Alkylation of 6-*N*-acylated adenosine derivatives by the use of phase transfer catalysis

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6-*N*- or N^1-Alkylation of 6-*N*-acyl adenosine derivatives with alkyl halides in CH_2Cl_2–1 mol dm^{-3} NaOH in the presence of Bu_4NBr has been studied. A variety of *N*-acyl groups have been examined. Consequently, the use of the acetyl and 2-(trimethylsilyl)ethoxycarbonyl groups resulted in the corresponding 6-*N*-alkylated products in high yields. It was also found that, when the benzoyl group was chosen as the *N*-acyl group, N^1-alkylated products were obtained along with 6-*N*-alkylated products. The structure of the 6-*N*- and N^1-alkylated adenosine derivatives has been determined by ^1H and ^{13}C NMR spectroscopy.

Introduction

Since, among naturally occurring modified nucleosides, 6-*N*- or N^1-substituted adenosine derivatives have potent biological activities,[1] a number of papers dealing with the base-alkylation of adenosines has appeared.[2–27] Generally, two methods for the synthesis of 6-*N*-alkylated adenosines have been utilized: one is the N^1-alkylation of adenosines followed by Dimroth rearrangement,[2–11] and the other involves nucleophilic displacement of 6-substituted purine ribosides with alkylamines.[12–27] Further, N^1-alkylated adenosines have been prepared by direct alkylation with alkylating reagents.

Here, we report a detailed study of 6-*N*- or N^1-alkylation of adenosines *via* 6-*N*-acylated species by the use of phase transfer catalysis (PTC).

Results and discussion

Numerous applications of PTC to the *N*-alkylation of amides and imides have been reported,[28] although few are concerned with nucleic acids except for those concerning glycosyl bond formation,[29] 2′,3′-*O*-methylenation of ribonucleosides,[30] 4-*O*-acylation and N^3-alkylation of uridines[31] and *O*-acylation of thymidines and uridines.[32] Therefore, our interest was focused on PTC which would provide a new strategy for the 6-*N*- or N^1-alkylation of adenosine *via* *N*-acyladenosines. 6-*N*-Acylated adenosines are accessible as well-known common intermediates in oligonucleotide synthesis. If such *N*-acylated compounds could be dissociated under PTC conditions, the resulting amide anion species would become more reactive towards alkyl halides than the parent *N*-unprotected adenosines. To ascertain this possibility as a new route to 6-*N*- or N^1-alkyladenosines, several *N*-acylated adenosines **4a**, **4b**, **4d** and **4e** were synthesized by the reaction of 2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)adenosine **2**[33] with acyl halides or anhydrides. An *N*-benzoylated adenosine **4c** and 6-*N*-[2-(trimethylsilyl)ethoxycarbonyl]adenosine **4f** were synthesized by silylation of the corresponding *N*-acylated adenosines **3c** and **3f**[34] with *tert*-butyldimethylsilyl chloride in the presence of imidazole in pyridine. These results are summarized in Table 1. We chose the *tert*-butyldimethylsilyl (TBDMS) group as the hydroxy protecting group throughout this study so that the effect of *N*-acyl groups on the phase transfer *N*-acylation could be estimated clearly under standard conditions.

The *N*-acetylated adenosine **4a** was alkylated with 4 mol equiv. of benzyl bromide, methyl iodide, or allyl bromide in the presence of tetrabutylammonium bromide (Bu_4NBr) as phase transfer catalyst in CH_2Cl_2–NaOH (1 mol dm^{-3}) to give the corresponding 6-*N*-alkyl-6-*N*-acetyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)adenosines **5a**, **6a** and **7a** in high yields (see Table 2). It is noteworthy that these reactions went to completion within 30 min without coloration, selective alkylation occurring at the 6-*N* position.

To study the effect of substituents [phenoxyacetyl, 4-nitrobenzoyl, 2,2,2-trichloro-1,1-dimethylethoxycarbonyl (CMEC), and 2-(trimethylsilyl)ethoxycarbonyl (TEOC) groups] on the above PTC reaction, compounds **4b** and **4d–f** were allowed to react with the same alkyl halides under similar conditions. These reactions resulted in exclusive formation of 6-*N*-alkylated adenosines. In particular, the use of the TEOC group gave excellent yields of the 6-*N*-alkylated products **5f**, **6f** and **7f**.

In contrast, it was found that the N^1-alkylated products **8c** and **10c** were obtained along with the 6-*N*-alkylated products **5c** and **7c** in the reactions of 6-*N*-benzoyladenosine derivative **4c** with methyl iodide and allyl bromide, respectively. However, compound **4c** when treated with benzyl bromide gave compound **6c** together with its debenzoylated product **11** (see Table 2). This shows a clear difference between the first two reagents and benzyl bromide. An independent experiment showed that product **6c**, once isolated, was stable and was not converted into compound **11** under phase transfer conditions. A different mechanism was suggested in this case.

The 4-nitrobenzoyl group when employed as the 6-*N*-acyl substituent failed to give **8d**, **11** and **10d** as products, the 6-*N*-alkylated adenosines **5d**, **6d** and **7d** being exclusively obtained instead. In terms of the yield of 6-*N*-alkylated products, the acetyl and TEOC groups were superior to the other acyl groups tested (see Table 2).

The phase transfer reaction required use of an equimolar amount of Bu_4NBr since with less (0.05 mmol), the reaction rate was extremely slow and 12 h reaction time was necessary to ensure completion. The reaction also proceeded very slowly when a weaker base (1 mol dm^{-3} Na_2CO_3) was used as the aqueous phase. A new phosphazene-type phosphonium salt **12**[35] also proved effective in inducing *N*-alkylation, giving **5a** in 90% yield.

Early attempts to obtain 6-*N*- or N^1-alkylated adenosines showed that more straightforward metallation of 6-*N*-acylated adenosines with reagents such as NaH and BuLi followed by 6-*N*-alkylation gave unsatisfactory results.

Structural assignments for the 6-*N* and N^1-alkylated products were established on the basis of ^1H and ^{13}C NMR spectroscopic results. The structure of N^1-alkylated product **8c** were determined by NOE experiments which showed strong NOEs between the methyl and 2-H groups (Fig. 1B). Compound **10c** exhibited a similar NOE effect between CH_2 of

Table 1 Synthesis of 6-*N*-acylated 2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)adenosine derivatives

Compound	Method	Acylation R	RCOCl (mol equiv.)	$(RCO)_2O$ (mol equiv.)	Time (*t*/min)	Treatment with NH_3 (Method A) (*t*/min)	Product	Yield of **4** (%)
2	A	Me		1.5	4	30	**4a**	49
2	A	$PhOCH_2$		1.5	3.5	30	**4b**	54
3c	B	Ph	4		1		**4c**	78
2	A	$PhNO_2$	1.5		4	30	**4d**	52
2	A	$OC(Me)_2CCl_3$	1.2		2 h	30	**4e**	83
3f	B	$OCH_2CH_2SiMe_3$	5		1		**4f**	60

Table 2 Alkylation of 6-*N*-acylated 2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)adenosine derivatives

	R = Me		$PhOCH_2$		Ph		$4\text{-}O_2NC_6H_4$		$OC(Me)_2CCl_3$		$OCH_2CH_2SiMe_3$	
R′X	Product	Yield (%)	Product	Yield (%)	Product	Yield (%)	Product	Yield (%)	Product	Yield (%)	Product	Yield (%)
MeI	**5a**	96	**5b**	82	**5c** **8c**	59 39	**5d**	67	**5e**	77	**5f**	89
BnBr	**6a**	90	**6b**	77	**6c** **11**	51 38	**6d**	61	**6e**	71	**6f**	91
$CH_2{=}CH{-}CH_2Br$	**7a**	94	**7b**	65	**7c** **10c**	51 28	**7d**	61	**7e**	66	**7f**	92

Table 3 ^1H NMR data of 6-*N*-alkylated adenosine derivatives **5c**, **6c**, **7c**, **8c** and **10c**

Compd.	2-H	8-H	*o*-Proton of Bz group	*m*-Proton of Bz group	*p*-Proton of Bz group
5c	8.53	8.25	7.41	7.13	7.22
6c	8.51	8.19	7.42	7.12	7.21
7c	8.55	8.20	7.44	7.13	7.23
8c	7.95	7.87	8.15	7.39	7.45
10c	7.91	7.87	8.11	7.38	7.45

Table 4 ^{13}C NMR data of 6-*N*- and N^1-alkylated adenosine derivatives **5c**, **6c**, **7c**, **8c** and **10c**

Compd.	2-C	4-C	5-C	6-C	8-C
5c	152.63	151.77	126.68	155.50	142.49
6c	152.59	151.80	127.08	154.03	142.46
7c	152.61	151.84	127.09	154.07	142.51
8c	146.52	145.44	122.42	147.65	138.58
10c	138.54	135.99	127.94	146.27	132.00

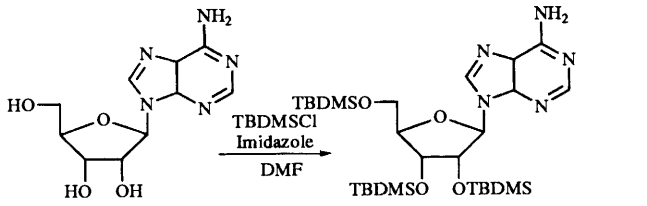
the N^1-allyl group and 2-H (data not shown). Although in contrast to this result, the 6-*N* alkylated products showed the absence of NOEs between the alkyl and 2-H groups, weak NOEs between 8-H and 1′-H or 2′-H were observed in compounds **5c** and **8c** (Fig. 1A and 1B). In general, for the 6-*N*- and N^1-alkylated products, there is a significant difference in the chemical shift for 2-H and 8-H. The signals for 8-H in 6-*N*-alkylated products appeared at 8.19–8.45 ppm while those for the N^1-alkylated products **8c** and **10c** were observed at 7.87 ppm each. The signals for 2-H in compounds **8c** and **10c** are shifted upfield compared with those for the 6-*N*-alkylated products **5c**, **6c** and **7c** (see Table 3). More interestingly, it is found that the *ortho*-protons of the benzoyl group for N^1-alkylated products consistently appeared downfield compared with those for 6-*N*-alkylated products. In the ^{13}C NMR spectra, the resonances for 2-C, 4-C and 8-C in the N^1-alkylated products **8c** and **10c** are shifted markedly upfield compared with those for the 6-*N*-alkylated products (see Table 4). Slight upfield shifts for 5-C and 6-C of compounds **8c** and **10c** were also observed.

The acyl groups of 6-*N*-alkylated 6-*N*-acyladenosine derivatives can be readily removed by treatment with ammonia or tetrabutylammonium fluoride (TBAF) as follows. Treatment of 6-*N*-acetyl-6-*N*-methyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-adenosine **5a** with $TABF{\cdot}H_2O$ (4 mol equiv.) in THF gave 6-*N*-acetyl-6-*N*-methyladenosine **13** quantitatively. Further treatment of **13** with concentrated ammonia gave 6-*N*-methyladenosine[4] **14** in 72% yield. 6-*N*-Allyladenosine[10] **15** was also obtained in quantitative yield by treatment of **7f** with $TBAF{\cdot}H_2O$ (6 mol equiv.) in THF. Treatment of 6-*N*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)adenosine **6e** with zinc in acetic acid gave **11** in quantitative yield. The acyl groups such as acetyl, phenoxyacetyl, 4-nitrobenzoyl, and benzoyl could be selectively removed from the corresponding 6-*N* masked adenosine derivatives **5a–d**, **6a–d** and **7a–d** by treatment for 30 min with NaOMe–MeOH.

Conclusion

The present method for the 6-*N*-alkylation of adenosine would be useful for introduction of functional groups into easily accessible starting materials, 5′-*O*-dimethoxytrityldeoxyadenosine derivatives, masked with *N*-protecting groups such as the acetyl, phenoxyacetyl and 2-(trimethylsilyl)ethoxycarbonyl groups, and for the synthesis of base-base bridged oligodeoxyribonucleotides.[37] Our preliminary results suggested that less reactive alkyl halides such as alkyl bromides can be used in the phase-transfer catalysed *N*-alkylation.

During this study we observed that the N^1-alkylation occurred only in the case of 6-*N*-benzoyladenosine derivative **4c**. This finding is also of great importance since it suggests the possibility of there being a still unexplored route to a series of N^1-ribosylated adenosine derivatives involving N^1-(5′-phosphoribosyl)-ATP[38,39] and cyclic ADP-ribose.[40,41] However, further studies of N^1-alkylation using more suitable *N*-protecting groups that can be removed under neutral conditions are necessary in order to synthesize more complex molecules.



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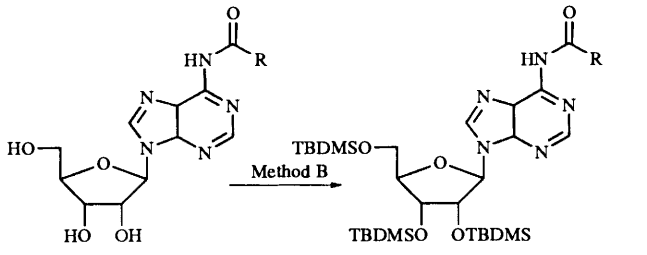
(1) RCOCl or $(RCO)_2O$
(2) NH_3 aq

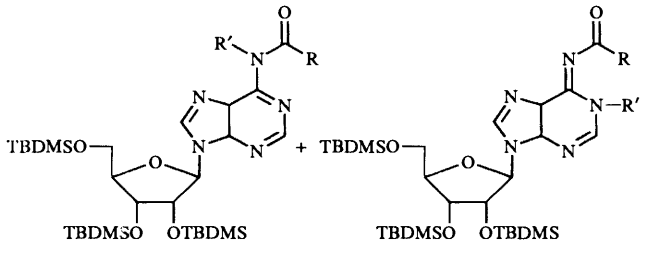
Method A



3a–f
a: R = Me
b: R = CH_2OPh
c: R = Ph
d: R = $C_6H_4NO_2$-4
e: R = $OC(Me)_2CCl_3$
f: R = $OCH_2CH_2SiMe_3$

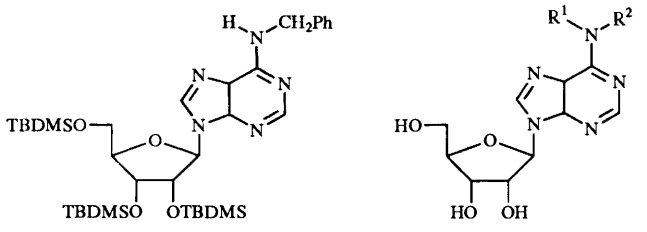
4a–f

R′X–Bu_4NBr
CH_2Cl_2/
1 mol dm^{-3} NaOH



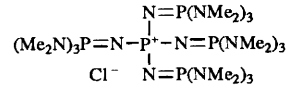
5a–f: R′ = Me
6a–f: R′ = $PhCH_2$
7a–f: R′ = $CH_2CH{=}CH_2$

8a–f: R′ = Me
9a–f: R′ = $PhCH_2$
10a–f: R′ = $CH_2CH{=}CH_2$



11

13: R^1 = Me, R^2 = Ac
14: R^1 = H, R^2 = Me
15: R^1 = H, R^2 = $CH_2CH{=}CH_2$



12

Scheme 1

Experimental

^1H and ^{13}C NMR spectra were measured at 270 and 67.8 MHz, respectively, on a JEOL-EX 270 spectrometer with $SiMe_4$ as the internal standard. *J* Values are given in Hz. UV spectra were taken on a Hitachi U-2000 spectrophotometer. TLC was performed by the use of Merck Kieselgel 60-F-254 (0.25 mm) with a developing solvent of hexane–ethyl acetate (5:1, v/v). Column chromatography was performed with silica gel C-200 purchased from Waco Co. Ltd., and a minipump, designed for a goldfish bowl, was conveniently used to attain sufficient pressure for rapid chromatographic separation. TBAF·H_2O and Bu_4NBr were purchased from Tokyo Kasei Co. Ltd. Compound **2** was prepared according to the method reported by Ogilvie.[33] Elemental analyses were performed by the Microanalytical Laboratory, Tokyo Institute of Technology, Nagatsuta.

Method A: typical procedure for *N*-acylation of 2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)adenosine 2

6-*N*-(2,2,2-Trichloro-1,1-dimethylethoxycarbonyl)-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)adenosine 4e. Compound **2** (1.0 g, 1.63 mmol) was rendered anhydrous by repeated co-evaporation with dry pyridine (10 cm^3 × 2) and finally dissolved in dry pyridine (16 cm^3). To the mixture was added dropwise 2,2,2-trichloro-1,1-dimethylethoxycarbonyl chloride (472 mg, 1.96 mmol) at 0 °C. The resulting mixture was kept at room temperature for 2 h after which concentrated ammonia (5 cm^3) was added to it. The solution was stirred for 30 min and then subjected to extractive work-up; chromatography of the crude product on silica gel (75 g) was CH_2Cl_2–MeOH (99:1, v/v) as eluent gave *compound* **4e** (1.1 g, 83%) (Found: C, 48.6; H, 7.4; N, 8.45. $C_{33}H_{60}Cl_3N_5O_6Si_3$ requires C, 48.7; H, 7.4; N, 8.6%); $\delta_H(CDCl_3)$ −0.30 (3 H, s, $SiCH_3$), −0.06 (3 H, s, $SiCH_3$), 0.09 (3 H, s, $SiCH_3$), 0.13 (3 H, s, $SiCH_3$), 0.14 (6 H, s, $SiCH_3$), 0.76 (9 H, s, Bu′), 0.92 (9 H, s, Bu′), 0.95 (9 H, s, Bu′), 3.79 (1 H, dd, $J_{4',5'}$ 2.6 and J_{gem} 11.6, 5′-H^a), 4.01 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.6, 5′-H^b), 4.13 (1 H, 4′-H), 4.27 (1 H, t, $J_{3',4'}$ 3.9, 3′-H), 4.63 (1 H, t, $J_{2',3'}$ 4.6, 2′-H), 6.10 (1 H, d, $J_{1',2'}$ 5.2, 1′-H), 8.35 (1 H, s, 2-H), 8.41 (1 H, br s, NH) and 8.77 (1 H, s, 8-H); $\delta_C(CDCl_3)$ 152.80, 152.48, 151.24, 149.02, 141.88, 122.71, 88.43, 85.61, 76.32, 71.80, 62.49, 26.03, 25.81, 25.63, 21.38, 18.48, 18.05, 17.80, −4.41, −4.69, −4.80, −5.09 and −5.42.

6-*N*-Acetyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)adenosine 4a (Found: C, 55.4; H, 8.9; N, 10.6. $C_{30}H_{57}N_5O_5Si_3$ requires C, 55.26; H, 8.81; N, 10.74%); $\delta_H(CDCl_3)$ −0.25 (3 H, s, $SiCH_3$), −0.04 (3 H, s, $SiCH_3$), 0.10 (3 H, s, $SiCH_3$), 0.13 (3 H, s, $SiCH_3$), 0.14 (6 H, s, $SiCH_3$), 0.78 (9 H, s, Bu′), 0.92 (9 H, s, Bu′), 0.95 (9 H, s, Bu′), 2.61 [3 H, s, $CH_3C(O)$], 3.78 (1 H, dd, $J_{4',5'}$ 2.6 and J_{gem} 11.6, 5′-H^a), 4.01 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.6, 5′-H^b), 4.14 (1 H, m, 4′-H), 4.30 (1 H, t, $J_{3',4'}$ 4.0, 3′-H), 4.64 (1 H, t, $J_{2',3'}$ 4.3, 2′-H), 6.08 (1 H, d, $J_{1',2'}$ 5.0, 1′-H), 8.34 (1 H, s, 2-H), 8.51 (1 H, br s, NH) and 8.67 (1 H, s, 8-H); $\delta_C(CDCl_3)$ 170.30, 152.30, 151.10, 149.09, 141.78, 121.97, 88.41, 85.58, 76.01, 71.86, 62.44, 23.92, 26.04, 25.80, 25.62 18.49, 18.04, 17.81, −4.42, −4.70, −4.74, −5.08 and −5.42.

2′,3′,5′-Tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-phenoxyacetyl-adenosine 4b (Found: C, 58.0; H, 8.4; N, 9.2. $C_{36}H_{61}N_5O_5Si_3$ requires C, 58.10; H, 8.26; N, 9.41%); $\delta_H(CDCl_3)$ −0.25 (3 H, s, $SiCH_3$), −0.03 (3 H, s, $SiCH_3$), 0.11 (3 H, s, $SiCH_3$), 0.14 (3 H, s, $SiCH_3$), 0.15 (6 H, s, $SiCH_3$), 0.79 (9 H, s, Bu′), 0.93 (9 H, s, Bu′), 0.96 (9 H, s, Bu′), 3.79 (1 H, dd, $J_{4',5'}$ 2.6 and J_{gem} 11.6, 5′-H^a), 4.03 (1 H, dd, $J_{4',5'}$ 4.3 and J_{gem} 11.6, 5′-H^b), 4.14 (1 H, m, 4′-H), 4.32 (1 H, t, $J_{3',4'}$ 4.0, 3′-H), 4.68 (1 H, t, $J_{2',3'}$ 4.6, 2′-H), 4.86 (2 H, s, CH_2), 6.09 (1 H, d, $J_{1',2'}$ 5.3, 1′-H), 7.03–7.08 (3 H, m, *p*-H of Ph), 7.32–7.38 (2 H, m, *o*-H of Ph), 8.36 (1 H, s, 2-H), 8.79 (1 H, s, 8-H) and 9.43 (1 H, br s, NH); $\delta_C(CDCl_3)$ 166.73, 152.32, 151.55, 148.23, 142.23, 129.63, 129.36, 122.73,

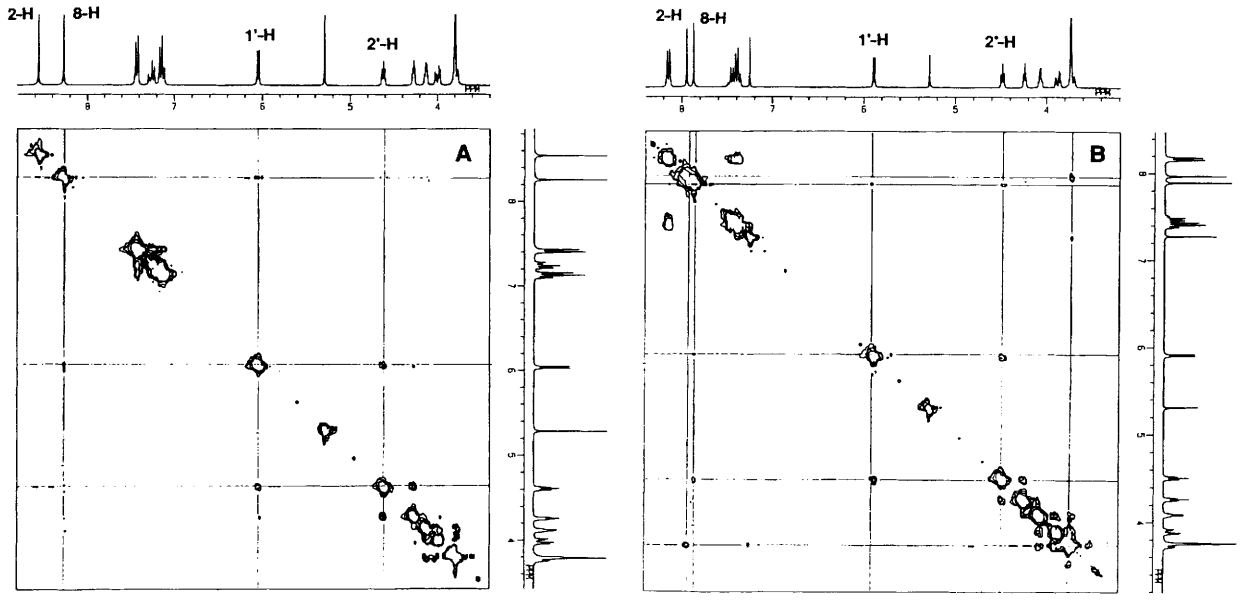


Fig. 1 NOESY spectra (270 MHz) of 6-*N*-methyladenosine derivative **5c** (A) and N^1-methyladenosine derivative **8c** (B) in $CDCl_3$

122.17, 114.86, 88.35, 85.52, 75.76, 71.79, 60.08, 62.33, 25.95, 25.71, 25.52, 18.38, 17.93, 17.72, −4.52, −4.77, −4.83, −5.17 and −5.49.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-(4-nitrobenzoyl)-adenosine 4d (Found: C, 55.1; H, 8.0; N, 10.9. $C_{35}H_{59}N_5O_7Si_3$ requires C, 55.30; H, 7.83; N, 11.06%); $\delta_H(CDCl_3)$ −0.23 (3 H, s, $SiCH_3$), −0.02 (3 H, s, $SiCH_3$), 0.10 (3 H, s, $SiCH_3$), 0.14 (3 H, s, $SiCH_3$), 0.15 (6 H, s, $SiCH_3$), 0.79 (9 H, s, Bu^t), 0.93 (9 H, s, Bu^t), 0.96 (9 H, s, Bu^t), 3.80 (1 H, dd, $J_{4',5'}$ 2.6 and J_{gem} 11.6, 5'-H^a), 4.02 (1 H, dd, $J_{4',5'}$ 3.6 and J_{gem} 11.6, 5'-H^b), 4.15 (1 H, m, 4'-H), 4.31 (1 H, t, $J_{3',4'}$ 4.0, 3'-H), 4.64 (1 H, t, $J_{2',3'}$ 4.3, 2'-H), 6.12 (1 H, d, $J_{1',2'}$ 5.0, 1'-H), 8.17–8.44 (4 H, m, ArH), 8.44 (1 H, s, 2-H), 8.81 (1 H, s, 8-H) and 9.32 (1 H, br s, NH); $\delta_C(CDCl_3)$ 168.25, 152.59, 151.31, 149.13, 147.31, 142.30, 141.04, 129.14, 123.93, 129.18, 88.44, 85.76, 76.12, 71.86, 62.44, 26.06, 25.80, 25.62, 18.51, 18.06, 17.82, −4.40, −4.67, −4.72, −5.04 and −5.37.

Typical procedure for silylation of *N*-acylated adenosines with *tert*-butyldimethylsilyl chloride

6-*N*-Benzoyl-2',3',5'-tris-*O*-(*tert*-butyldimethylsilyl)adenosine 4c. Compound **3c** (2.68 mmol) was dissolved in dry DMF (13 cm^3) and to the solution were added *tert*-butyldimethylsilyl chloride (1.78 g, 11.8 mmol) and imidazole (1.60 g, 23.5 mmol). After being stirred for 4 h, the mixture was evaporated under reduced pressure and the residue extracted with EtOAc. After work-up chromatography using silica gel (100 g) with CH_2Cl_2–MeOH (99:1, v/v) as eluent gave *compound* **4c** (Found: C, 58.8; H, 8.3; N, 9.9. $C_{35}H_{59}N_5O_5Si_3$ requires C, 58.86; H, 8.32; N, 9.80%); $\delta_H(CDCl_3)$ −0.25 (3 H, s, $SiCH_3$), −0.04 (3 H, s, $SiCH_3$), 0.10 (3 H, s, $SiCH_3$), 0.13 (3 H, s, $SiCH_3$), 0.14 (6 H, s, $SiCH_3$), 0.79 (9 H, s, Bu^t), 0.93 (9 H, s, Bu^t), 0.95 (9 H, s, Bu^t), 3.79 (1 H, dd, $J_{4',5'}$ 3.0 and J_{gem} 11.6, 5'-H^a), 4.02 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.6, 5'-H^b), 4.14 (1 H, m, 4'-H), 4.31 (1 H, t, $J_{3',4'}$ 4.0, 3'-H), 4.68 (1 H, t, $J_{2',3'}$ 4.6, 2'-H), 6.11 (1 H, d, $J_{1',2'}$ 5.3, 1'-H), 7.48–7.59 (3 H, m, *m*,*p*-H of Ph), 8.00–8.03 (2 H, m, *o*-H of Ph), 8.36 (1 H, s, 2-H), 8.80 (1 H, s, 8-H) and 9.10 (1 H, br s, NH); $\delta_C(CDCl_3)$ 164.54, 152.70, 151.62, 149.45, 141.92, 133.85, 132.66, 128.82, 127.79, 123.16, 88.41, 85.67, 76.53, 71.96, 62.53, 26.07, 25.82, 25.64, 18.51, 18.06, 17.82, −4.42, −4.67, −4.72, −5.06 and −5.37.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-(2-trimethylsilylethoxycarbonyl)adenosine 4f (Found: C, 54.3; H, 8.9; N, 9.4. $C_{34}H_{67}N_5O_6Si_4$ requires C, 54.14; H, 8.95; N, 9.29%); $\delta_H(CDCl_3)$ −0.26 (3 H, s, $SiCH_3$), −0.04 (3 H, s, $SiCH_3$), 0.07 (9 H, s, $SiCH_2CH_3$), 0.10 (3 H, s, $SiCH_3$), 0.13 (3 H, s, $SiCH_3$), 0.14 (6 H, s, $SiCH_3$), 0.78 (9 H, s, Bu^t), 0.93 (9 H, s, Bu^t), 0.95 (9 H, s, Bu^t), 0.98–1.08 (2 H, m, $SiCH_2CH_3$), 3.79 (1 H, dd, $J_{4',5'}$ 2.6 and J_{gem} 11.2, 5'-H^a), 4.02 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.2, 5'-H^b), 4.13 (1 H, m, 4'-H), 4.29–4.39 (3 H, m, 3'-H and CH_2CH_2Si), 4.66 (1 H, t, $J_{2',3'}$ 4.6, 2'-H), 6.07 (1 H, d, $J_{1',2'}$ 5.2, 1'-H), 8.09 (1 H, br s, NH), 8.31 (1 H, s, 2-H) and 8.73 (1 H, s, 8-H); $\delta_C(CDCl_3)$ 152.79, 151.07, 149.45, 141.50, 127.20, 88.37, 85.04, 76.53, 71.95, 64.51, 62.49, 26.04, 25.80, 25.62, 18.49, 18.04, 17.81, 17.64, −1.52, −4.43, −4.70, −5.11 and −5.39.

Typical procedure for the *N*-alkylation of acyladenosines: synthesis of 6-*N*-acyl-6-*N*-alkyl-2',3',5'-tris-*O*-(*tert*-butyldimethylsilyl)adenosines

An appropriate 6-*N*-acyladenosine derivative (1 mmol) and alkyl halide (4 mmol) were dissolved in CH_2Cl_2, and tetrabutylammonium bromide (1 mmol) and 1 mol dm^{-3} aq. NaOH (10 cm^3) were added to the solution. After vigorous stirring of the mixture for 10–30 min, work-up followed by silica gel column chromatography with hexane–ethyl acetate (7:1, v/v) as eluent gave an *N*-alkylated product as a colourless syrup.

6-*N*-Acetyl-2',3',5'-tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-methyladenosine 5a (Found: C, 54.3; H, 8.9; N, 10.5. $C_{31}H_{59}N_5O_5Si_3H_2O$ requires C, 54.31; H, 8.69; N, 10.24%); $\delta_H(CDCl_3)$ 2.26 (3 H, s, CH_3), 3.54 (3 H, s, NCH_3), 3.79 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.4, 5'-H^a), 4.00 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.4, 5'-H^b), 4.13 (1 H, m, 4'-H), 4.31 (3 H, m, 3'-H), 4.64 (1 H, dd, $J_{2',3'}$ 4.6, 2'-H), 6.11 (1 H, d, $J_{1',2'}$ 5.3, 1'-H), 8.41 (1 H, s, 2-H) and 8.74 (1 H, s, 8-H); $\delta_C(CDCl_3)$ −5.24, −5.20, −4.72, −4.45 (MeSi), 17.79, 18.02, 18.47 [$(CH_3)_3CSi$], 24.02 (Ac), 25.55, 25.78, 26.02 [$(CH_3)_3CSi$)], 35.11 (Me), 62.44 (C-5'), 71.89 (C-3'), 76.01 (C-2'), 85.71 (C-4'), 88.28 (C-1'), 126.88 (C-5), 142.69 (C-8), 151.75 (C-4), 152.95 (C-2), 154.01 (C-6) and 171.57 (C=O).

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-methyl-6-*N*-phenoxyacetyladenosine 5b (Found: C, 58.7; H, 8.4; N, 9.1. $C_{37}H_{63}N_5O_6Si_3$ requires C, 58.61; H, 8.38; N, 9.24%); $\delta_H(CDCl_3)$ 3.75 (3 H, s, NCH_3), 3.82 (1 H, dd, $J_{4',5'}$ 3.6 and J_{gem} 11.3, 5'-H^a), 4.04 (1 H, dd, $J_{4',5'}$ 3.6 and J_{gem} 11.3, 5'-H^b), 4.16 (1 H, m, 4'-H), 4.34 (3 H, dd, $J_{3',4'}$ 3.7, 3'-H), 4.55 (1 H, dd, $J_{2',3'}$ 4.3, 2'-H), 6.13 (1 H, d, $J_{1',2'}$ 5.0, 1'-H), 6.73, 6.91, 7.20 (5 H, m, Ph), 8.45 (1 H, s, 2-H) and 8.69 (1 H, s, 8-H); $\delta_C(CDCl_3)$

−5.42, −5.33, −4.99, −4.70, −4.63, −4.42 (MeSi), 17.82, 18.04, 18.51 [$(CH_3)_3CSi$], 25.54, 25.80, 26.06 [$(CH_3)_3CSi$], 34.99 (Me), 62.33 (C-5′), 68.73 ($PhOCH_2$), 71.71 (C-3′), 76.08 (C-2′), 85.49 (C-4′), 88.39 (C-1′), 114.50, 121.27, 129.30 (PacPh), 125.69 (C-5), 142.46 (C-8), 151.42 (C-4), 152.86 (C-2), 157.89 (C-6) and 170.47 (C=O).

6-*N*-Benzoyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl-6-*N*-methyladenosine 5c (Found: C, 59.5; H, 8.4; N, 9.6. $C_{36}H_{61}N_5O_5Si_3$ requires C, 59.38; H, 8.44; N, 9.62%); $\delta_H(CDCl_3)$ −0.37, −0.08, 0.08, 0.11 (3 H, s, MeSi), 0.74, 0.92, 0.94 (9 H, s, Bu^{t}Si), 3.76 (1 H, dd, $J_{4',5'}$ 3.0 and J_{gem} 11.2, 5′-H^a), 3.78 (3 H, s, Me), 3.98 (1 H, dd, $J_{4',5'}$ 4.3 and J_{gem} 11.2, 5′-H^b), 4.10 (1 H, m, 4′-H), 4.24 (1 H, t, $J_{3',4'}$ 4.3, 3′-H), 4.60 (1 H, t, $J_{2',3'}$ 4.3, 2′-H), 6.03 (1 H, d, $J_{1',2'}$ 5.6, 1′-H), 8.25 (1 H, s, 2-H) and 8.53 (1 H, s, 8-H); $\delta_C(CDCl_3)$ −4.42, −4.63, −4.72, −5.15, −5.46 (MeSi), 18.49, 18.04, 17.77 [$(CH_3)_3CSi$], 26.06, 25.80, 25.61 [$(CH_3)_3CSi$], 35.77 (Me), 62.60 (C-5′), 72.11 (C-3′), 76.28 (C-2′), 85.91 (C-4′), 88.10 (C-1′), 126.68 (C-5), 136.26, 130.45, 128.60, 127.78 (Bz), 142.49 (C-8), 151.77 (C-4), 152.63 (C-2), 155.50 (C-6) and 171.01 (C=O).

2′,3′,5′-Tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-methyl-6-*N*-(4-nitrobenzoyl)adenosine 5d (Found: C, 55.8; H, 7.9; N, 10.8. $C_{36}H_{61}N_6O_7Si_3$ requires C, 55.85; H, 7.94; N, 10.86%); $\delta_H(CDCl_3)$ −0.42, −0.10, 0.07, 0.10, 0.11 (3 H, s, MeSi), 0.73, 0.91, 0.94 (9 H, s, Bu^{t}Si), 3.75 (1 H, dd, $J_{4',5'}$ 2.6 and J_{gem} 11.2, 5′-H^a), 3.80 (3 H, s, Me), 3.96 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.2, 5′-H^b), 4.11 (1 H, m, 4′-H), 4.23 (1 H, t, $J_{3',4'}$ 3.0, 3′-H), 4.54 (1 H, t, $J_{2',3'}$ 4.6, 2′-H), 6.03 (1 H, d, $J_{1',2'}$ 5.6, 1′-H), 7.56 (2 H, d, *J* 8.9, *m*-ArH), 7.99 (2 H, d, *J* 8.9, *o*-ArH), 8.30 (1 H, s, 2-H), 8.53 (1 H, s, 8-H); $\delta_C(CDCl_3)$ −5.44, −5.28, −4.72, −4.69, −4.50 (MeSi), 17.72, 18.02, 18.47 [$(CH_3)_3CSi$], 25.54, 25.77, 26.04 [$(CH_3)_3CSi$], 35.67 (Me), 62.59 (C-5′), 72.13 (C-3′), 75.99 (C-2′), 86.02 (C-4′), 88.14 (C-1′), 126.47 (C-5), 123.00, 129.36, 142.51, 148.44 (NO_2Bz), 142.98 (C-8), 151.82 (C-4), 152.88 (C-2), 153.80 (C-6) and 169.95 (C=O).

2′,3′,5′-Tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-6-*N*-methyladenosine 5e (Found: C, 49.5; H, 7.4; N, 8.3. $C_{34}H_{62}Cl_3N_5O_6Si_3$ requires C, 49.35; H, 7.55; N, 8.46%); $\delta_H(CDCl_3)$ −0.26, −0.04, 0.10, 0.11, 0.12 (3 H, s, MeSi), 0.72, 0.91, 0.93 (9 H, s, Bu^{t}Si), 1.99 (6 H, s, TcBocMe), 3.76 (3 H, s, Me), 3.78 (1 H, dd, $J_{4',5'}$ 2.9 and J_{gem} 11.5, 5′-H^a), 4.01 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.5, 5′-H^b), 4.14 (1 H, m, 4′-H), 4.30 (1 H, t, $J_{3',4'}$ 3.8, 3′-H), 4.59 (1 H, t, $J_{2',3'}$ 4.2, 2′-H), 6.06 (1 H, d, $J_{1',2'}$ 5.0, 1′-H), 8.40 (1 H, s, 2-H) and 8.77 (1 H, s, 8-H); $\delta_C(CDCl_3)$ −5.41, −4.99, −4.79, −4.73, −4.40 (MeSi), 17.81, 18.03, 18.47 [$(CH_3)_3CSi$], 25.62, 25.78, 26.05 [$(CH_3)_3CSi$], 21.25 (TcBoc), 35.28 (Me), 62.47 (C-5′), 71.50 (C-3′), 75.92 (C-2′), 85.26 (C-4′), 88.56 (C-1′), 127.81 (C-5), 151.92 (C-4), 142.50 (C-8), 152.91 (C-6) and 152.36 (C-2).

2′,3′,5′-Tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-methyl-6-*N*-(2-trimethylsilylethoxycarbonyl)adenosine 5f (Found: C, 54.5; H, 9.1; N, 9.0. $C_{35}H_{69}N_5O_6Si_4$ requires C, 54.69; H, 9.06; N, 9.12%); $\delta_H(CDCl_3)$ −0.24, −0.05, 0.09, 0.10, 0.12 (3 H, s, MeSi), −0.02 (9 H, s, TMS), 0.78, 0.93, 0.94 (9 H, s, Bu^{t}Si), 3.78 (1 H, dd, $J_{4',5'}$ 3.0 and J_{gem} 11.2, 5′-H^a), 3.79 (3 H, s, CH_3), 4.01 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.2, 5′-H^b), 4.13 (1 H, m, 4′-H), 4.28–4.34 (3 H, m, 3′-H and OCH_2CH_2TMS), 4.65 (1 H, t, $J_{2',3'}$ 4.6, 2′-H), 6.09 (1 H, d, $J_{1',2'}$ 5.3, 1′-H), 8.34 (1 H, s, 2-H) and 8.72 (1 H, s, 8-H); $\delta_C(CDCl_3)$ −5.39, −5.03, −4.72, −4.68, −4.42 (MeSi), 17.54 [$CH_2CH_2Si(CH_3)_3$], 17.75, 18.04, 18.49 [$(CH_3)_3CSi$], 62.50 (C-5′), 64.94 [$CH_2CH_2Si(CH_3)_3$], 71.88 (C-3′), 75.81 (C-2′), 85.43 (C-4′), 88.28 (C-1′), 127.40 (C-5), 141.98 (C-8), 151.66 (C-4), 152.40 (C-2), 154.98 (C-6) and 153.62 (C=O).

6-*N*-Acetyl-6-*N*-benzyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)adenosine 6a (Found: C, 59.5; H, 8.4; N, 9.4. $C_{37}H_{63}N_5O_5Si_3$ requires C, 59.88; H, 8.56; N, 9.44%); $\delta_H(CDCl_3)$ 2.32 (3 H, s, CH_3), 3.80 (1 H, dd, $J_{4',5'}$ 4.3 and J_{gem} 11.3, 5′-H^a), 4.02 (1 H, dd, $J_{4',5'}$ 4.3 and J_{gem} 11.3, 5′-H^b), 4.15 (1 H, m, 4′-H), 4.30 (3 H, dd, $J_{3',4'}$ 4.3, 3′-H), 4.65 (1 H, dd, $J_{2',3'}$ 4.3, 2′-H), 5.56 (3 H, s, NCH_2), 6.1 (1 H, d, $J_{1',2'}$ 5.6, 1′-H), 7.10–7.27 (5 H, m, ArH), 8.40 (1 H, s, 2-H) and 8.74 (1 H, s, 8-H); $\delta_C(CDCl_3)$ −5.24, −5.20, −4.72, −4.45 (MeSi), 17.72, 18.02, 18.47 [$(CH_3)_3CSi$], 24.11 (Ac), 26.04, 25.79, 25.50 [$(CH_3)_3CSi$], 49.77 (CH_2), 62.60 (C-5′), 72.13 (C-3′), 75.90 (C-2′), 86.02 (C-4′), 88.14 (C-1′), 126.90 (C-4), 126.90 (C-5), 127.58, 128.21, 137.53 (ArC), 142.78 (C-8), 151.86 (C-2), 153.61 (C-6) and 171.82 (C=O).

6-*N*-Benzyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-phenoxyacetyladenosine 6b (Found: C, 60.3; H, 8.1; N, 8.2. $C_{43}H_{67}N_5O_6Si_3H_2O$ requires C, 60.59; H, 8.16; N, 8.21%); $\delta_H(CDCl_3)$ 3.80 (1 H, dd, $J_{4',5'}$ 3.6 and J_{gem} 11.2, 5′-H^a), 4.02 (1 H, dd, $J_{4',5'}$ 3.6 and J_{gem} 11.2, 5′-H^b), 4.14 (1 H, m, 4′-H), 4.29 (3 H, dd, $J_{3',4'}$ 4.0, 3′-H), 4.59 (1 H, dd, $J_{2',3'}$ 4.0, 2′-H), 5.66 (2 H, s, CH_2), 6.08 (1 H, d, $J_{1',2'}$ 5.0, 1′-H), 6.67, 6.91, 7.21–7.28 (5 H, m, ArH), 7.11–7.28 (5 H, m, Ph), 8.42 (1 H, s, 2-H) and 8.66 (1 H, s, 8-H); $\delta_C(CDCl_3)$ −5.39, −5.22, −4.72, −4.96, −4.41 (MeSi), 17.76, 18.06, 18.51 [$(CH_3)_3CSi$], 25.54, 25.82, 26.06 [$(CH_3)_3CSi$], 49.77 (CH_2), 62.48 (C-5′), 68.70 ($PhOCH_2$), 71.95 (C-3′), 76.05 (C-2′), 85.78 (C-4′), 88.24 (C-1′), 114.44, 121.31, 129.30, 152.68 (PacPh), 126.34 (C-5), 127.08, 127.90, 128.23, 137.16 (ArC), 142.55 (C-8), 151.59 (C-4), 151.84 (C-2), 157.77 (C-6) and 170.54 (C=O).

6-*N*-Benzoyl-6-*N*-benzyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)adenosine 6c (Found: C, 62.7; H, 8.2; N, 8.8. $C_{42}H_{65}N_5O_5Si_3{\cdot}H_2O$ requires C, 62.7; H, 8.21; N, 8.51%); $\delta_H(CDCl_3)$ −0.57, −0.16, 0.09, 0.12 (3 H, s, MeSi), 0.68, 0.92, 0.94 (9 H, s, Bu^{t}Si), 3.76 (1 H, dd, $J_{4',5'}$ 3.6 and J_{gem} 11.6, 5′-H^a), 3.95 (1 H, dd, $J_{4',5'}$ 4.2 and J_{gem} 11.6, 5′-H^b), 4.08 (1 H, m, 4′-H), 4.22 (1 H, t, $J_{3',4'}$ 3.9, 3′-H), 4.5 (1 H, t, $J_{2',3'}$ 4.6, 2′-H), 5.63 (2 H, s, CH_2Ph), 5.98 (1 H, d, $J_{1',2'}$ 4.9, 1′-H), 7.50–7.08 (10 H, m, ArH), 8.19 (1 H, s, 2-H), 8.51 (1 H, s, 8-H); $\delta_C(CDCl_3)$ −5.42, −5.38, −5.23, −4.68, −4.61, −4.49 (MeSi), 17.74, 18.06, 18.49 [$(CH_3)_3CSi$], 25.55, 25.80, 26.08 [$(CH_3)_3CSi$], 51.27 (CH_2), 62.77 (C-5′), 72.33 (C-3′), 75.55 (C-2′), 86.18 (C-4′), 87.98 (C-1′), 127.08 (C-5), 128.01, 128.30, 137.46 (Ph), 127.79, 128.80, 136.35, 137.47 (Bz), 142.46 (C-8), 151.80 (C-4), 154.03 (C-6), 152.59 (C-2) and 172.50 (C=O).

6-*N*-Benzyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-(4-nitrobenzoyl)adenosine 6d (Found: C, 59.3; H, 7.7; N, 9.8. $C_{42}H_{64}N_6O_7Si_3$ requires C, 59.40; H, 7.60; N, 9.90%); $\delta_H(CDCl_3)$ −0.58, −0.15, 0.09, 0.11, 0.12 (3 H, s, MeSi), 0.68, 0.91, 0.94 (9 H, s, Bu^{t}Si), 3.75 (1 H, dd, $J_{4',5'}$ 2.6 and J_{gem} 11.6, 5′-H^a), 3.95 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.6, 5′-H^b), 4.08 (1 H, m, 4′-H), 4.20 (1 H, t, $J_{3',4'}$ 4.3, 3′-H), 4.52 (1 H, t, $J_{2',3'}$ 5.0, 2′-H), 5.65 (2 H, s, CH_2), 5.99 (1 H, d, $J_{1',2'}$ 5.6, 1′-H), 7.15–7.42 (5 H, m, Ph), 7.63 (2 H, d, *J* 8.9, *m*-NO_2Bz), 8.02 (2 H, d, *J* 8.9, *o*-NO_2Bz), 8.23 (1 H, s, 2-H) and 8.53 (1 H, s, 8-H); $\delta_C(CDCl_3)$ −5.44, −4.72, −4.67, −4.52, −3.59 (MeSi), 17.67, 18.04, 18.47 [$(CH_3)_3CSi$], 25.62, 25.77, 26.04 [$(CH_3)_3CSi$], 49.65 (CH_2), 62.73 (C-5′), 72.34 (C-3′), 75.80 (C-2′), 86.32 (C-4′), 87.97 (C-1′), 123.03, 129.56, 142.53, 144.24 (NO_2Bz), 127.40, 128.41, 136.78 (ArC), 126.82 (C-5), 142.91 (C-8), 151.89 (C-4), 152.79 (C-2), 152.90 (C-6) and 170.00 (C=O).

6-*N*-Benzyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)adenosine 6e (Found: C, 53.3; H, 7.5; N, 7.5. $C_{40}H_{66}Cl_3N_5O_6Si_3$ requires C, 53.17; H, 7.36; N, 7.75%); $\delta_H(CDCl_3)$ −0.27, −0.04, 0.10, 0.11, 0.12 (3 H, s, MeSi), 0.77, 0.93, 0.94 (9 H, s, Bu^{t}Si), 1.66 (6 H, s, TcBocMe), 3.78 (1 H, dd, $J_{4',5'}$ 3.0 and J_{gem} 11.6, 5′-H^a), 4.00 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.6, 5′-H^b), 4.14 (1 H, m, 4′-H), 4.31 (1 H, t, $J_{3',4'}$ 4.0, 3′-H), 4.61 (1 H, t, $J_{2',3'}$ 4.3, 2′-H), 5.38 (2 H, s, CH_2), 6.06 (1 H, d, $J_{1',2'}$ 5.0, 1′-H), 7.13–7.28 (5 H, m, Ph), 8.37 (1 H, s, 2-H) and 8.74 (1 H, s, 8-H); $\delta_C(CDCl_3)$ −5.38, −4.99, −4.96, −4.72, −4.40 (MeSi), 17.81, 18.01, 18.49 [$(CH_3)_3CSi$], 21.25 (TcBoc), 25.62, 25.79, 26.06 [$(CH_3)_3CSi$], 51.57 (CH_2), 62.57 (C-5′), 71.84 (C-3′), 75.99 (C-2′), 85.44 (C-4′), 88.50 (C-1′),

127.36 (C-5), 128.58, 128.44, 128.98, 137.96 (Ph), 142.89 (C-8), 152.00 (C-4), 152.48 (C-2), 152.32 (C=O) and 152.93 (C-6).

6-*N*-Benzyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-[2-(trimethylsilyl)ethoxycarbonyl]adenosine 6f (Found: C, 58.2; H, 8.9; N, 8.1. $C_{41}H_{73}N_5O_6Si_4$ requires C, 58.32; H, 8.71; N, 8.29%); δ_H($CDCl_3$) −0.37, −0.08, 0.10, 0.12 (3 H, s, MeSi), −0.03 (9 H, s, TMS), 0.73, 0.93, 0.94 (9 H, s, Bu^{t}Si), 3.78 (1 H, dd, $J_{4',5'}$ 3.0 and J_{gem} 11.2, 5′-H^a), 4.00 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.2, 5′-H^b), 4.12 (1 H, m, 4′-H), 4.27–4.30 (2 H, m, OCH_2CH$_2$TMS), 4.33 (1 H, t, $J_{3',4'}$ 3.0, 3′-H), 4.67 (1 H, t, $J_{2',3'}$ 4.6, 2′-H), 5.33 (2 H, s, CH_2), 6.06 (1 H, d, $J_{1',2'}$ 5.6, 1′-H), 7.16–7.37 (5 H, m, Ph), 8.29 (1 H, s, 2-H) and 8.70 (1 H, s, 8-H); δ_C($CDCl_3$) −5.42, −5.39, −5.26, −4.72, −4.69, −4.48 (MeSi), −1.13 [$CH_2CH_2Si(CH_3)_3$], 17.47 [$CH_2CH_2Si(CH_3)_3$], 17.75, 18.04, 18.49 [$(CH_3)_3CSi$], 50.74 (CH_2), 62.66 (C-5′), 65.10 [$CH_2CH_2Si(CH_3)_3$], 72.11 (C-3′), 75.63 (C-2′), 85.76 (C-4′), 88.10 (C-1′), 126.95 (C-5), 127.51, 127.90, 128.23, 137.86 (Ph), 142.08 (C-8), 151.66 (C-4), 152.45 (C-2), 152.77 (C=O) and 155.04 (C-6).

6-*N*-Acetyl-6-*N*-allyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-adenosine 7a (Found: C, 57.4; H, 8.6; N, 10.2. $C_{33}H_{61}N_5O_5Si_3$ requires C, 57.27; H, 8.80; N, 10.12%); δ_H($CDCl_3$) 2.24 (3 H, s, CH_3), 3.80 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.3, 5′-H^a), 4.02 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.3, 5′-H^b), 4.13 (1 H, m, 4′-H), 4.31 (3 H, dd, $J_{3',4'}$ 4.0, 3′-H), 4.67 (1 H, dd, $J_{2',3'}$ 4.3, 2′-H), 4.87 (2 H, s, CH_2), 4.97–5.10 (2 H, m, C=CH_2), 5.78–5.92 (1 H, m, C=CH), 6.11 (1 H, d, $J_{1',2'}$ 5.6, 1′-H), 8.40 (1 H, s, 2-H) and 8.76 (1 H, s, 8-H); δ_C($CDCl_3$) −5.40, −5.28, −4.68, −4.45 (MeSi), 17.79, 18.06, 18.49 [$(CH_3)_3CSi$], 24.04 (Ac), 25.57, 25.80, 26.04 [$(CH_3)_3CSi$], 49.18 (CH_2=CHCH_2), 62.64 (C-5′), 72.17 (C-3′), 76.01 (C-2′), 86.03 (C-4′), 88.17 (C-1′), 116.96 (CH_2=CHCH_2), 127.56 (C-5), 133.20 (CH_2=$CHCH_2$), 142.83 (C-8), 151.91 (C-4), 152.99 (C-2), 153.22 (C-6) and 171.10 (C=O).

6-*N*-Allyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-phenoxyacetyladenosine 7b (Found: C, 59.7; H, 8.5; N, 8.8. $C_{39}H_{65}N_5O_6Si_3$ requires C, 59.72; H, 8.35; N, 8.93%); δ_H($CDCl_3$) 3.80 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.5, 5′-H^a), 4.03 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.5, 5′-H^b), 4.15 (1 H, m, 4′-H), 4.31 (3 H, dd, $J_{3',4'}$ 3.6, 3′-H), 4.62 (1 H, dd, $J_{2',3'}$ 4.6, 2′-H), 4.89–5.17 (2 H, s, CH_2), 4.89–5.17 (2 H, m, C=CH_2), 5.80–5.92 (1 H, m, C=CH), 6.11 (1 H, d, $J_{1',2'}$ 5.0, 1′-H), 6.67–6.70, 6.87–6.93, 7.14–7.22 (5 H, m, Ph), 8.42 (1 H, s, 2-H) and 8.69 (1 H, s, 8-H); δ_C($CDCl_3$) −5.39, −5.13, −4.70, −4.67, −4.40 (MeSi), 17.81, 18.06, 18.51 [$(CH_3)_3CSi$], 25.59, 25.82, 26.07 [$(CH_3)_3CSi$], 49.07 (CH_2=CHCH_2), 62.49 (C-5′), 68.73 (CH_2), 71.95 (C-3′), 76.10 (C-2′), 85.77 (C-4′), 88.28 (C-1′), 117.15 (CH_2=$CHCH_2$), 114.48, 121.31, 129.30, 152.83 (PacPh), 126.21 (C-5), 129.30 (CH_2=$CHCH_2$), 142.53 (C-8), 151.60 (C-4), 151.93 (C-2), 157.80 (C-6) and 170.15 (C=O).

6-*N*-Allyl-6-*N*-benzoyl-2′,3′,5′-*O*-tris(*tert*-butyldimethylsilyl)adenosine 7c (Found: C, 60.7; H, 8.5; N, 9.5. $C_{38}H_{62}N_5O_5Si_3$ requires C, 60.60; H, 8.30; N, 9.30%); δ_H($CDCl_3$) −0.45, −0.10, 0.09, 0.11, 0.12 (3 H, s, MeSi), 0.79, 0.92, 0.94 (9 H, s, Bu^{t}Si), 3.77 (1 H, dd, $J_{4',5'}$ 2.6 and J_{gem} 11.6, 5′-H^a), 3.97 (1 H, dd, $J_{4',5'}$ 4.6 and J_{gem} 11.6, 5′-H^b), 4.11 (1 H, m, 4′-H), 4.24 (1 H, t, $J_{3',4'}$ 2.6, 3′-H), 4.62 (1 H, t, $J_{2',3'}$ 4.6, 2′-H), 4.98–5.06 (3 H, m, CH_2=CHCH_2), 5.20 (1 H, dd, J 1.3 and 7.2), (CH_2=$CHCH_2$), 6.02 (1 H, d, $J_{1',2'}$ 5.9, 1′-H), 6.06–5.95 (1 H, m, CH_2=CHCH_2), 8.20 (1 H, s, 2-H) and 8.55 (1 H, s, 8-H); δ_C($CDCl_3$) −5.42, −5.38, −5.23, −4.68, −4.61, −4.43 (MeSi), 17.76, 18.06, 18.49 [$(CH_3)_3CSi$], 25.59, 25.80, 26.06 [$(CH_3)_3CSi$], 50.46 (CH_2=CHCH_2), 67.76 (C-5′), 72.36 (C-3′), 75.61 (C-2′), 86.20 (C-4′), 87.96 (C-1′), 117.59 (CH_2=$CHCH_2$), 127.09 (C-5), 127.79, 128.71, 130.58, 136.28 (Bz), 133.04 (CH_2=$CHCH_2$), 142.51 (C-8), 151.84 (C-4), 154.07 (C-6), 151.84 (C-4), 152.61 (C-2) and 171.78 (C=O).

6-*N*-Allyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-(4-nitrobenzoyl)adenosine 7d (Found: C, 57.3; H, 7.4; N, 10.3. $C_{38}H_{58}N_6O_7Si_3$ requires C, 57.40; H, 7.35; N, 10.57%); δ_H($CDCl_3$) −0.50, −0.12, 0.08, 0.11, 0.12 (3 H, s, MeSi), 0.71, 0.91, 0.94 (9 H, s, Bu^{t}Si), 3.77 (1 H, dd, $J_{4',5'}$ 2.6 and J_{gem} 11.2, 5′-H^a), 3.96 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.2, 5′-H^b), 4.11 (1 H, m, 4′-H), 4.21 (1 H, dd, $J_{3',4'}$ 4.0, 3′-H), 4.56 (1 H, dd, $J_{2',3'}$ 4.6, 2′-H), 5.04 (3 H, m, CH_2=CHCH_2), 5.21 (1 H, dd, J 1.3 and 17.2, CH_2=CHCH_2), 5.93–5.99 (1 H, m, CH_2=CHCH_2), 6.02 (1 H, d, $J_{1',2'}$ 6.3, 1′-H), 7.63–7.58 (2 H, m, *m*-ArH), 7.93–8.04 (2 H, m, *o*-ArH), 8.26 (1 H, s, 2-H) and 8.56 (1 H, s, 8-H); δ_C($CDCl_3$) −5.42, −5.37, −4.67, −4.52, −3.59 (MeSi), 17.70, 18.04, 18.47 [$(CH_3)_3CSi$], 25.62, 26.04 [$(CH_3)_3CSi$], 50.42 (CH_2=CHCH_2), 62.77 (C-5′), 72.38 (C-3′), 75.92 (C-2′), 86.34 (C-4′), 87.99 (C-1′), 123.01 (CH_2=$CHCH_2$), 129.49 (C-5), 132.34 (CH_2=CCH_2), 123.19, 129.56, 142.49, 148.51 (NO_2ArCO), 142.98 (C-8), 151.91 (C-4), 152.84 (C-2), 152.95 (C-6) and 169.64 (C=O).

6-*N*-Allyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)adenosine 7e (Found: C, 50.5; H, 7.6; N, 8.1. $C_{36}H_{64}Cl_3N_5O_6Si_3$ requires C, 50.66; H, 7.56; N, 8.21%); δ_H($CDCl_3$) −0.20, −0.03, 0.09, 0.10, 0.12 (3 H, s, MeSi), 0.79, 0.92, 0.94 (9 H, s, Bu^{t}Si), 1.99 (6 H, s, TcBocMe), 3.78 (1 H, dd, $J_{4',5'}$ 2.6 and J_{gem} 11.6, 5′-H^a), 4.00 (1 H, dd, $J_{4',5'}$ 3.6 and J_{gem} 11.6, 5′-H^b), 4.13 (1 H, m, 4′-H), 4.31 (1 H, t, $J_{3',4'}$ 4.3, 3′-H), 4.62 (1 H, t, $J_{2',3'}$ 3, 2′-H), 4.72 (2 H, d, J 5.6, CH_2=CHCH_2), 5.03 (1 H, dd, J 1.3 and 10.2, CH_2=CHCH_2), 5.20 (1 H, dd, J 1.2 and 17.2, CH_2=CHCH_2), 5.86–6.00 (1 H, m, CH_2=CHCH_2), 6.08 (1 H, d, $J_{1',2'}$ 4.6, 1′-H), 8.38 (1 H, s, 2-H) and 8.76 (1 H, s, 8-H); δ_C($CDCl_3$) −5.40, −4.99, −4.77, −4.76, −4.42 (MeSi), 17.83, 18.06, 18.51 [$(CH_3)_3CSi$], 25.64, 25.82, 26.06 [$(CH_3)_3CSi$], 21.47 (TcBoc), 50.49 (CH_2=CHCH_2), 62.28 (C-5′), 71.53 (C-3′), 75.81 (C-2′), 85.10 (C-4′), 88.53 (C-1′), 116.96 (CH_2=$CHCH_2$), 128.30 (C-5), 133.18 (CH_2=$CHCH_2$), 142.89 (C-8), 152.00 (C-4), 152.70 (C-6) and 152.18 (C-2).

6-*N*-Allyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-6-*N*-(2-trimethylsilylethoxycarbonyl)adenosine 7f (Found: C, 55.8; H, 9.1; N, 8.8. $C_{37}H_{71}N_5O_6Si_4$ requires C, 55.95; H, 9.01; N, 8.82%); δ_H($CDCl_3$) −0.29, −0.06, 0.10, 0.12 (3 H, s, MeSi), −0.02 (9 H, s, TMS), 0.76, 0.93, 0.94 (9 H, s, Bu^{t}Si), 3.79 (1 H, dd, $J_{4',5'}$ 2.6 and J_{gem} 11.2, 5′-H^a), 4.00 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.2, 5′-H^b), 4.14 (1 H, m, 4′-H), 4.27–4.33 (3 H, m, 3′-H and OCH_2CH$_2$TMS), 4.65–4.72 (3 H, m, 2′-H and CH_2=CHCH_2), 5.04 (1 H, dd, CH_2=$CHCH_2$), 5.20 (1 H, dd, CH_2=$CHCH_2$), 5.89–5.99 (1 H, m, CH_2=CHCH_2), 6.09 (1 H, d, $J_{1',2'}$ 5.3, 1′-H), 8.31 (1 H, s, 2-H) and 8.72 (1 H, s, 8-H); δ_C($CDCl_3$) −5.40, −5.37, −5.13, −4.70, −4.45 (MeSi), 17.81, 18.06, 18.51 [$(CH_3)_3CSi$], 25.60, 25.63, 26.06 [$(CH_3)_3CSi$], 17.54 [$CH_2CH_2Si(CH_3)_3$], 49.92 (CH_2=CHCH_2), 62.64 (C-5′), 64.96 [$CH_2CH_2Si(CH_3)_3$], 72.07 (C-3′), 75.74 (C-2′), 85.69 (C-4′), 88.18 (C-1′), 116.74 (CH_2=$CHCH_2$) 127.85 (C-5), 133.54 (CH_2=$CHCH_2$), 142.68 (C-8), 151.72 (C-4), 152.45 (C-2), 152.86 (C=O) and 154.72 (C-6).

6-*N*-Benzoyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-N^1-methyladenosine 8c (Found: C, 59.5; H, 8.5; N, 9.7. $C_{36}H_{61}N_5O_5Si_3$ requires C, 59.38; H, 8.44; N, 9.62%); δ_H($CDCl_3$) −0.20, −0.03, 0.05, 0.06, 0.08 (3 H, s, MeSi), 0.80, 0.88, 0.91 (9 H, s, Bu^{t}Si), 3.72 (1 H, dd, $J_{4',5'}$ 3.6 and J_{gem} 11.5, 5′-H^a), 3.74 (3 H, s, Me), 3.87 (1 H, dd, $J_{4',5'}$ 4.3 and J_{gem} 11.5, 5′-H^b), 4.06 (1 H, q, J 3.6, $J_{4',5'}$ 4.3, 4′-H), 4.24 (1 H, t, $J_{3',4'}$ 4.0, 3′-H), 4.49 (1 H, t, $J_{2',3'}$ 4.6, 2′-H), 5.89 (1 H, d, $J_{1',2'}$ 5.0, 1′-H), 7.87 (1 H, s, 8-H) and 7.95 (1 H, s, 2-H); δ_C($CDCl_3$) −5.42, −5.34, −4.93, −4.72, −4.67, −4.43 (MeSi), 17.84, 18.04, 18.49 [$(CH_3)_3CSi$], 25.68, 25.82, 26.04 [$(CH_3)_3CSi$], 36.85 (Me), 62.64 (C-5′), 71.91 (C-3′), 75.90 (C-2′), 85.33 (C-4′), 87.99 (C-1′), 122.42 (C-5), 127.94, 129.73, 135.71, 135.93 (Bz), 138.58 (C-8), 145.44 (C-4), 146.52 (C-2), 147.65 (C-6) and 177.07 (C=O).

N^1-Allyl-6-*N*-benzoyl-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-adenosine 10c (Found: C, 60.8; H, 8.4; N, 9.45. $C_{38}H_{58}N_5O_5Si_3$ requires C, 60.60; H, 8.30; N, 9.30%); δ_H($CDCl_3$) −0.20,

−0.03, 0.09, 0.10, 0.11 (3 H, s, MeSi), 0.80, 0.88, 0.91 (9 H, s, Bu^{t}Si), 3.72 (1 H, dd, $J_{4',5'}$ 3.6 and J_{gem} 11.2, 5'-H^a), 3.87 (1 H, dd, $J_{4',5'}$ 4.0 and J_{gem} 11.2, 5'-H^b), 4.08 (1 H, m, 4'-H), 4.24 (1 H, t, $J_{3',4'}$ 4.0, 3'-H), 4.47 (1 H, t, $J_{2',3'}$ 4.6, 2'-H), 4.81–5.38 (4 H, m, CH_2=CHCH_2), 5.90 (1 H, d, $J_{1',2'}$ 5.3, 1'-H), 6.08–6.14 (1 H, m, CH_2=CHCH$_2$), 7.87 (1 H, s, 8-H) and 7.91 (1 H, s, 2-H); δ_C($CDCl_3$) −5.42, −5.33, −4.99, −4.70, −4.63, −4.42 (MeSi), 17.84, 18.01, 18.49 [(CH_3)$_3$CSi], 25.66, 25.28, 26.04 [(CH_3)$_3$CSi], 50.58 (CH_2=CHCH_2), 62.62 (C-5'), 71.87 (C-3'), 75.95 (C-2'), 85.35 (C-4'), 87.97 (C-1'), 118.92 (CH_2=CHCH$_2$), 127.94 (C-5), 128.08, 129.63, 129.73 (Bz), 131.71 (CH_2=CHCH$_2$), 132.00 (C-8), 135.99 (C-4), 138.54 (C-2), 146.27 (C-6) and 170.61 (C=O).

6-*N*-Methyladenosine 14. Compound **5a** (650 mg, 0.924 mmol) was dissolved in THF (10 cm^3) and TBAF·H_2O (942 mg, 3.68 mmol) was added to the solution. After being stirred at room temperature for 10 min, the mixture was evaporated under reduced pressure. The residue was dissolved in methanol (5 cm^3) and the solution was applied to a column of Dowex 50W X8 (pyridinium form, 50 cm^3). The column was eluted with water–pyridine (5:2, v/v; 250 cm^3). The eluate was evaporated under reduced pressure and the residue was chromatographed on a column of silica gel (10 g) with CH_2Cl_2–MeOH (95:5, v/v) to give compound **13** as a syrup (295 mg, 98%). Part (100 mg, 0.307 mmol) of this material was further treated with concentrated ammonia–pyridine (9:1, v/v; 30 cm^3) at 60 °C for 12 h after which the mixture was evaporated under reduced pressure. The residue was dissolved in water (10 cm^3) and the aqueous solution was washed with CH_2Cl_2 (10 cm^3 × 3). The aqueous layer was collected and evaporated under reduced pressure. The residue was dissolved in water (5 cm^3) and the solution was lyophilized to give compound **14** (62 mg, 72%). This compound was identified by comparison of its ^{1}H NMR with that of the authentic sample:[11] δ_H(D_2O) 2.99 (3 H, s, CH_3), 3.80 (1 H, dd, $J_{4',5'}$ 3.3 and J_{gem} 13.0, 5'-H^a), 3.91 (1 H, dd, $J_{4',5'}$ 3.0 and J_{gem} 13.0, 5'-H^b), 4.26 (1 H, q, $J_{4',5'}$ 3.3, $J_{4',5'}$ 3.0, 4'-H), 4.39 (1 H, t, $J_{3',4'}$ 3.9, 3'-H), 4.72 (1 H, t, $J_{2',3'}$ 5.0, 2'-H), 5.96 (1 H, d, $J_{1',2'}$ 5.9, 1'-H), 8.06 (1 H, s, 2-H) and 8.14 (1 H, s, 8-H).

6-*N*-Allyladenosine 15. Compound **6f** (226 mg, 0.285 mmol) was dissolved in THF (28 cm^3) and TBAF·H_2O (446 mg, 1.71 mmol) was added to the solution. After being stirred at room temperature for 1 h, the mixture was evaporated under reduced pressure. The residue was dissolved in water (1 cm^3) and the solution was applied to a column of Dowex 50W X8 (pyridinium form, 40 cm^3). The column was eluted with water (250 cm^3). The elutate was evaporated under reduced pressure and the residue was dissolved in water (5 cm^3). The solution was lyophilized to give compound **15** (92 mg, quant.). This compound was identified by comparison of its ^{1}H NMR with that of the authentic sample.[17] δ_H(D_2O) 3.78 (1 H, dd, $J_{4',5'}$ 2.6 and J_{gem} 12.9, 5'-H^a), 3.87 (1 H, dd, $J_{4',5'}$ 3.6 and J_{gem} 12.9, 5'-H^b), 4.11 (2 H, br s, CH_2CH=CH$_2$), 4.23 (1 H, m, 4'-H), 4.36 (1 H, dd, $J_{2',3'}$ 5.3 and $J_{3',4'}$ 3.3, 3'-H), 5.11–5.22 (2 H, m, C=CH_2), 5.89 and 6.03 (2 H, m, $J_{1',2'}$ 6.3, 1'-H and CH=CH$_2$), 8.11 (1 H, s, 2-H) and 8.21 (1 H, s, 8-H).

Treatment of 6e with zinc. Compound **6e** (73 mg, 0.08 mmol) was dissolved in acetic acid (0.8 cm^3) and zinc powder (26 mg, 0.4 mmol) was added to the solution. The mixture was vigorously stirred for 1 h after which zinc powder (26 mg, 0.4 mmol) was added to it and stirring was continued for an additional 2 h. The mixture was filtered through Celite which was then washed with CH_2Cl_2. The filtrate was evaporated and the residue chromatographed on a column of silica gel to give compound **11** (48 mg, 85%); δ_H($CDCl_3$) −0.21, −0.03, 0.05, 0.07, 0.08 (3 H, s, MeSi), 0.79, 0.88, 0.92 (9 H, s, Bu^{t}Si), 3.77 (1 H, dd, $J_{4',5'}$ 2.2 and J_{gem} 11.3, 5'-H^a), 3.84 (1 H, dd, $J_{4',5'}$ 2.8 and J_{gem} 11.3, 5'-H^b), 4.06 (1 H, q, $J_{4',5'}$ 2.2 and $J_{4',5'}$ 2.8, 4'-H), 4.22 (1 H, t, $J_{3',4'}$ 3.2, 3'-H), 4.45 (1 H, t, $J_{2',3'}$ 4.1, 2'-H), 5.39 (2 H, d, CH_2), 5.89 (1 H, d, $J_{1',2'}$ 5.9, 1'-H), 7.39 (4 H, m, *m,p*-H of Ar), 7.84–7.87 (2 H, m, *o*-H of Ar), 7.86 (1 H, s, 2-H) and 8.03 (1 H, s, 8-H); δ_C($CDCl_3$) −5.38, −5.06, −4.72, −4.41, 17.86, 18.07, 18.51, 24.68, 25.67, 25.84, 26.05, 62.49 (C-5'), 76.93 (C-3'), 75.74 (C-2'), 85.39 (C-4'), 88.32 (C-1'), 120.05 (C-5), 127.43, 127.78, 128.62 (Ph), 138.41, 138.99, 153.11 and 154.55.

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