, NH_3) 236 (MH^+, 100%) [Found: (CI, NH_3) 236.1147 (MH^+, $C_9H_{14}N_5O_2$ requires 236.1147)].

Methyl (N^6-Boc-N^9-adeninyl)acetate 15

N^6-Boc-Adenine **14** (1.07 g, 4.57 mmol) was suspended in DMF (5 ml). Potassium carbonate (0.63 g, 4.57 mmol) and caesium carbonate (0.15 g, 0.46 mmol) were added and the mixture was stirred for five minutes. Methyl bromoacetate (0.52 ml, 5.48 mmol) was then added drop-wise and the solution was stirred overnight. The solution was then diluted with ethyl acetate (60 ml) and washed with water (3 × 30 ml). The dried organic phase was evaporated *in vacuo* to give the product as a pale yellow solid (0.93 g, 66%). Mp 134–138 °C; ν_{max}($CHCl_3$)/cm^{-1} 2986 (m), 1739 (s), 1601 (m); δ_H ($CDCl_3$) 1.5 (9H, s), 3.8 (3H, s), 5.0 (2H, s), 8.0 (1H, s), 8.2 (1H, br), 8.7 (1H, s); δ_C ($CDCl_3$) 28.1, 44.1, 53.0, 82.1, 121.7, 142.7, 149.9, 150.0, 151.3, 153.1, 167.3; *m*/*z* (CI, NH_3) 308 (MH^+, 23%), 208 (100) [Found: (CI, NH_3) 308.1359 (MH^+, $C_{13}H_{18}N_5O_4$ requires 308.1359)].

N^6-Boc-Adeninylacetic acid 16

Methyl (N^6-(Boc)-N^9-adeninyl)acetate **15** (0.118 g, 0.4 mmol) was dissolved in methanol (10 ml). Sodium hydroxide (2 M) was added drop-wise to the stirred solution and the saponification was monitored by TLC (eluting with ethyl acetate). After the

disappearance of the starting material, the solution was stirred for a further thirty minutes. The solution was then neutralized with hydrochloric acid (2 M) producing a white precipitate. The solvent was evaporated *in vacuo* to leave a white solid which was stirred in methanol (5 ml), filtered and concentrated *in vacuo* to give the product as a white solid (0.112 g, 100%). Mp >260 °C dec.; ν_{max}(KBr)/cm^{-1} 3429 (br), 1741 (w), 1618 (s); δ_H (d$_6$-DMSO) 1.5 (9H, s), 4.6 (2H, s), 8.3 (1H, s), 8.5 (1H, s), 10.0 (1H, br); δ_C (d$_6$-DMSO) 28.0, 47.1, 80.0, 123.0, 145.6, 149.3, 151.0, 151.4, 152.2, 169.3.

exo-N^6-Boc-adenine monomer

exo-Amine **2** trifluoroacetate (2.15 g, 6.7 mmol) was dissolved in a mixture of triethylamine (2.34 ml, 16.8 mmol) and DMF (9 ml). HOBt (1.00 g, 7.4 mmol) was added followed by N^6-Boc-adeninylacetic acid **16** (1.89 g, 6.7 mmol). Finally, DCC (1.52 g, 7.4 mmol) was added in portions and the mixture was stirred overnight at ambient temperature. The solution was then diluted with ethyl acetate (230 ml) and washed with water (3 × 40 ml). The dried ($MgSO_4$) organic phase was evaporated to a yellow solid, which was purified by flash chromatography (10% MeOH–90% EtOAc) to yield the title compound as a white solid (0.97 g, 30%). R_f = 0.15 (10% MeOH–90% EtOAc); Mp 178–182 °C; ν_{max}(KBr)/cm^{-1} 3324 (br), 2981 (m), 1698 (s), 1612 (s); δ_H ($CDCl_3$) 1.0 (1H, d *J* 9.1 Hz), 1.45–1.55 (10H, m), 2.6 (2H, s), 3.1 (2H, s), 3.35–3.45 (2H, m), 3.55–3.65 (2H, m), 4.8 (2H, s), 6.2 (2H, s), 6.8 (1H, br), 8.0 (1H, s), 8.7 (1H, s); δ_C ($CDCl_3$) 28.1, 37.9, 39.0, 42.8, 45.1, 46.3, 47.9, 82.3, 121.2, 137.7, 143.1, 149.7, 149.9, 151.1, 153.0, 166.2, 178.4; *m*/*z* (FAB) 504 (M + Na$^+$, 72%), 483 (MH$^+$, 22), 382 (100) [Found: (FAB) 482.2145 (MH$^+$, $C_{23}H_{28}N_7O_5$ requires 482.2152)].

exo-Adenine monomer 17

Trifluoroacetic acid (1 ml, 13 mmol) was added drop-wise to a solution of *exo*-N^6-Boc-adenine monomer (0.200 g, 0.415 mmol) in dichloromethane (20 ml) and the mixture was stirred overnight. The organic phase was then diluted with ethyl acetate (50 ml) and washed carefully with saturated aqueous sodium hydrogen carbonate solution (2 × 15 ml). The dried ($MgSO_4$) organic phase was evaporated *in vacuo* to give the product as a white solid (0.133 g, 90%). Mp 218–222 °C; ν_{max}(KBr)/cm^{-1} 3350–3100 (br s), 1772 (m), 1696 (s), 1592 (s), 1573 (s); δ_H (d$_6$-DMSO) 1.1 (1H, d *J* 9.7 Hz), 1.3 (1H, d *J* 9.7 Hz), 2.6 (2H, s), 3.1 (2H, s), 3.25–3.30 (2H, m), 3.35–3.45 (2H, m), 4.7 (2H, s), 6.3 (2H, s), 7.2 (2H, br s), 8.0 (1H, s), 8.1 (1H, s), 8.4 (1H, br t *J* 5.7 Hz); δ_C (d$_6$-DMSO) 36.4, 37.6, 42.6, 44.4, 44.9, 47.4, 118.3, 137.7, 141.6, 149.8, 152.4, 155.9, 166.8, 177.7; *m*/*z* (EI) 382 (MH$^+$, 40%), 381 (M$^+$, 100) [Found: (EI) 381.1550 (M$^+$, $C_{18}H_{19}N_7O_3$ requires 381.1549)].

endo-Chloroacetamide 18

endo-Amine **1** (3.00 g, 14.5 mmol) was dissolved in a mixture of triethylamine (8.08 ml, 58 mmol) and dichloromethane (80 ml). A solution of chloroacetyl chloride (1.16 ml, 14.5 mmol) in dichloromethane (50 ml) was added drop-wise and the mixture was stirred overnight at room temperature. The organic phase was then washed with saturated brine solution (3 × 100 ml) and water (2 × 100 ml). The dried ($MgSO_4$) organic layer was then evaporated *in vacuo* to leave a pale yellow solid (3.15 g, 77%). Mp 82–84 °C (Anal. Calcd. for $C_{13}H_{15}N_2O_3Cl$: C, 55.30; H, 5.36; N, 9.93. Found: C, 55.19; H, 5.46; N, 9.64%); ν_{max}($CHCl_3$)/cm^{-1} 3365 (br), 1770 (s), 1697 (s); δ_H ($CDCl_3$) 1.6 (1H, d *J* 8.8 Hz), 1.8 (1H, d *J* 8.8 Hz), 3.3–3.6 (8H, m), 4.0 (2H, s), 6.1 (2H, s), 7.0 (1H, br); δ_C ($CDCl_3$) 36.3, 39.1, 42.4, 44.9, 45.8, 52.3, 134.4, 166.3, 177.9; *m*/*z* (CI, NH_3) 300 (M + NH_4^+, 56%), 283 (MH$^+$, 100) [Found: (CI, NH_3) 283.0849 (MH$^+$, $C_{13}H_{16}N_2O_3Cl^{35}$ requires 283.0894)].

exo-Chloroacetamide 19

exo-Amine **2** trifluoroacetate (1.00 g, 3.1 mmol) was dissolved in a mixture of dichloromethane (30 ml) and triethylamine (1.31 ml, 9.4 mmol). A solution of chloroacetyl chloride (0.35 ml, 3.4 mmol) in dichloromethane (30 ml) was added drop-wise and the mixture was stirred overnight at room temperature. The organic phase was then washed with saturated brine solution (2 × 30 ml) and water (2 × 30 ml). The dried ($MgSO_4$) organic layer was evaporated *in vacuo* to leave a pale yellow solid (0.74 g, 83%). Mp 94–95 °C (Anal. Calcd. for $C_{13}H_{15}N_2O_3Cl$: C, 55.30; H, 5.36; N, 9.93. Found: C, 55.20; H, 5.52; N, 9.78%); ν_{max}($CHCl_3$)/cm^{-1} 3365 (br), 3068 (w), 2949 (m), 1770 (m), 1694 (s); δ_H ($CDCl_3$) 1.0 (1H, d *J* 9.9 Hz), 1.3 (1H, d *J* 9.9 Hz), 2.5 (2H, s), 3.0 (2H, s), 3.25–3.35 (2H, m), 3.45–3.55 (2H, m), 3.8 (2H, s), 6.1 (2H, s), 7.2 (1H, br); δ_C ($CDCl_3$) 38.0, 38.9, 42.4, 42.8, 45.1, 47.8, 137.7, 166.6, 178.3; *m*/*z* (CI, NH_3) 300 (M + NH_4^+, 40%), 283 (MH$^+$, 31), 77(100) [Found: (CI, NH_3) 283.0852 (MH$^+$, $C_{13}H_{16}N_2O_3Cl^{35}$ requires 283.0849)].

exo-*N*-(Bn)-Chloroacetamide 20

N-Benzylamine **13** (1.45 g, 4.9 mmol) and triethylamine (1.37 ml, 9.8 mmol) were dissolved in dichloromethane (50 ml). A solution of chloroacetyl chloride (0.78 ml, 9.8 mmol) in dichloromethane (10 ml) was added drop-wise and the mixture was stirred overnight. The organic phase was washed with dilute hydrochloric acid (2 M, 3 × 20 ml), saturated aqueous sodium hydrogen carbonate solution (3 × 20 ml) and water (2 × 20 ml). The dried ($MgSO_4$) organic phase was evaporated *in vacuo* to give the product as a pale yellow oil which solidified under high vacuum to a white solid (1.62 g, 90%). Mp 55–59 °C (Anal. Calcd. for $C_{20}H_{21}N_2O_3Cl$: C, 64.49; H, 5.69; N, 7.53. Found: C, 64.44; H, 5.89; N, 7.66%); ν_{max}($CDCl_3$)/cm^{-1} 3066 (w), 3031 (w), 2989 (w), 1700 (s), 1656 (s); δ_H ($CDCl_3$, room temperature, rotamers present) 1.15–1.25 (1H, m), 1.45–1.55 (1H, m), 2.55–2.65 (2H, m), 3.15–3.25 (2H, m), 3.4–3.6 (4H, m), 4.0 + 4.2 (2H, 2 × s), 4.55–4.65 (2H, m), 6.15–6.25 (2H, m), 7.1–7.4 (5H, m); δ_C ($CDCl_3$, room temperature, rotamers present) 35.6 and 36.2, 40.9 and 41.2, 42.8 and 43.0, 43.4 and 43.8, 44.9 and 45.1, 48.0, 48.4 and 50.8, 126.4–130.1 (6 peaks), 135.6 and 136.3, 137.7, 167.0 and 167.7, 177.7 and 178.0; *m*/*z* (CI, NH_3) 390 (M + NH_4^+, 50%), 373 (MH$^+$, 61), 339 (100), 106 (100) [Found: (CI, NH_3) 373.1313 (MH$^+$, $C_{20}H_{22}N_2O_3Cl^{35}$ requires 373.1319)].

endo-N^6-Boc-adenine monomer 21

N^6-Boc-Adenine **14** (0.34 g, 1.4 mmol), *endo*-chloride derivative **18** (0.25 g, 0.88 mmol) and 18-crown-6 (0.47 g, 1.77 mmol) were suspended in DMF (0.9 ml). Sodium hydride (0.07 g of a 60% dispersion, 1.77 mmol) was added and the mixture was stirred overnight at room temperature under an argon atmosphere. The solution was quenched with water (10 ml) and extracted with ethyl acetate (3 × 20 ml). The dried ($MgSO_4$) organic phase was concentrated *in vacuo* to a yellow oil which was purified by flash chromatography (10% MeOH–90% EtOAc) to yield the product as a white solid (0.13 g, 31%). Recrystallization from 10% MeOH–90% EtOAc yielded crystals suitable for X-ray analysis. R_f = 0.15 (10% MeOH–90% EtOAc); Mp 194–195 °C (Anal. Calcd. for $C_{23}H_{27}N_7O_5$: C, 57.37; H, 5.65; N, 20.36. Found: C, 57.27; H, 5.62; N, 20.16%); ν_{max}($CHCl_3$)/cm^{-1} 3217 (br), 1756 (m), 1697 (m), 1670 (m); δ_H ($CDCl_3$) 1.55–1.65 (10H, m), 1.8 (1H, d *J* 8.7 Hz), 3.25–3.30 (2H, m), 3.35–3.40 (4H, m), 3.45–3.55 (2H, m), 4.9 (2H, s), 6.1 (2H, pseudo-t *J* 1.8 Hz), 6.8 (1H, br), 8.1 (1H, s), 8.2 (1H, br s), 8.8 (1H, s); δ_C ($CDCl_3$) 28.1, 37.3, 39.5, 44.9, 45.8, 46.3, 52.3, 82.3, 121.4, 134.4, 142.9, 149.5, 150.0, 151.8, 153.1, 166.0, 178.1; *m*/*z* (CI, NH_3) 482 (MH$^+$, 76%), 382 (100), 318 (100), 136 (100) [Found: (FAB) 482.2176 (MH$^+$, $C_{23}H_{28}N_7O_5$ requires 482.2152)].

Crystal data:‡ $C_{23}H_{27}N_7O_5$, M = 481.5, monoclinic, $C2/c$ (no. 15), a = 37.962(4), b = 12.655(1), c = 9.552(1) Å, β = 91.59(1), V = 4587.0(7) Å^3, Z = 8, D_c = 1.395 g cm^{-3}, μ(Cu-Kα) = 8.40 cm^{-1}, T = 293 K, colourless platy needles; 3812 independent measured reflections, F^2 refinement, R_1 = 0.063, wR_2 = 0.155, 2853 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 128°$], 325 parameters.

Adenine monomer 22

endo-(Boc)-adenine derivative **21** (0.048 g, 0.1 mmol) was suspended in dichloromethane (1 ml). Trifluoroacetic acid (1 ml) was added drop-wise and the mixture was stirred at room temperature overnight. The solution was then evaporated *in vacuo* to an oil which was dissolved in dichloromethane (20 ml) and washed with saturated aqueous sodium hydrogen carbonate solution (2 × 10 ml). The dried ($MgSO_4$) organic phase was reduced to a white solid (0.034 g, 91%). Mp 207 °C; ν_{max}(KBr)/cm^{-1} 3326 (br), 1697 (s); δ_H ($CDCl_3$) 1.5 (1H, d J 8.5 Hz), 1.7 (1H, d J 8.5 Hz), 3.15–3.20 (2H, m), 3.25–3.30 (4H, m), 3.45–3.55 (2H, m), 4.8 (2H, s), 5.7 (2H, br), 6.1 (2H, s), 6.6 (1H, br), 7.9 (1H, s), 8.4 (1H, s); δ_C (d_6-DMSO) 36.5, 37.0, 44.3, 45.0, 45.4, 51.7, 118.3, 134.5, 141.8, 149.8, 152.5, 156.0, 166.8, 177.5; *m*/*z* (CI, NH_3) 382 (MH^+, 100%) [Found: 382.1627 (MH^+ requires 382.1628)].

N^6-Boc-protected *exo*-(Bn)-adenine monomer

N^6-Boc-Adenine **14** (2.00 g, 8.5 mmol) was suspended in DMF (15 ml) and sodium hydride (0.51 g of a 60% dispersion, 12.8 mmol) was added in portions. A mixture of chloroacetamide **20** (4.00 g, 10.7 mmol) and tetrabutylammonium iodide (0.31 g, 0.85 mmol) was added in portions and the mixture stirred overnight under an argon atmosphere. The solution was then diluted with ethyl acetate (100 ml) and washed with water (5 × 20 ml). The dried ($MgSO_4$) organic phase was evaporated *in vacuo* to a yellow solid which was purified by flash chromatography (10% MeOH–90% EtOAc) to leave the product as a white solid (2.17 g, 53%). R_f = 0.56 (10% MeOH–90% EtOAc); Mp 85–86 °C; ν_{max}($CHCl_3$)/cm^{-1} 3410 (m), 3063 (w), 2934 (w), 1749 (s), 1699 (s), 1670 (s), 1613 (s), 1591 (s); δ_H($CDCl_3$, room temperature, rotamers present) 1.2 (1H, d J 9.8 Hz), 1.4 (1H, d J 9.8 Hz), 1.6 (9H, s), 2.6 and 2.7 (2H, 2 × s), 3.2 and 3.3 (2H, 2 × s), 3.5–3.8 (4H, m), 4.6 and 4.7 (2H, 2 × s), 5.0 and 5.2 (2H, 2 × s), 6.3 and 6.4 (2H, 2 × s), 7.2–7.5 (5H, m), 7.9 and 8.1 (1H, 2 × s), 7.95 and 8.0 (1H, 2 × br s), 8.7 (1H, 2 × s); δ_C ($CDCl_3$, room temperature, rotamers present) 28.0, 35.7, 43.0, 44.1 and 44.3, 44.9 and 45.1, 48.0 and 48.1, 49.0 and 50.3, 82.0, 120.9, 126.3 and 128.0, 128.3 and 128.4, 128.9 and 129.4, 135.0, 137.8, 143.2, 149.7, 149.9, 151.2, 152.7, 165.0, 166.8, 178.0 and 178.2; *m*/*z* (EI) 497 (100%), 471 (92), 59 (100) [Found: (FAB) 572.2628 (MH^+, $C_{30}H_{34}N_7O_5$ requires 572.2621)].

exo-(Bn)-adenine monomer 23

exo-(Bn)-N^6-Boc-adenine derivative (0.80 g, 1.4 mmol) was dissolved in dichloromethane (10 ml) and trifluoroacetic acid (1.1 ml, 14 mmol) was added drop-wise. The mixture was stirred overnight at ambient temperature. The solution was then diluted with ethyl acetate (60 ml) and washed carefully with saturated aqueous sodium hydrogen carbonate solution (2 × 15 ml). The dried ($MgSO_4$) organic phase was evaporated *in vacuo* to leave the product as a white solid (0.61 g, 92%). Mp 172–174 °C; ν_{max}($CHCl_3$) 3411 (br s), 3068 (w), 2949 (w), 1698 (s), 1635 (s), 1597 (s); δ_H ($CDCl_3$, room temperature, rotamers present) 1.1–1.3 (1H, m), 1.4–1.6 (1H, m), 2.6 + 2.8 (2H, 2 × s), 3.2 and 3.3 (2H, 2 × s), 3.5–3.8 (4H, m), 4.6 and 4.7 (2H, 2 × s), 4.9 and 5.1 (2H, 2 × s), 5.95–6.05 (2H, br m), 6.2 and 6.3 (2H, 2 × s), 7.2–7.4 (5H, m), 7.8 and 7.9 (1H, 2 × s), 8.3 (1H, s); δ_C (d_6-DMSO, room temperature, rotamers present) 35.2 and 35.9, 42.3 and 42.6, 42.9, 43.6, 44.1, 44.3 and 44.4, 47.3 and 47.6, 48.1, 49.1, 118.2, 127.2, 127.6, 128.5, 128.9, 136.4 and 137.0, 137.6, 141.9, 149.9, 152.3, 155.8, 166.2 and 166.7, 177.6 and 177.8; *m*/*z* (EI) 472 (MH^+, 29%), 471 (M^+, 88), 295 (100), 91 (100) [Found: (EI) 471.2017 (M^+, $C_{25}H_{25}N_7O_3$ requires 471.2019)].

Aminol 24

Sodium borohydride (0.066 g, 1.7 mmol) was dissolved in ethanol (10 ml). The benzylidene imine of amine **1** (0.515 g, 1.7 mmol) was added in portions and the mixture was stirred for four and a half hours. The solution was evaporated *in vacuo* and the residue was dissolved in dichloromethane (40 ml). The organic phase was washed with saturated aqueous sodium hydrogen carbonate (2 × 10 ml) and water (10 ml). The dried ($MgSO_4$) organic phase was then evaporated *in vacuo* to a colourless oil which was purified by flash chromatography using a solvent gradient (EtOAc, 10% MeOH–90% EtOAc) to yield compounds **12** and **24** (0.046 g, 9%) as white solids. R_f = 0.06 (10% MeOH–90% EtOAc); Mp 118–119 °C (Anal. Calcd. for $C_{18}H_{22}N_2O_2$: C, 72.44; H, 7.44; N, 9.39. Found: C, 72.26; H, 7.47; N, 9.33%); ν_{max}($CHCl_3$)/cm^{-1} 3415 (br s), 1670 (s); δ_H ($CDCl_3$) 1.4 (1H, d J 8.4 Hz), 1.6 (1H, d J 8.4 Hz), 2.55–2.60 (2H, m), 2.65–2.70 (1H, m), 2.85–2.95 (1H, m), 3.1 (1H, s), 3.15–3.25 (2H, m), 3.7 (2H, s), 3.95–4.05 (1H, m), 4.4 (1H, s), 5.95–6.00 (1H, m), 6.05–6.10 (1H, m), 7.3–7.4 (5H, m); δ_C ($CDCl_3$) 42.3, 44.7, 45.0, 45.5, 48.2, 49.3, 51.1, 53.5, 85.9, 127.7, 128.4, 128.8, 133.2, 136.1, 138.0, 175.8; *m*/*z* (CI, NH_3) 299 (MH^+, 58%), 281 (100) [Found: (CI, NH_3) 299.1757 (MH^+, $C_{18}H_{23}N_2O_2$ requires 299.1759)].

endo-Cytosine monomer 25

Cytosine (0.39 g, 3.5 mmol) was suspended in DMF (3 ml) and triethylamine (0.74 ml, 5.31 mmol). Sodium hydride (0.20 g of 60% dispersion, 4.9 mmol) was added and the effervescent suspension stirred for five minutes. *endo*-Chloride **18** (1.00 g, 3.5 mmol) was added in portions and the mixture was stirred overnight at room temperature under an argon atmosphere. The reaction mixture was concentrated *in vacuo* and purified by flash chromatography (20% MeOH–80% CH_2Cl_2) to give the product as a white solid (1.22 g, 98%); R_f = 0.31 (20% MeOH–80% CH_2Cl_2); Mp 176–180 °C (Anal. Calcd. for $C_{17}H_{19}N_5O_4 \cdot \frac{1}{3}H_2O$: C, 56.19; H, 5.46; N, 19.27. Found: C, 56.17; H, 5.34; N, 19.20%); ν_{max}(KBr)/cm^{-1} 3389 (s), 3343 (s), 3190 (m), 2995 (w), 1763 (m), 1687 (s), 1654 (s), 1605 (s); δ_H (d_6-DMSO) 1.5 (2H, s), 3.0–3.4 (8H, m), 4.2 (2H, s), 5.7 (1H, d J 7.2 Hz), 6.0 (2H, pseudo-t J 1.7 Hz), 7.0 (1H, br s), 7.3 (1H, br s), 7.4 (1H, d J 7.2 Hz), 8.2 (1H, br t J 5.7 Hz); δ_C (d_6-DMSO) 36.2, 36.9, 44.2, 45.3, 50.7, 51.7, 93.2, 134.4, 146.9, 155.9, 166.2, 167.8, 177.5; *m*/*z* (CI, NH_3) 358 (MH^+, 47%), 112 (100) [Found: (CI, NH_3) 358.1515 (MH^+, $C_{17}H_{20}N_5O_4$ requires 358.1515)].

exo-Cytosine monomer 26

Cytosine (0.18 g, 1.6 mmol) was suspended in DMF (1 ml) and triethylamine (0.34 ml, 2.4 mmol). Sodium hydride (0.09 g, of a 60% dispersion, 2.3 mmol) was then added in portions. After five minutes, *exo*-chloroacetamide **19** (0.46 g, 1.6 mmol) was added and the mixture was stirred overnight under an argon atmosphere. The solution was then evaporated *in vacuo* and purified by flash chromatography (20% MeOH–80% CH_2Cl_2) to give the product as a white solid (0.48 g, 85%). R_f = 0.35 (20% MeOH–80% CH_2Cl_2); Mp 245–250 °C dec. (Anal. Calcd. for $C_{17}H_{19}N_5O_4$: C, 57.14; H, 5.36; N, 19.60. Found: C, 57.17; H, 5.38; N, 19.68%); ν_{max} (Nujol®)/cm^{-1} 3385 (m), 3345 (m), 3185 (m), 1761 (w), 1693 (s), 1652 (s), 1606 (s); δ_H (d_6-DMSO) 1.1 (1H, d J 9.4 Hz), 1.3 (1H, d J 9.4 Hz), 2.7 (2H, s), 3.1 (2H,

‡ CCDC reference numbers 168679–168681. See http://www.rsc.org/suppdata/p1/b1/b107139d/ for crystallographic files in .cif or other electronic format.

s), 3.15–3.25 (2H, m), 3.35–3.45 (2H, m), 4.2 (2H, s), 5.6 (1H, d *J* 7.1 Hz), 6.3 (2H, s), 7.0 (1H, br), 7.1 (1H, br), 7.4 (1H, d *J* 7.1 Hz), 8.1 (1H, br); δ_C (d_6-DMSO) 36.2, 37.7, 42.7, 44.5, 47.5, 50.9, 93.3, 137.8, 146.9, 156.0, 166.3, 168.0, 177.8; *m*/*z* (CI, NH_3) 358 (MH^+, 100%) [Found: (CI, NH_3) 358.1515 (MH^+, $C_{17}H_{20}N_5O_4$ 358.1515)].

exo-(Bn)-cytosine monomer 27

Sodium hydride (0.235 g of a 60% dispersion, 5.9 mmol) was added in portions to a suspension of cytosine (0.467 g, 4.2 mmol) in DMF (7 ml). After five minutes, a mixture of *exo*-(Bn)-chloride **20** (2.031 g, 5.4 mmol) and tetrabutylammonium iodide (0.155 g, 0.4 mmol) was added in portions to the stirred suspension and the mixture was stirred overnight under an argon atmosphere. The crude product was then precipitated from ether (to remove DMF and unreacted **20**) and purified by flash chromatography (10% MeOH–90% CH_2Cl_2) to leave the title compound as a white solid (1.16 g, 62%). R_f = 0.23 (10% MeOH–90% CH_2Cl_2); Mp 186–190 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3337 (br), 3198 (br), 3060 (w), 2943 (w), 1769 (m), 1698 (s), 1652 (s), 1608 (s); δ_H ($CDCl_3$, room temperature, rotamers present) 1.1 (1H, d *J* 9.4 Hz), 1.4–1.6 (1H, m), 2.5 and 2.7 (2H, 2 × s), 3.1 (2H, 2 × s), 3.2–3.7 (4H, m), 4.4–4.6 (4H, m), 5.8 (1H, d *J* 7.2 Hz), 6.9 (2H, br), 7.1–7.4 (6H, m); δ_C ($CDCl_3$, room temperature, rotamers present) 35.7 and 36.0, 42.9, 43.4 and 43.8, 45.0, 47.8 and 48.0, 48.9 and 50.0, 50.3 and 50.7, 95.4, 127.0–129.1 (6 peaks), 135.7 and 136.4, 137.7, 146.3 and 146.6, 157.0, 166.2, 168.0 and 168.5, 178.3; *m*/*z* (EI) 447 (M^+, 16%), 229 (100), 66 (100) [Found: (EI) 447.1913 (M^+, $C_{24}H_{25}N_5O_4$ requires 447.1907)].

endo-Boc-cytosine derivative 28

endo-Cytosine monomer **25** (1.45 g, 4.0 mmol) was suspended in DMF (5 ml) and sodium hydride (0.21 g, of a 60% dispersion, 5.3 mmol) was added in portions, producing a yellow coloured suspension. After five minutes di-*tert*-butyl dicarbonate (1.15 g, 5.3 mmol) was added turning the solution a dark red colour. The mixture was stirred overnight under an argon atmosphere. The solution was then evaporated *in vacuo* and purified by flash chromatography (5% MeOH–95% CH_2Cl_2) to give compound **28** as a white solid (0.79 g, 43%). R_f = 0.36 (5% MeOH–95% CH_2Cl_2); Mp 178–184 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3410 (br), 1734 (w), 1697 (s), 1654 (m); δ_H ($CDCl_3$) 1.45–1.55 (10H, m), 1.7 (1H, d *J* 8.7 Hz), 3.2–3.3 (6H, m), 3.25–3.35 (2H, m), 4.5 (s, 2H), 6.1 (2H, s), 7.3 (1H, d *J* 7.3 Hz), 7.4 (1H, br), 7.7 (1H, d *J* 7.3 Hz); δ_C ($CDCl_3$) 28.0, 37.3, 38.1, 44.7, 45.9, 52.2, 52.5, 82.7, 95.6, 134.5, 149.2, 151.3, 156.4, 163.3, 167.0, 178.3; *m*/*z* (FAB) 480 (M + Na^+, 72%), 458 (MH^+, 23), 152 (100) [Found: (FAB) 458.2047 (MH^+, $C_{22}H_{27}N_5O_6$ requires 457.2040)].

exo-Boc-cytosine derivative 29

exo-Cytosine monomer **26** (0.10 g, 0.28 mmol) was suspended in DMF (1 ml) and sodium hydride (0.02 g of 60% dispersion, 0.36 mmol) was added. After five minutes, di-*tert*-butyl dicarbonate (0.08 g, 0.36 mmol) was added and the mixture was stirred overnight under an argon atmosphere. The solution was then evaporated *in vacuo* and purified by flash chromatography (5% MeOH–95% CH_2Cl_2) to give the product as a white solid (0.048 g, 38%). R_f = 0.36 (5% MeOH–95% CH_2Cl_2); Mp 149–153 °C; δ_H ($CDCl_3$) 1.2 (1H, d *J* 10.0 Hz), 1.45–1.55 (10H, m), 2.6 (2H, d *J* 1.1 Hz), 3.2 (2H, s), 3.35–3.45 (2H, m), 3.55–3.65 (2H, m), 4.4 (2H, s), 6.2 (2H, pseudo-t *J* 1.7 Hz), 7.2 (1H, d *J* 7.4 Hz), 7.4 (1H, br), 7.6 (1H, d *J* 7.4 Hz), 7.9 (1H, br); δ_C ($CDCl_3$) 28.0, 37.8, 38.3, 43.0, 45.0, 47.9, 52.9, 82.8, 95.7, 137.7, 148.8, 151.2, 156.4, 163.2, 167.0, 178.5; *m*/*z* (Electrospray) 480 (M + Na^+, 80%), 380 (100) [Found: (Electrospray) 480.1860 (M + Na^+, $C_{22}H_{27}N_5O_6Na$ requires 480.1859)].

endo-Cytosine monomer trifluoroacetate 30

endo-Cytosine monomer **25** (0.100 g, 0.3 mmol) was suspended in dichloromethane (1 ml) and trifluoroacetic acid (4 drops) was added. The solution was stirred overnight at ambient temperature. The solution was then evaporated *in vacuo* to leave a white solid (0.130 g, 99%). Recrystallization from methanol yielded a crystal suitable for X-ray analysis. Crystal data: ‡ $[C_{17}H_{20}N_5O_4][CF_3CO_2]$, M = 471.4, orthorhombic, *Pccn* (no. 56), a = 13.873(1), b = 30.229(3), c = 9.879(6) Å, V = 4143.0(5) Å^3, Z = 8, D_c = 1.512 g cm^{-3}, μ(Cu-Kα) = 11.4 cm^{-1}, T = 293 K, colourless platy needles; 3437 independent measured reflections, F^2 refinement, R_1 = 0.064, wR_2 = 0.160, 2258 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 128°$], 327 parameters.

exo-(Bn)-N^2-Ac-guanine derivatives 31 and 33

Sodium hydride (0.24 g of a 60% dispersion, 6.1 mmol) was added in portions to a suspension of N^2-acetylguanine[16] (0.73 g, 3.8 mmol) in DMF (5 ml). After five minutes, a mixture of *exo*-(Bn)-chloride derivative **20** (1.97 g, 5.3 mmol) and tetrabutylammonium iodide (0.14 g, 0.38 mmol) in DMF (5 ml) was added slowly to the suspension. The mixture was stirred overnight under an argon atmosphere. The reaction mixture was then diluted with dichloromethane (100 ml), filtered (to remove unreacted N^2-acetylguanine) and evaporated *in vacuo* to leave a brown residue, which was purified by flash chromatography (10% MeOH–90% EtOAc) to give the products as white solids. Data for N^7-regio-isomer **31**: white solid (0.96 g, 48%). R_f = 0.22 (10% MeOH–90% EtOAc); Mp 208–209 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3178 (br w), 3064 (w), 2939 (w), 1769 (w), 1698 (s), 1614 (m); δ_H ($CDCl_3$, room temperature, rotamers present) 1.1–1.7 (2H, m), 2.3 (3H, s), 2.6 and 2.7 (2H, 2 × s), 3.2 and 3.3 (2H, 2 × s), 3.3–3.8 (4H, m), 4.7 (2H, 2 × s), 5.3 and 5.4 (2H, 2 × s), 6.2 and 6.3 (2H, 2 × s), 7.2–7.5 (5H, m, Ph), 7.9 and 8.0 (1H, 2 × s), 11.0 (1H, br), 12.3 (1H, br); δ_C (d_6-DMSO, room temperature, rotamers present) 23.7, 35.1 and 35.7, 42.3 and 42.5, 42.9, 44.4 and 44.5, 47.3 and 47.5, 48.2, 49.1, 112.1, 127.3 and 127.6, 128.5, 128.8, 136.3 and 137.0, 137.6, 145.4, 146.9, 152.7 and 152.8, 156.7 and 156.8, 166.8 and 167.1, 173.3, 177.5 and 177.7; *m*/*z* (EI) 529 (M^+, 20%), 242 (100), 66 (100) [Found: (EI) 529.2075 (M^+, $C_{27}H_{27}N_7O_5$ requires 529.2074)]. Data for N^9-regio-isomer **33**: white solid (0.59 g, 29%); R_f = 0.17 (10% MeOH–90% EtOAc); mp 224–227 °C; ν_{max}(KBr)/cm^{-1} 3454 (br w), 3201 (br w), 3060 (w), 2978 (w), 1772 (w), 1700 (s), 1610 (m), 1560 (m); δ_H ($CDCl_3$, room temperature, rotamers present) 1.1–1.5 (2H, m), 2.3 (3H, 2 × s), 2.5 and 2.7 (2H, 2 × s), 3.1 and 3.2 (2H, 2 × s), 3.5–3.9 (4H, m), 4.6 (2H, m), 4.8 and 5.0 (2H, 2 × s), 6.2 and 6.3 (2H, 2 × s), 7.2–7.4 (5H, m, Ph), 7.7 and 7.9 (1H, 2 × s), 10.3 and 10.6 (1H, 2 × br s), 12.0 (1H, br s); δ_C (d_6-DMSO, room temperature, rotamers present) 23.8, 35.0 and 35.8, 42.3, 42.8, 43.9, 44.4 and 44.5, 47.3 and 47.5, 48.5 and 49.1, 119.6 and 119.7, 127.4, 127.8, 128.6, 128.9, 136.3 and 137.0, 137.6, 140.8, 147.6 and 147.7, 149.3, 154.9, 166.4 and 166.8, 173.5, 177.6; *m*/*z* (CI, NH_3) 530 (MH^+, 100%), 297 (13), 194 (40), 108 (26), 106 (29), 77 (59) [Found: (CI, NH_3) 530.2148 (MH^+, $C_{28}H_{28}N_7O_5$ requires 530.2152)]

exo-(Bn)-N^7-alkylated guanine monomer 32

exo-(Bn)-N^2-Ac-guanine derivative **31** (0.150 g, 0.3 mmol) was dissolved in a solution of methanol (6 ml) and dichloromethane (3 ml). Ammonium hydroxide solution (3 ml, 35% aqueous NH_3) was added drop-wise and the mixture was stirred at 40 °C for 48 hours (the ammonolysis was monitored by TLC eluting with 15% MeOH–85% EtOAc). The reaction mixture was evaporated *in vacuo*, triturated with water to remove acetamide and dried *in vacuo* to give the product as a white solid (0.125 g, 91%). Mp >282 °C dec.; ν_{max}(KBr)/cm^{-1} 3317 (m), 3158 (m), 3060 (w), 2932 (w), 1771 (w), 1701 (s), 1684 (s), 1667 (s), 1619 (m); δ_H (d_6-DMSO, room temperature, rotamers present)

1.1–1.4 (2H, m), 2.6 and 2.7 (2H, 2 × s), 3.1 (2H, 2 × s), 3.3–3.7 (4H, m), 4.6 and 4.7 (2H, 2 × s), 5.2 and 5.3 (2H, 2 × s), 6.1 (2H, s), 6.3 (2H, 2 × s), 7.2–7.4 (5H, m), 7.8 (1H, 2 × s), 10.8 (1H, br); δ_C (d_6-DMSO, room temperature, rotamers present) 35.1 and 35.6, 42.2, 42.6, 44.4 and 44.5, 47.2 and 48.0, 47.3 and 47.5, 49.0, 108.7, 127.4, 127.6, 128.5, 128.8, 136.4 and 137.1, 137.7, 144.2, 152.8, 154.7, 159.4 and 159.5, 167.1 and 167.4, 177.6 and 177.8; *m/z* (CI, NH_3) 488 (MH^+, 100%) [Found: (CI, NH_3) 488.2034 (MH^+, $C_{25}H_{26}N_7O_4$ requires 488.2046)].

exo-(Bn)-guanine monomer 34 from N^2-acetyl derivative 33

exo-(Bn)-N^2-Ac-guanine derivative **33** (0.100 g, 0.19 mmol) was dissolved in a mixture of dichloromethane (1 ml) and methanol (8 ml). Ammonium hydroxide (3 ml, 35% aqueous NH_3) was added drop-wise and the solution was stirred at 40 °C, the ammonolysis was monitored by TLC eluting with 15% MeOH–85% EtOAc. After forty eight hours, a white precipitate was observed and the suspension was evaporated *in vacuo*, triturated with THF (10 ml) and water (2 × 10 ml) and dried *in vacuo* to give the product as a white solid (0.085 g, 92%). Mp 278–282 °C dec.; ν_{max}(KBr)/cm^{-1} 3419 (m), 3148 (m), 3028 (w), 2981 (w), 1768 (w), 1700 (s), 1660 (s), 1596 (m); δ_H (d_6-DMSO, room temperature, rotamers present) 1.1–1.4 (2H, m), 2.6 and 2.7 (2H, 2 × s), 3.06 and 3.11 (2H, 2 × s), 3.3–3.7 (4H, m), 4.6 and 4.7 (2H, 2 × s), 4.9 and 5.1 (2H, 2 × s), 6.3–6.4 (4H, m), 7.2–7.5 (5H, m), 7.55 and 7.64 (1H, 2 × s), 10.6 (1H, br); δ_C (d_6-DMSO, room temperature, rotamers present) 35.3 and 36.0, 42.5, 43.2, 43.8, 44.3, 47.3, 48.9 and 49.2, 116.0 and 116.1, 127.3, 127.6, 128.6, 128.9, 136.4 and 137.1, 137.6, 138.5, 151.6, 153.4, 156.8, 166.8 and 167.2, 177.6; *m/z* (CI, NH_3) 488 (MH^+, 12%), 77 (100) [Found: (CI, NH_3) 488.2035 (MH^+, $C_{25}H_{26}N_7O_4$ requires 488.2046)].

exo-(Bn)-N^2-acetyl-O^6-diphenylcarbamoylguanine derivative 36

N^2-Acetyl-O^6-diphenylcarbamoylguanine[18] **35** (0.81 g, 2.1 mmol) was suspended in DMF (3 ml). Sodium hydride (0.07 g, 1.7 mmol of a 60% dispersion) was slowly added, forming a transparent red solution. A mixture of chloride **20** (0.65 g, 1.7 mmol) and tetrabutylammonium iodide (0.08 g, 0.2 mmol) was added in portions and the solution was stirred overnight under an argon atmosphere. The reaction solution was then purified directly by flash chromatography (EtOAc) to give the product as a white solid (0.72 g, 71%). R_f = 0.23 (EtOAc); Mp 126–130 °C; ν_{max} (KBr)/cm^{-1} 3064 (w), 3031 (w), 2981 (w), 1744 (s), 1700 (s), 1622 (s), 1589 (s); δ_H ($CDCl_3$, room temperature, rotamers present) 1.2–1.3 (1H, m), 1.4–1.6 (1H, m), 2.5 (3H, 2 × s), 2.6 and 2.7 (2H, 2 × s), 3.2 and 3.3 (2H, 2 × s), 3.5–3.8 (4H, m), 4.6 and 4.7 (2H, 2 × s), 4.9 and 5.2 (2H, 2 × s), 6.2 and 6.3 (2H, 2 × s), 7.2–7.5 (5H, m), 7.9 and 8.1 (1H, 2 × s), 8.1 and 8.2 (1H, 2 × br s); δ_C ($CDCl_3$, room temperature, rotamers present) 25.1, 36.0 and 36.5, 42.9, 43.5 and 44.1, 44.3 and 44.8, 44.9 and 45.1, 47.9, 49.7 and 50.6, 120.0, 126.3, 126.9, 128.0, 128.3, 128.4, 128.9, 129.2, 129.4, 135.2 and 136.2, 137.8, 141.7, 145.0 and 145.2, 150.3, 152.1, 155.3, 156.0 and 156.4, 166.0 and 166.9, 170.9, 177.9 and 178.2; *m/z* 725 (MH^+, 40%), 590 (100), 170 (100) [Found: (CI, NH_3) 725.2832 (MH^+, $C_{40}H_{37}N_8O_6$ requires 725.2836)].

exo-(Bn)-guanine monomer 34 from derivative 36

exo-(Bn)-N^2-(Ac)-O^6-diphenylcarbamoylguanine derivative **36** (0.100 g, 0.16 mmol) was dissolved in a mixture of methanol (4 ml) and dichloromethane (1 ml). Ammonium hydroxide (3 ml, 35% aqueous NH_3) was added and the mixture was stirred at 40 °C for seventy-two hours. The solution was then evaporated *in vacuo* and triturated with water (10 ml) and THF (3 × 10 ml). The residue was dried *in vacuo* to give the title compound as a white solid (0.064 g, 82%).

Imine 37

Amine **2** trifluoroacetate (5.0 g, 15.6 mmol) and triethylamine (2.28 ml, 16.4 mmol) were dissolved in dichloromethane (60 ml). Magnesium sulfate (0.5 g) was added to the stirred solution. A solution of 2-naphthaldehyde (2.4 g, 15.6 mmol) in dichloromethane (10 ml) was added and the mixture was stirred overnight under an argon atmosphere. The solution was then evaporated *in vacuo* to a white solid which was stirred with ether (60 ml) and cooled in ice to precipitate the triethylammonium trifluoroacetate by-product. The solution was filtered and evaporated *in vacuo* to give the title compound as a white solid (5.0 g, 93%). Mp 123–125 °C; δ_H ($CDCl_3$) 1.4 (2H, s), 2.7 (2H, s), 3.3 (2H, s), 3.9 (4H, s), 6.3 (2H, pseudo-t *J* 1.8 Hz), 7.3 (1H, s), 7.5 (2H, m), 7.7–8.0 (4H, m), 8.4 (1H, s); δ_C ($CDCl_3$) 39.4, 42.7, 45.2, 47.8, 57.7, 123.6, 126.5, 127.2, 127.9, 128.5, 128.6, 130.2, 133.0, 133.6, 134.8, 137.8, 162.9, 178.0; *m/z* (CI, NH_3) 345 (MH^+, 8%) [Found: (CI, NH_3) 345.1599 (MH^+, $C_{22}H_{21}N_2O_2$ requires 345.1603)].

Amine 38

Imine **37** (2.2 g, 6.4 mmol) and sodium cyanoborohydride (0.4 g, 6.4 mmol) were mixed as solids. A solution of acetic acid (10 drops) in methanol (10 ml) was then added and the mixture was stirred for four hours under an argon atmosphere. The solvent was evaporated *in vacuo* to leave a white solid which was dissolved in ethyl acetate (80 ml) and washed with saturated aqueous sodium hydrogen carbonate (4 × 40 ml) and water (40 ml). The dried ($MgSO_4$) organic phase was evaporated *in vacuo* to give the title compound as a white solid (1.6 g, 80%). R_f = 0.31 (2% MeOH–98% EtOAc); mp 83–84 °C (Anal. Calcd. for $C_{22}H_{22}N_2O_2$: C, 76.26; H, 6.41; N, 8.09. Found: C, 76.26; H, 6.21; N, 8.02%); ν_{max} (KBr)/cm^{-1} 3289 (m), 3078 (w), 3054 (w), 3017 (w), 2993 (m), 2928 (m) 1760 (m), 1678 (s); δ_H ($CDCl_3$) 1.5 (2H, s), 1.6 (1H, br s), 2.7 (2H, s), 2.9 (2H, t *J* 6.1 Hz), 3.3 (2H, s), 3.7 (2H, t *J* 6.1 Hz), 3.9 (2H, s), 6.3 (2H, d *J* 1.5 Hz), 7.4–7.8 (7H, m); δ_C ($CDCl_3$) 38.2, 42.8, 45.3, 46.4, 47.9, 53.4, 125.5, 126.0, 126.4, 126.5, 127.6, 127.7, 128.0, 132.6, 133.4, 137.6, 137.8, 178.3; *m/z* (EI) 346 (M^+, 5%), 141 (100) [Found: (EI) 346.1681 (M^+, $C_{22}H_{22}N_2O_2$ requires 346.1681)].

Chloride 39

Amine **38** (1.00 g, 2.89 mmol) and triethylamine (0.65 ml, 4.6 mmol) were dissolved in dichloromethane (30 ml). A solution of chloroacetyl chloride (0.37 ml, 4.6 mmol) in dichloromethane (10 ml) was added drop-wise and the mixture was stirred overnight at ambient temperature. The organic phase was diluted with dichloromethane (40 ml) and washed with dilute hydrochloric acid (2 M, 2 × 35 ml), saturated aqueous sodium hydrogen carbonate solution (2 × 35 ml) and water (35 ml). The dried ($MgSO_4$) organic phase was evaporated *in vacuo* to leave the product as a pale brown foam (1.08 g, 88%). R_f = 0.28 (Et_2O); mp 57–59 °C; ν_{max} (KBr)/cm^{-1} 3057 (w), 2984 (w), 1770 (w), 1699 (s), 1654 (m); δ_H ($CDCl_3$, room temperature, rotamers present) 1.1–1.3 (1H, m), 1.5 (1H, d *J* 8.8 Hz), 2.7 (2H, 2 × s), 3.2 (2H, s), 3.6–3.8 (4H, m), 4.0 and 4.3 (2H, 2 × s), 4.8 (2H, 2 × s), 6.3 (2H, s), 7.3–7.9 (7H, m); δ_C ($CDCl_3$, room temperature, rotamers present) 35.5 and 36.1, 40.8 and 41.0, 42.7 and 42.9, 43.4 and 43.6, 44.8 and 45.0, 47.8 and 48.3, 50.9 and 52.0, 124.1, 124.8, 126.0, 126.2, 126.6, 127.1, 127.6, 128.7, 129.0, 132.8 and 133.2, 167.1 and 167.8, 177.6 and 178.0; *m/z* (CI, NH_3) 440 (M + NH_4^+, 80%), 423 (MH^+, 92), 389 (100) [Found: (EI) 422.1400 ($C_{24}H_{23}N_2O_3Cl$ requires 422.1397)].

Protected guanine derivative 40

N^2-Acetyl-O^6-diphenylcarbamoylguanine[18] **35** (0.69 g, 1.8 mmol) was suspended in DMF (5 ml). Sodium hydride (0.09 g of a 60% dispersion, 2.1 mmol) was added in portions

producing a clear red solution. A mixture of chloride **39** (0.90 g, 2.1 mmol) and tetrabutylammonium iodide (0.07 g, 0.18 mmol) was added slowly and the solution was stirred overnight under an argon atmosphere. The reaction solution was then purified directly by flash chromatography (EtOAc) to give the product as a white solid (1.30 g, 95%). R_f = 0.25 (EtOAc); mp 116–120 °C; ν_{max} (KBr)/cm^{-1} 3291 (br w), 3059 (w), 2982 (w), 1743 (s), 1700 (s), 1669 (s), 1622 (s), 1589 (s); δ_H ($CDCl_3$, room temperature, rotamers present) 1.1–1.5 (2H, m), 2.4 (3H, 2 × s), 2.5 and 2.6 (2H, 2 × s), 3.1 and 3.2 (2H, 2 × s), 3.5–3.8 (4H, m), 4.8 (2H, 2 × s), 4.9 and 5.2 (2H, 2 × s), 6.2 (2H, 2 × s), 7.1–7.8 (17H, m), 7.9 and 8.1 (1H, 2 × s), 8.5 and 8.6 (1H, 2 × br s); δ_C ($CDCl_3$, room temperature, rotamers present) 24.9, 36.1 and 36.5, 42.9, 43.5, 44.3 and 44.8, 44.9 and 45.1, 47.9, 49.8 and 50.9, 120.0, 124.2, 125.1, 126.1, 126.2, 126.5, 126.9, 127.4, 127.8, 128.8, 129.2, 129.3, 132.7, 132.9, 133.3, 133.6, 137.7, 141.7, 145.1, 150.4, 152.1, 155.3, 155.9 and 156.3, 166.2 and 167.1, 170.8, 177.9 and 178.2; *m*/*z* (ES) 797 (M + Na^+, 12%) 96 (100) [Found: (ES) 797.2814 (M + Na^+, $C_{44}H_{38}N_8O_6Na$ requires 797.2812)].

Guanine imine 41

Protected guanine derivative **40** (1.05 g, 1.4 mmol) was dissolved in a mixture of dichloromethane (2 ml) and methanol (9 ml). Ammonium hydroxide (4 ml, 35% aqueous NH_3) was added, initially causing precipitation. The suspension was warmed to 40 °C eventually forming a homogeneous solution which was maintained at 40 °C for forty eight hours. The solution was then evaporated to dryness *in vacuo* and triturated with ether (3 × 50 ml), removing *N*,*N*-diphenylurea and acetamide impurities. The remaining white solid was dried *in vacuo* to give the title compound as a white solid (0.70 g, 96%). R_f = 0.14 (10% MeOH–90% CH_2Cl_2); mp 162–166 °C dec.; ν_{max} (KBr)/cm^{-1} 3346 (br m), 3134 (br m), 3059 (w), 2983 (w), 1768 (m), 1697 (s), 1598 (s); δ_H (d_6-DMSO, room temperature, rotamers present) 1.1–1.4 (2H, m), 2.6 and 2.7 (2H, 2 × s), 3.1 (2H, 2 × s), 3.4–3.7 (4H, m), 4.7 and 4.9 (2H, 2 × s), 5.0 and 5.1 (2H, 2 × s), 6.3 (2H, 2 × s), 6.4 (2H, 2 × s), 7.4–8.0 (8H, m), 10.5 (1H, m); δ_C (d_6-DMSO, room temperature, rotamers present) 35.5 and 36.2, 42.6, 43.7, 44.1, 44.5 and 44.6, 47.5, 49.0 and 49.7, 116.1, 125.6, 126.0, 126.3, 127.7, 128.4, 128.7, 132.4, 132.6, 133.1, 134.2, 134.8, 137.6, 137.9, 138.4, 151.8, 153.6 and 153.7, 157.0, 167.1 and 167.4, 177.7; *m*/*z* [Found: (EI) 537.2312 (MH^+, $C_{29}H_{29}N_8O_3$ requires 537.2125)].

Guanine monomer 42

Imine **41** (0.70 g, 1.3 mmol) was suspended in a solution of methanol (2 ml) and water (20 ml), and the suspension was stirred for seventy-two hours. The solution was then allowed to settle and the excess liquid was decanted off. The remaining residue was triturated with ether (50 ml) and dried *in vacuo* to give the title compound as a white solid (0.67 g, 97%). Mp >165 °C dec.; ν_{max} (KBr)/cm^{-1} 3389 (br), 3154 (br), 2926 (w), 1596 (m); δ_H (d_6-DMSO, room temperature, rotamers present) 1.1–1.4, 2.5 and 2.7 (2H, 2 × s), 3.0 and 3.1 (2H, 2 × s), 3.3–3.7 (4H, m), 4.7 and 4.8 (2H, 2 × s), 5.0 and 5.1 (2H, 2 × s), 6.2–6.3 (2H, 2 × s), 6.4–6.5 (2H, 2 × s), 7.3–8.0 (8H, m), 10.7 (1H, 2 × s); δ_C (d_6-DMSO, room temperature, rotamers present) 35.1 and 35.9, 42.3 (11′-CH_2[a]), 42.5 and 43.1, 43.3 and 43.7, 44.1 and 44.4, 47.1 and 47.2, 48.7 and 49.3, 116.0, 125.3, 125.7, 125.9, 126.1, 126.2, 127.4, 127.6, 128.1, 128.4, 128.9, 132.3, 132.5, 133.0, 134.1, 134.7, 137.4, 138.3, 151.7, 153.6 and 153.7, 156.8, 167.0 and 167.3, 177.6; *m*/*z* (CI, NH_3) 538 (MH^+, 8%) 142 (100) [Found: (CI, NH_3) 538.2202 (MH^+, $C_{29}H_{28}N_7O_4$ requires 538.2203)].

endo-Alcohol 43

endo-Norborn-5-ene-2,3-dicarboxylic anhydride (6.0 g, 37 mmol) was dissolved in warm toluene (60 ml) and ethanolamine (5 ml, 83 mmol) was added. The mixture was then heated to reflux temperature overnight. The cooled solution was filtered and evaporated *in vacuo* to give the product as a white solid (5.5 g, 72%). Mp 74–75 °C (Anal. Calcd. for $C_{11}H_{13}NO_3$: C, 63.74; H, 6.33; N, 6.76. Found: C, 63.78; H, 6.34; N, 6.86%); ν_{max}($CHCl_3$)/cm^{-1} 3448 (br), 2990 (m), 2944 (m), 2873 (m), 1766 (m), 1691 (s); δ_H($CDCl_3$) 1.8 (1H, d *J* 8.8 Hz), 2.0 (1H, d *J* 8.8 Hz), 3.1 (1H, br), 3.45–3.50 (2H, m), 3.55–3.65 (2H, m), 3.75–3.80 (2H, m), 3.85–3.95 (2H, m), 6.4 (2H, pseudo-t *J* 1.8 Hz); δ_C($CDCl_3$) 40.8, 44.8, 45.7, 52.0, 59.9, 134.4, 178.3; *m*/*z* (CI, NH_3) 225 (M + NH_4^+, 34%), 208 (MH^+, 100) [Found: (CI, NH_3) 208.0974 (MH^+, $C_{11}H_{13}NO_3$ requires 207.0874)].

exo-Alcohol 44

exo-Norborn-5-ene-2,3-dicarboxylic anhydride[20] (10.0 g, 61 mmol) was added to a solution of ethanolamine (7.36 ml, 122 mmol) in toluene (100 ml) and the mixture was heated to reflux temperature overnight. The cooled solution was diluted with dichloromethane (130 ml) and washed with water (4 × 70 ml). The solvent was evaporated *in vacuo* to leave the product as a white solid (10.6 g, 84%). Mp 134–135 °C (Anal. Calcd. for $C_{11}H_{13}NO_3$: C, 63.74; H, 6.33; N, 6.76. Found: C, 63.81; H, 6.44; N, 6.61%); ν_{max}($CHCl_3$)/cm^{-1} 3442 (br), 3060 (w), 2943 (w), 2884 (w), 1767 (w), 1697 (s); δ_H ($CDCl_3$) 1.3 (1H, d *J* 10.0 Hz), 1.5 (1H, d *J* 10.0 Hz), 2.3 (1H, br), 2.7 (2H, s), 3.3 (2H, s), 3.65–3.70 (2H, m), 3.75–3.85 (2H, m), 6.3 (2H, s); δ_C ($CDCl_3$) 41.2, 42.8, 45.2, 47.9, 60.1, 137.8, 178.7; *m*/*z* (CI, NH_3) 225 (M + NH_4^+, 88%), 208 (MH^+, 100) [Found: (CI, NH_3) 208.0975 (MH^+, $C_{11}H_{14}NO_3$ requires 208.0973)].

endo-Chloride 45

endo-Alcohol **43** (1.00 g, 4.8 mmol) was dissolved in a mixture of triethylamine (1.35 ml, 9.7 mmol) and dichloromethane (40 ml). A solution of chloroacetyl chloride (0.79 ml, 9.7 mmol) in dichloromethane (10 ml) was added drop-wise and the mixture was stirred overnight. The organic phase was washed with dilute hydrochloric acid (2 M, 3 × 20 ml), saturated aqueous sodium hydrogen carbonate solution (3 × 20 ml) and water (2 × 20 ml). The solvent was evaporated *in vacuo* to give a yellow oil which solidified under high vacuum to yield the product as a pale yellow solid (1.18 g, 86%). Mp 64–65 °C (Anal. Calcd. for $C_{13}H_{14}NO_4Cl$: C, 55.11; H, 4.98; N, 4.95. Found: C, 54.90; H, 5.09; N, 4.96%); ν_{max}($CDCl_3$)/cm^{-1} 3065 (w), 2995 (m), 2957 (m), 2872 (w), 1767 (s), 1696 (s); δ_H ($CDCl_3$) 1.5 (1H, d *J* 8.8 Hz), 1.7 (1H, d *J* 8.8 Hz), 3.25–3.35 (2H, m), 3.4 (2H, s), 3.6 (2H, t *J* 5.2 Hz), 4.0 (2H, s), 4.2 (2H, t *J* 5.2 Hz), 6.1 (2H, s); δ_C ($CDCl_3$) 36.9, 40.7, 44.9, 45.8, 52.2, 62.7, 134.4, 167.1, 177.4; *m*/*z* (CI, NH_3) 301 (M + NH_4^+, 78%), 284 (MH^+, 8), 77 (100) [Found: (CI, NH_3) 284.0687 (MH^+, $C_{13}H_{15}NO_4Cl$ requires 284.0689)].

exo-Chloride 46

exo-Alcohol **44** (3.28 g, 0.0158 mol) was dissolved in a mixture of dichloromethane (30 ml) and triethylamine (2.21 ml, 0.0317 mol). A solution of chloroacetyl chloride (2.52 ml, 0.0317 mol) in dichloromethane (20 ml) was added drop-wise and the mixture was stirred overnight. The organic phase was then washed with dilute hydrochloric acid (2 M, 3 × 15 ml) and water (15 ml). The dried ($MgSO_4$) organic phase was evaporated *in vacuo* to give a yellow oil which solidified under high vacuum to yield the title compound as an off-white solid (4.24 g, 95%); Mp 45–47 °C (Anal. Calcd. for $C_{13}H_{14}NO_4Cl$: C, 55.11; H, 4.98; N, 4.95. Found: C, 55.15; H, 5.00; N, 4.90%); ν_{max}($CDCl_3$)/cm^{-1} 3070 (w), 2991 (m), 2960 (m), 2882 (w), 1766 (s), 1700 (s); δ_H ($CDCl_3$) 1.3 (1H, d *J* 9.9 Hz), 1.5 (1H, d *J* 9.9 Hz), 2.7 (2H, s), 3.3 (2H, s), 3.8 (2H, t *J* 5.2 Hz), 4.0 (2H, s), 4.4 (2H, t *J* 5.2 Hz), 6.3 (2H, s); δ_C ($CDCl_3$) 37.2, 40.6, 42.7, 45.2, 47.7, 62.4,

137.7, 167.0, 177.8; *m/z* (CI, NH_3) 301 (M + NH_4^+, 35%), 208 (100) [Found: (CI, NH_3) 301.0961 (M + NH_4^+, $C_{13}H_{18}N_2O_4Cl^{35}$ requires 301.0955)].

endo-Thymine monomer 47

Thyminylacetic acid[14] **4** (4.45 g, 24.2 mmol), *endo*-alcohol **43** (2.50 g, 12.1 mmol) and DMAP (0.45 g, 1.2 mmol) were suspended in DMF (4 ml). EDC (4.62 g, 24.1 mmol) was added portion-wise and the mixture was stirred overnight. The solution was then diluted with ethyl acetate (100 ml) and washed with dilute hydrochloric acid (3 × 30 ml), saturated aqueous sodium hydrogen carbonate solution (3 × 30 ml) and water (2 × 30 ml). The solvent was evaporated *in vacuo* to leave the crude product which was purified by flash chromatography (EtOAc) to give the title compound as a white solid (1.55 g, 35%). R_f = 0.36 (EtOAc); mp 54.5–55 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3397 (br), 1758 (m), 1697 (s); δ_H ($CDCl_3$) 1.5 (1H, d *J* 8.8 Hz), 1.8 (1H, d *J* 8.8 Hz), 1.9 (3H, s), 3.3 (2H, s), 3.4 (2H, s), 3.6 (2H, t *J* 4.9 Hz), 4.2 (2H, t *J* 4.9 Hz), 4.9 (2H, s), 6.1 (2H, s), 7.1 (1H, s), 9.0 (1H, br s); δ_C ($CDCl_3$) 12.1, 36.8, 44.8, 45.7, 48.3, 52.1, 62.9, 111.1, 134.4, 140.5, 151.0, 164.4, 167.6, 177.8; *m/z* (CI, NH_3) 391 (M + NH_4^+, 14%), 374 (MH^+, 27), 60 (100) [Found: (CI, NH_3) 374.1354 (MH^+, $C_{18}H_{20}N_3O_6$ requires 374.1352)].

exo-Thymine monomer 48

Thyminylacetic acid[14] **4** (2.60 g, 14.1 mmol), *exo*-alcohol **44** (1.50 g, 7.2 mmol) and DMAP (catalytic quantity) were suspended in DMF (4 ml). EDC (2.70 g, 14.5 mmol) was added portion-wise and the mixture was stirred overnight. The solution was then diluted with ethyl acetate (100 ml) and washed with dilute hydrochloric acid (3 × 30 ml), saturated aqueous sodium hydrogen carbonate solution (3 × 30 ml) and water (2 × 30 ml). The solvent was evaporated *in vacuo* to leave the crude product, which was purified by flash chromatography (EtOAc) to give the title compound as a white solid (1.47 g, 55%). R_f = 0.39 (EtOAc); mp 49–50 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3206 (br w), 3063 (w), 2958 (w), 2882 (w), 1758 (s), 1700 (s); δ_H ($CDCl_3$) 1.2 (1H, d *J* 9.8 Hz), 1.5 (1H, d *J* 9.8 Hz), 1.8 (3H, s), 2.6 (2H, s), 3.1 (2H, s), 3.6 (2H, t *J* 4.7 Hz), 4.1 (2H, t *J* 4.7 Hz), 4.3 (2H, s), 6.2 (2H, s), 7.0 (1H, s), 10.0 (1H, br s); δ_C ($CDCl_3$) 12.3, 37.3, 42.6, 45.1, 47.8, 48.3, 62.5, 110.9, 137.7, 140.6, 151.1, 164.6, 167.6, 178.1; *m/z* (CI, NH_3) 391 (M + NH_4^+, 26%), 374 (MH^+, 53), 127 (100) [Found: (CI, NH_3) 374.1346 (MH^+, $C_{18}H_{20}N_3O_6$ requires 374.1352)].

Uracil monomer 49

Alcohol **44** (0.68 g, 3.3 mmol) and uracilylacetic acid[19] **5** (1.11 g, 6.5 mmol) were suspended in DMF (5 ml). EDC (1.25 g, 6.5 mmol) was added in portions and the mixture was stirred overnight under an argon atmosphere. The solution was then evaporated *in vacuo* and the crude product was purified by flash chromatography (5% MeOH–95% EtOAc) to give the title compound as a white solid (0.38 g, 33%). R_f = 0.38 (5% MeOH–95% EtOAc); mp 120.5–122 °C; ν_{max} (KBr)/cm^{-1} 3097 (w), 2976 (m), 1771 (s), 1700 (s); δ_H (d_6-DMSO) 1.2 (1H, d *J* 9.8 Hz), 1.4 (1H, d *J* 9.8 Hz), 2.7 (2H, s), 3.1 (2H, s), 3.6 (2H, t *J* 5.3 Hz), 4.2 (2H, t *J* 5.3 Hz), 4.4 (2H, s), 5.6 (1H, d *J* 7.9 Hz), 6.3 (2H, s), 7.5 (1H, d *J* 7.9 Hz), 11.4 (1H, br s); δ_C (d_6-DMSO) 36.6, 42.2, 44.3, 47.0, 48.2, 61.3, 100.9, 137.4, 145.4, 150.6, 163.4, 167.7, 177.3; *m/z* (CI, NH_3) 377 (M + NH_4^+, 38%) 360 (MH^+, 24), 267 (100) [Found: (EI) 359.1118 (M^+, $C_{17}H_{17}N_3O_6$ requires 359.1117)].

Boc-adenine derivative 50

Sodium hydride (0.16 g of a 60% dispersion, 3.9 mmol) was added in portions to a suspension of N^6-Boc-adenine **14** (0.61 g, 2.6 mol) in DMF (2 ml). Chloride **46** (0.73 g, 2.6 mmol) and tetrabutylammonium iodide (0.09 g, 0.26 mmol) were mixed and added in portions to the suspension, after which the mixture was stirred overnight under an argon atmosphere. The reaction solution was then diluted with ethyl acetate (40 ml) and washed with water (5 × 8 ml). The organic phase was evaporated *in vacuo* to leave a yellow foam which was purified by flash chromatography (5% MeOH–95% CH_2Cl_2) to give the product as a white solid (0.69 g, 55%). R_f = 0.18 (5% MeOH–95% CH_2Cl_2); mp 105–106 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3407 (w), 2993 (m), 1753 (s), 1700 (s), 1612 (s); δ_H ($CDCl_3$) 1.1 (1H, d *J* 9.9 Hz), 1.4 (1H, d *J* 9.9 Hz), 1.5 (9H, s), 2.6 (2H, s), 3.2 (2H, s), 3.7 (2H, t *J* 4.7 Hz), 4.3 (2H, t *J* 4.7 Hz), 4.9 (2H, s), 6.2 (2H, s), 8.1 (1H, s), 8.3 (1H, br s), 8.7 (1H, s); δ_C ($CDCl_3$) 28.1, 37.3, 42.7, 44.0, 45.2, 47.8, 62.9, 82.1, 121.1, 137.7, 143.0, 146.6, 150.0, 151.3, 153.1, 166.9, 178.0; *m/z* (CI, NH_3) 483 (M + H^+, 39%), 383 (100), 77 (100) [Found: (CI, NH_3) 483.1988 (MH^+, $C_{23}H_{27}N_6O_6$ requires 483.1992)].

Adenine monomer 51

Trifluoroacetic acid (1.1 ml, 14 mmol) was added drop-wise to a solution of compound **50** (0.71 g, 1.5 mmol) in dichloromethane (15 ml) and the mixture was stirred overnight. The reaction solution was diluted with ethyl acetate (80 ml) and washed carefully with saturated aqueous sodium hydrogen carbonate solution (3 × 15 ml) and water (10 ml). The dried ($MgSO_4$) organic phase was evaporated to give the title product as a white solid (0.51 g, 92%). Mp 183–184 °C; ν_{max}(KBr)/cm^{-1} 3355 (br), 3141 (br), 2977 (w), 1768 (s), 1700 (s), 1657 (s), 1603 (s); δ_H ($CDCl_3$) 1.2 (1H, d *J* 9.9 Hz), 1.5 (1H, d *J* 9.9 Hz), 2.7 (2H, s), 3.3 (2H, s), 3.8 (2H, t *J* 5.0 Hz), 4.3 (2H, t *J* 5.0 Hz), 4.9 (2H, s), 5.6 (2H, br s), 6.3 (2H, s), 7.9 (1H, s), 8.4 (1H, s); δ_C (d_6-DMSO) 36.8, 42.4, 43.8, 44.5, 47.3, 61.7, 118.2, 137.6, 141.2, 149.6, 152.4, 155.6, 167.8, 177.6; *m/z* (EI) 383 (MH^+, 25%), 382 (M^+, 100), 66 (100) [Found: 382.1385 (M^+, $C_{18}H_{18}N_6O_4$ requires 382.1390)]. Recrystallization from 15% MeOH–85% CH_2Cl_2 yielded crystals suitable for X-ray analysis. Crystal data:‡ $C_{18}H_{18}N_6O_4$, M_r = 382.38, T = 293(2) K, triclinic, space group $P\bar{1}$, a = 6.7111(2), b = 9.2637(5), c = 15.5593(8) Å, α = 103.438(2), β = 98.437(3), γ = 102.274(3)°, V = 899.54(7) Å^3, ρ_{calc} = 1.412 g cm^{-3}, μ = 0.104 mm^{-1}, Z = 2, reflections collected: 11622, independent reflections: 3097 (R_{int} = 0.0711), final R indices [$I > 2\sigma I$]: $R1$ = 0.0431, $wR2$ = 0.1108, R indices (all data): $R1$ = 0.0567. $wR2$ = 0.1206.

Cytosine monomer 52

Cytosine (0.50 g, 4.5 mmol) was suspended in DMF (5 ml) and sodium hydride (0.25 g of a 60% dispersion, 6.3 mmol) was added in portions. After five minutes, a mixture of chloride **46** (1.79 g, 6.3 mmol) and tetrabutylammonium iodide (0.17 g, 0.45 mmol) was added in portions. The mixture was stirred overnight under an argon atmosphere. The solution was then evaporated *in vacuo* and purified by flash chromatography (20% MeOH–80% EtOAc) to give the title compound as a white solid (0.90 g, 56%). R_f = 0.23 (20% MeOH–80% EtOAc); Mp 184–185 °C; ν_{max}(KBr)/cm^{-1} 3346 (br), 3122 (br), 2984 (m), 1764 (s), 1701 (s), 1653 (s); δ_H ($CDCl_3$) 1.3 (1H, d *J* 9.6 Hz), 1.5 (1H, d *J* 9.6 Hz), 1.8 (2H, br), 2.7 (2H, s), 3.3 (2H, s), 3.8 (2H, t *J* 5.0 Hz), 4.3 (2H, t *J* 5.0 Hz), 4.5 (2H, s), 5.7 (1H, d *J* 7.2 Hz), 6.3 (2H, s), 7.3 (1H, d *J* 7.2 Hz); δ_H (d_6-DMSO) 1.2 (1H, d *J* 9.7 Hz), 1.4 (1H, d *J* 9.7 Hz), 2.7 (2H, s), 3.1 (2H, s), 3.6 (2H, t *J* 5.3 Hz), 4.2 (2H, t *J* 5.3 Hz), 4.3 (2H, s), 5.6 (1H, d *J* 7.2 Hz), 6.3 (2H, s), 7.1 (1H, br), 7.2 (1H, br), 7.5 (1H, d *J* 7.2 Hz); δ_C (d_6-DMSO) 36.9, 42.6, 44.7, 47.4, 50.0, 61.2, 93.9, 137.7, 146.2, 155.9, 166.5, 168.6, 177.6; *m/z* (ES) 358 (M^+, 11%), 242 (100), 66 (100) [Found: (ES) 359.1356 (MH^+ requires 359.1355)].

Guanine derivatives 53 and 54

Sodium hydride (0.65 g of a 60% dispersion, 16.2 mmol) was added in portions to a suspension of N^2-acetylguanine (1.95 g, 10.1 mmol) in DMF (10 ml). After five minutes, a mixture

of chloride **46** (4.01 g, 14.2 mmol) and tetrabutylammonium iodide (0.37 g, 1.0 mmol) was added in portions and the suspension was stirred overnight under an argon atmosphere. The mixture was then diluted with dichloromethane (120 ml), filtered (to remove N^2-acetylguanine) and evaporated *in vacuo* to leave a brown residue which was purified by flash chromatography (15% MeOH–85% EtOAc) to give the title compounds as white solids. Data for N^7-isomer **53**: white solid (0.68 g, 16%). $R_f = 0.30$ (15% MeOH–85% EtOAc); mp 234.5–236 °C; ν_{max}(KBr)/cm^{-1} 3112 (m), 2992 (m), 2966 (m), 1749 (s), 1701 (s), 1608 (s); δ_H (d_6-DMSO) 1.1 (1H, d *J* 9.7 Hz), 1.3 (1H, d *J* 9.7 Hz), 2.2 (3H, s), 2.6 (2H, s), 3.1 (2H, s), 3.6 (2H, t *J* 5.3 Hz), 4.2 (2H, t *J* 5.3 Hz), 5.1 (2H, s), 6.3 (2H, s), 8.1 (1H, s), 11.6 (1H, br s), 12.1 (1H, s); δ_C (d_6-DMSO) 23.8, 36.9, 42.5, 44.6, 47.4, 61.8, 111.8, 137.8, 144.9, 147.2, 152.8, 156.9, 167.7, 173.5, 177.6; *m*/*z* (CI, NH_3) 441 (MH^+, 100%) [Found: (CI, NH_3) 441.1523 (MH^+, $C_{20}H_{21}N_6O_6$ requires 441.1522)]. Data for N^9-isomer **54**: white solid (0.59 g, 13%). $R_f = 0.25$ (15% MeOH–90% EtOAc); mp 180–185 °C; ν_{max}(KBr)/cm^{-1} 3448 (br w), 3175 (br w), 3058 (w), 2984 (w), 1700 (s), 1617 (m); δ_H ($CDCl_3$) 1.2 (1H, d *J* 9.8 Hz), 1.6 (1H, d *J* 9.8 Hz), 2.3 (3H, s), 2.7 (2H, s), 3.3 (2H, s), 3.8 (2H, t *J* 3.8 Hz), 4.4 (2H, t *J* 3.8 Hz), 4.7 (2H, s), 6.3 (2H, s), 7.7 (1H, s), 9.5 (1H, s), 12.0 (1H, s); δ_C (d_6-DMSO) 23.9, 36.9, 42.5, 44.3, 44.6, 47.4, 62.0, 119.8, 137.8, 140.2, 148.1, 149.0, 155.0, 167.5, 173.7, 177.6; *m*/*z* (CI, NH_3) 441 (MH^+, 62%), 267 (100), 186 (100) [Found: (CI, NH_3) 441.1522 (MH^+, $C_{20}H_{21}N_6O_6$ requires 441.1522)].

N^2-Ac-guanine N^9-acetamide 55

Guanine derivative **54** (0.120 g, 0.3 mmol) was dissolved in THF (2 ml). Ammonium hydroxide (15 drops, 35% aqueous NH_3) was added and the mixture was stirred at ambient temperature. After two minutes, a white solid had precipitated. The reaction mixture was filtered and the white precipitate was washed with THF (3 × 10 ml), dichloromethane (10 ml), and dried *in vacuo* to give the title compound as a white solid (0.060 g, 88%); mp >264 °C dec.; ν_{max}(KBr)/cm^{-1} 3360 (m), 3186 (m), 2931 (w), 1690 (s), 1662 (s), 1618 (s), 1563 (m); δ_H (d_6-DMSO) 2.1 (3H, s), 4.7 (2H, s), 7.3 (1H, br), 7.7 (1H, br), 7.9 (1H, s); δ_C (d_6-DMSO) 23.9, 45.2, 119.6, 140.7, 148.2, 149.3, 155.3, 168.0, 173.7; *m*/*z* (CI, NH_3) 251 (MH^+, 5%), 77 (100) [Found: (EI) 250.0813 (M^+, $C_9H_{10}N_6O_3$ requires 250.0814)].

General procedure for NMR scale ROMP reactions

To a stirring solution of the initiator (0.0100 g in 200 µl $CDCl_3$ or CD_2Cl_2) in a nitrogen-filled glove box, was added the nucleotide base-derived monomer (3 equivalents) dissolved (or suspended) in the same deuterated solvent (600 µl). The resulting mixture was then transferred to an NMR tube equipped with a Teflon valve.

Preparative scale ROMP of 10

In a 10 ml vial in a glove box, **57** (5.3 mg, 5.55 × 10^{-6}mol) was dissolved in CH_2Cl_2 (0.5 ml) to afford a red solution. This was then added to a solution of **10** (0.1283 g; 2.77 × 10^{-4} mol; 50 equivalents) in CH_2Cl_2 (2 ml). Within 15 minutes the solution turned orange. After 24 hours the reaction was terminated by the addition of ethyl vinyl ether (50 µl). The reaction was then removed from the glove box and added dropwise to rapidly stirred acetone (50 ml) to give a white precipitate, which was filtered and dried (0.0219 g, 17%). δ_H ($CDCl_3$) 1.7 (m, br), 1.9 (s, br), 2.0 (m, br), 2.7 (m, br), 3.0 (m, br), 3.7 (m, br), 4.1 (s, br), 4.8 (s, br), 5.5 (s, br), 5.8 (s, br), 7.0 (s, br), 7.4–7.2 (m, br), 10.2 (s, br).

Preparative scale ROMP of Boc-17

Initiator **56** (5.0 mg; 6.07 × 10^{-6}mol) dissolved in $CHCl_3$ (0.5 ml) was added to a solution of the monomer (0.0580 g; 1.20 × 10^{-4}mol; 20 equivalents) in $CHCl_3$ (2 ml). The reaction was stirred for 24 hours by which time a solid had precipitated. Ethyl vinyl ether (50 µl) was then added and the solvent was removed under reduced pressure to afford an off-white solid. The solid was washed with methanol (3 × 10 ml) and dried *in vacuo* for several hours. Yield: 0.0070 g, 13%. δ_H (d_6-DMSO) 1.45 (s), 1.2 (m, br), 1.9 (m, br), 2.6 (m, br), 3.0 (m, br), 3.4 (m, br), 4.8 (m, br), 5.6 (m, br), 5.7 (m, br), 8.2–8.8 (m, br).

Preparative scale ROMP of 29

In an identical method to that described for the polymerization of Boc-**17**, the reaction between **29** (0.0550 g; 1.20 × 10^{-4} mol; 20 equivalents) and initiator **56** (5.0 mg; 6.07 × 10^{-6} mol) gave poly**29** (0.0080 g, 15%). δ_H (d_6-DMSO) 1.2 (m, br), 1.4 (s), 2.0 (m, br), 2.7 (m, br), 2.7 (m, br), 3.0 (m, br), 3.2 (m, br), 4.3 (s, br), 5.5 (m, br), 5.7 (m, br), 6.9 (d, *J* 6.6 Hz), 7.9 (d, *J* 6.6 Hz), 8.3 (m, br), 10.3 (s, br); δ_C (d_6-DMSO) 27.8, 36.1, 37.5, 41.5, 44.4, 50.2, 50.5, 131.5, 134.5, 137.6, 150.4, 152.1, 155.1, 163.2, 167.0, 178.2.

Preparative scale ROMP of 48

Initiator **57** (6.0 mg, 6.28 × 10^{-6} mol) dissolved in CH_2Cl_2 (0.5 ml) was added to a solution of **48** (0.1173 g; 3.14 × 10^{-4}mol; 50 equivalents) in CH_2Cl_2 (2 ml). After 10 minutes the red solution became cloudy and over the next 15 minutes the mixture became a pale yellow emulsion with red–pink oily droplets. After 24 hours, the red droplets had become a gel-like precipitate. The reaction was terminated with ethyl vinyl ether (50 µl) and the gel, which was insoluble in either THF or acetone, was triturated with hexane (50 ml) to afford a pale yellow solid (0.1136 g, 97%). δ_H (d_6-DMSO) 1.5 (m, br), 1.8 (s, br), 2.0 (m, br), 2.6 (m, br), 3.0 (m, br), 3.6 (s, br and m, br), 4.2 (s, br and m, br), 4.4 (s, br), 5.5 (s, br), 5.7 (s, br), 7.4 (s, br), 11.4 (s, br).

Acknowledgements

The authors thank the BBSRC for a postdoctoral fellowship (to P. J. W), and the EPSRC for a postdoctoral fellowship (to E. L. M), a studentship (to R. G. D) and for access to the national mass-spectrometry and X-ray crystallography services.

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