

Martin J. Wanner and Gerrit-Jan Koomen*

Laboratory of Organic Chemistry, Institute of Molecular Chemistry, University of Amsterdam, Nieuwe Achtergracht 129, NL-1018 WS Amsterdam, Netherlands.
E-mail: gjk@org.chem.uva.nl; Fax: +31-20-5255670

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A series of new 2-substituted adenosine derivatives was synthesised *via* addition and condensation reactions with 2-nitrosoadenosine triacetate **4**. The exceptional reactivity of the adenosine nitroso functionality was demonstrated by reaction with, *e.g.*, dienes (4 + 2 cycloaddition), cyclohexene ('ene' reaction), furans (addition/rearrangement) and with anilines (Mills coupling). 2-Nitrosoadenosine triacetate was prepared from 6-chloropurine riboside triacetate *via* nitration at the 2-position followed by reduction/oxidation of the nitro group. The vulnerable nitroso functionality of **4** had to be protected by 4 + 2 cycloaddition with cyclopentadiene to make deacylation of the ribose ring possible. Retro-Diels–Alder reaction of the deacylated product at 95 °C gave the title compound 2-nitrosoadenosine **7**. Dimerisation of the nitroso functionality of triacetate **4** was studied with ¹H NMR by changing the temperature, concentration and solvent. In particular, variation of temperature gave control over this dimerisation: 100% monomer at 65 °C gave complete dimerisation at –20 °C.

Introduction

The application of purine derivatives in the research areas of *e.g.*, purinergic receptors, cyclin-dependent protein kinase (CDK) inhibitors, antitumour and antiviral compounds has resulted in a large number of synthetic investigations. Besides substitution at the 6-, 8- and 9-position, modification of the 2-position of the purine ring has received much attention. The 2-position is in general substituted by conversion of an amino group, as it is present in guanine or guanosine derivatives, to halogen substituents *via* alkyl nitrite-catalyzed reactions (Fig. 1).^{1–3} Replacement of these halides with, *e.g.*, amines is often sluggish and requires high temperatures. Some recent examples show that substitution with suitable amines using Pd catalysis is effected under milder conditions.^{4,5} An alternative strategy for the introduction of amino substituents on the 2-position of the purine ring is based on nitroso chemistry (Fig. 2). We here report the synthesis of the hitherto unknown, but stable, 2-nitrosoadenosine from the corresponding 2-nitropurine ribosides. The required 2-nitronucleosides were prepared *via* selective nitration of the 2-position of 6-chloropurine triacetate with the nitrating mixture tetrabutylammonium nitrate and trifluoroacetic anhydride (TBAN–TFAA) as we described recently.^{6,7} The reactivity, dimerisation and in particular the conversion of 2-nitrosoadenosine triacetate to a number of new 2-substituted adenosine derivatives *via* addition and condensation reactions will be discussed in this paper.

Results and discussion

Synthesis

2-Nitrosoadenosine triacetate. Aromatic nitroso compounds are most conveniently prepared from the corresponding nitro derivatives in a 2-step reduction–oxidation process.^{8,9} This reduction–oxidation route towards nitroso compounds is precluded for most electron-deficient heterocycles since electrophilic nitration of these heterocycles to the required nitro compounds is not possible. To circumvent the nitration of pyridines an oxidative sequence was developed to obtain 2- and 3-nitrosopyridines from the corresponding amines.¹⁰ Since purines substituted with a nitro group at the 2-position are now

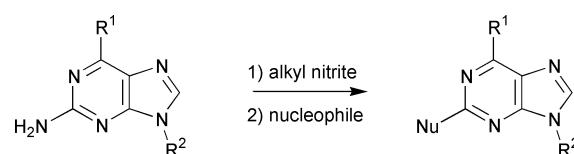


Fig. 1 Substitution of the guanosine C-2 position.

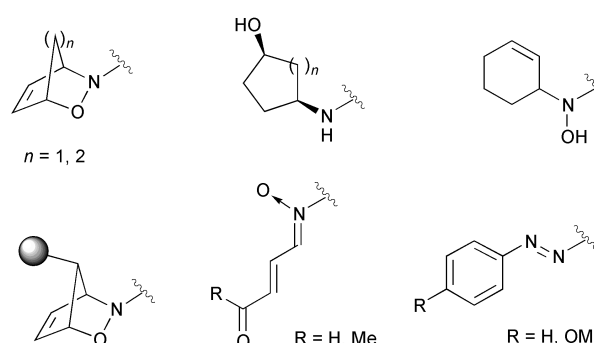
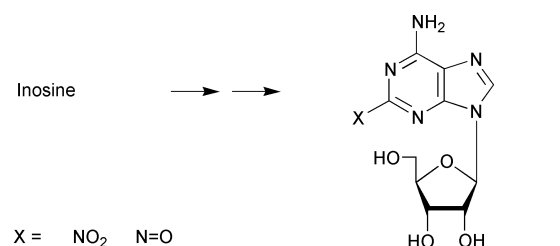


Fig. 2 Substitution of the purine C-2 position based on nitroso chemistry.

readily available *via* TBAN–TFAA nitration^{6,7} we examined the redox conversion of 2-nitro- to 2-nitrosopurines.

TBAN–TFAA nitration of triacetyl-protected 6-chloropurine riboside took place exclusively at the 2-position, as was shown by long-range correlation NMR experiments performed with **1** (Scheme 1).⁶ The highly reactive chloride **1** was converted to the corresponding azide **2** with one equivalent of sodium

Table 1 ^1H NMR dimerisation studies with 2-nitrosoadenosine triacetate **4**. The ratio monomer–dimer is based on the integral of 8-H at δ 8.2 and 8.3, respectively

(a) Concentration effects ^a			
Entry	Conc. ^b	Monomer	Dimer
1	0.5	63	37
2	2.0	38	62
3	5.0	25	75
(b) Solvent effects ^c			
Entry	Solvent	Monomer	Dimer
4	CDCl_3	32	68
5	CD_3OD	21	79
6	$\text{d}_6\text{-DMSO-D}_2\text{O}$ 4 : 1	14	86
7	$\text{d}_6\text{-DMSO-D}_2\text{O}$ 2 : 1	7	93
(c) Temperature effects ^c			
Entry	Temp. ($\theta/^\circ\text{C}$)	Monomer	Dimer
8	67 ^d	100	0
9	-20 ^e	0	100

^a In $\text{d}_6\text{-DMSO}$ at 27 °C. ^b In mg per 0.5 mL. ^c At 2 mg/0.5 mL, 27 °C. ^d In $\text{d}_6\text{-DMSO}$. ^e In CDCl_3 .

demonstrated by ^1H NMR. When a solution of **12** (single isomer) was kept at rt for 40 h in DMSO (1 mg in 0.5 mL), a 60 : 40 mixture of isomers had formed. At 50 °C complete equilibration to a 50 : 50 mixture already occurred within a few minutes, but now also small amounts of the precursors, cyclopentadiene and 2-nitrosoadenosine **7**, were observed. At still higher temperatures (100 °C) the formation of the Diels–Alder precursors was almost complete. Upon cooling to rt the 50 : 50 mixture of cycloaddition products **12** was reproduced in high yield.

To drive the retro-Diels–Alder reaction of **12** to completion in a synthetically useful procedure, it was essential to remove the cyclopentadiene from the reaction mixture. Initially we used dienophiles (e.g., maleimide) to trap the diene, but the C6-amino substituent appeared to react with these reagents. Satisfactory conversion was accomplished by heating cycloadduct **12** in DMF at 95 °C, under a vigorous stream of nitrogen gas. Crystalline 2-nitrosoadenosine **7** was obtained in this way in 58% yield. This compound was stable enough for biological investigations, but for reasons of availability and solubility we preferred to examine the reactivity of the nitroso substituent with the triacetyl-protected derivative **4**.

Properties of 2-nitrosoadenosine triacetate **4**

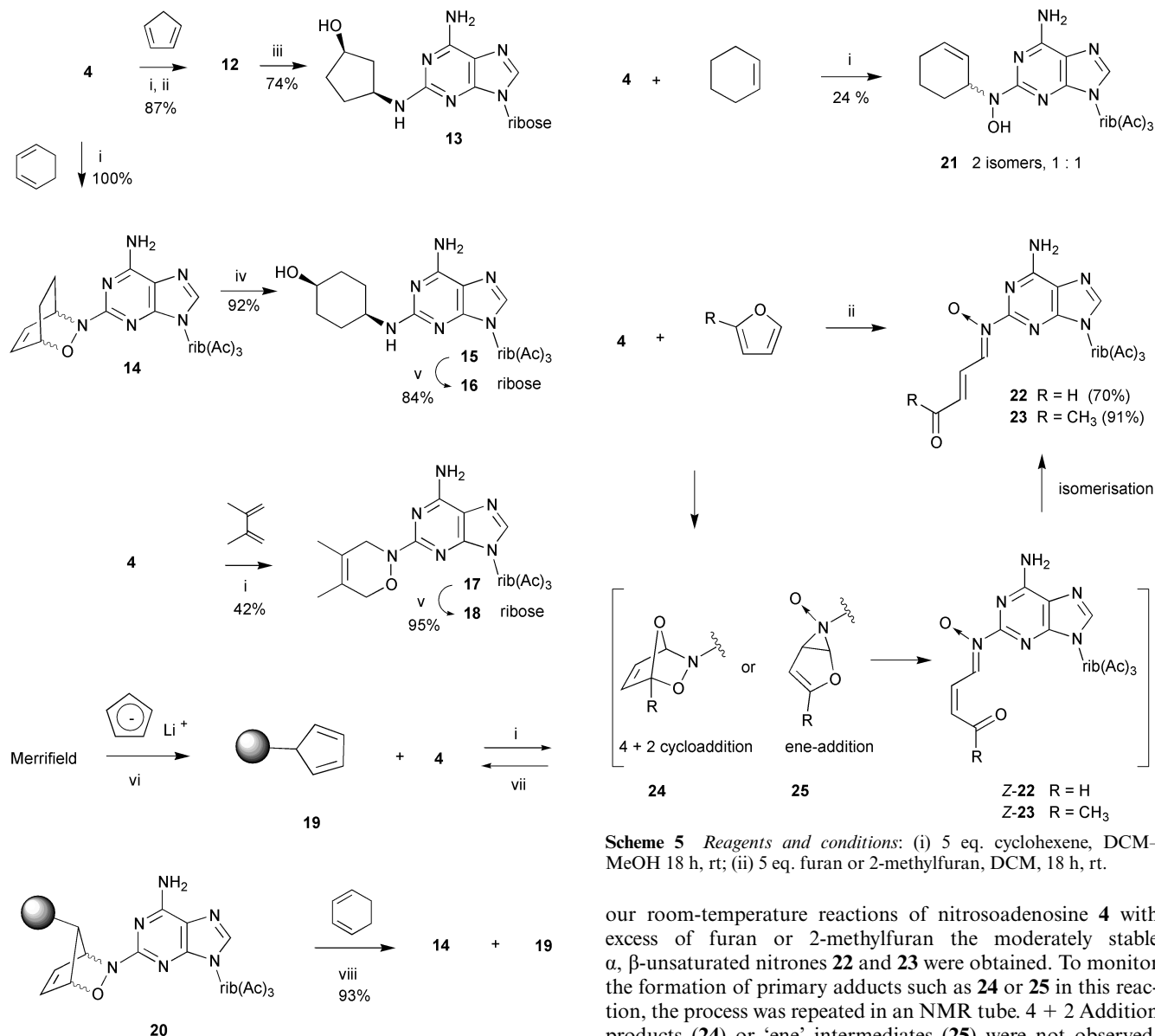
Dimerisation studies. Aromatic nitroso compounds show a strong tendency to form azodioxy dimers in a reversible process.^{17,18} The amount of dimerisation in solution not only depends on the presence of substituents on the aromatic system but also on concentration, temperature and solvent. The influence of those variables on the dimerisation of **4** to **5** (Scheme 1) was studied using ^1H NMR spectroscopy. As can be seen from Table 1, the monomer–dimer equilibrium of **4** is concentration dependent, as expected. Probably the amount of monomer will reach 100% at higher dilution, but NMR does not allow us to measure this. Replacement of CDCl_3 for $\text{d}_6\text{-DMSO}$ did not influence the equilibrium significantly, but a pronounced shift was observed when mixtures of DMSO with deuterium oxide were used. Hydrogen-bond stabilisation of the polar dimer probably plays a role here. This effect was also demonstrated

with nitrosobenzene, which is known to be completely in its monomeric form in organic solvents. When we dissolved nitrosobenzene in a 1 : 1 mixture of $\text{d}_6\text{-DMSO}$ and deuterium oxide (1 mg in 0.5 mL), formation of 21% of the dimer was observed.

Changing the temperature had the strongest effect on the equilibrium between **4** and **5**: after increasing the temperature to 65 °C in $\text{d}_6\text{-DMSO}$, the equilibrium shifted completely to the monomer. On the other hand, when a solution of **4** in CDCl_3 was cooled to -20 °C, only the dimer was present. In all examples only one of the *Z/E* isomers of dimer **5** was detected in the ^1H NMR spectra (>98%). In general, when no *ortho*-substituents are present in the aromatic ring, the *Z*-dimer is preferred in solution. The same tendency towards the formation of *Z*-dimers was observed for 2-nitrosopyridines.¹⁸ In analogy with these data, and in view of the absence of even hydrogen substituents in both *ortho* positions, the azodioxy dimer **5** of 2-nitrosoadenosine triacetate **4** in solution was assumed to be the *Z*-form.

Diels–Alder reactions. Two more dienes were used for cycloaddition with nitrosoadenosine **4** (Scheme 4). Cyclohexa-1,3-diene reacted rapidly and quantitatively to give adduct **14** in the same 50 : 50 ratio of diastereomers as was observed with cyclopentadiene. The acyclic diene 2,3-dimethylbuta-1,3-diene reacted less cleanly to give **17**. Lower abundance of the *s-cis* form in dimethylbutadiene compared with the cyclic dienes probably favour ene-type side reactions. Hydrogenation converted the cycloadducts to the corresponding cyclopentyl and cyclohexylamines. From crystalline cyclopentadiene isomer **12**, obtained as described in Scheme 3, the *cis*-3-aminocyclopentanol **13** (single isomer) was obtained. The absolute configuration of the cyclopentane part of the molecule was not determined. Hydrogenation of **14** and subsequent removal of the acetates produced the symmetrical *cis*-substituted 4-aminocyclohexanol **16**. In **17** both the tetra substituted double bond and the N–O bond resisted hydrogenation, so except for deacetylation of the ribose ring to **18**, cycloadduct **17** was not subjected to further transformations.

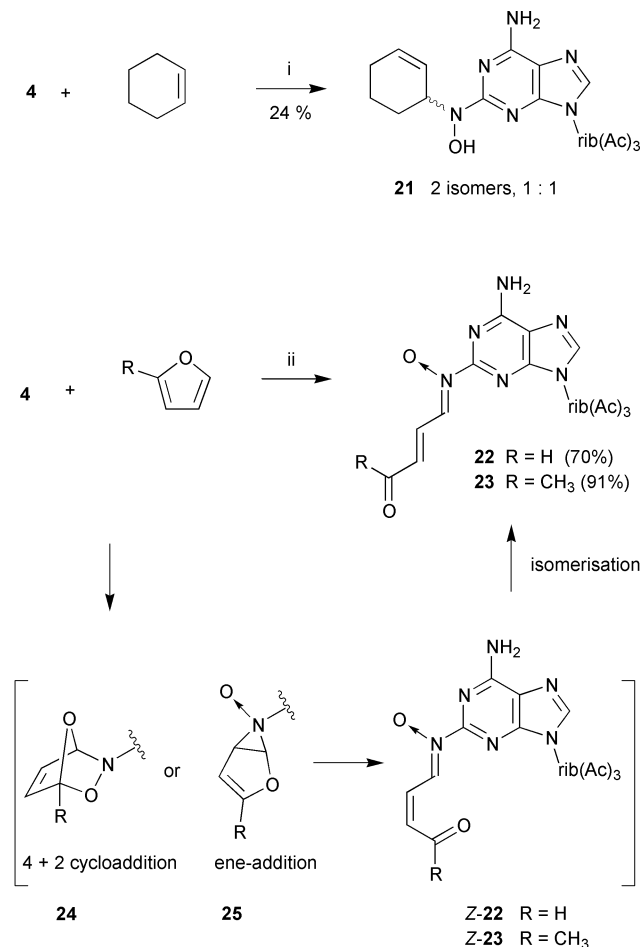
An additional example of the versatility of this cycloaddition was obtained from a solid-phase reaction of **4** with resin-bound cyclopentadiene (Scheme 4). In the synthesis of **7** (Scheme 3) removal of cyclopentadiene with a N_2 -stream in the retro-Diels–Alder process is the limiting step. If resin-bound cyclopentadiene is used, filtration of a hot Diels–Alder equilibration mixture will be sufficient to remove the cyclopentadiene. Immobilised cyclopentadiene **19** was prepared by the coupling of Merrifield resin with cyclopentadienyl lithium. Although **19** and **20** are depicted as 5-substituted cyclopentadienes in Scheme 4, it should be noted that (base-catalysed) 1,5-hydrogen shifts can also give the 1- and 2-substituted cyclopentadiene isomers. When a solution of **4** in DCM was stirred with resin **19** at rt, the yellow colour of the nitroso compound disappeared and within a few minutes complete cycloaddition to **20** had occurred. The retro-Diels–Alder of **20** in hot DMF could easily be monitored by the development of the yellow colour of the nitroso compound, allowing easy recovery of **4** by filtration and evaporation. The retro-Diels–Alder reaction of **20** in the presence of cyclohexadiene was very efficient, and produced **14** in almost quantitative yield. Although resin-bound cycloadduct **20** was prepared to allow us to obtain unprotected 2-nitrosoadenosine **7**, we have not been successful in removal of the ribose acetates from **20** without destroying the compound. Immobilised cyclopentadiene **19** has potential applications in handling other reactive nitroso compounds such as nitrosyl cyanide^{12,19} or *N*-acylnitroso derivatives.^{14,20} Often these unstable compounds are captured as cycloadducts with 9,10-dimethylanthracene that can be used as latent sources of the nitroso compound.



Scheme 4 Reagents and conditions: (i) DCM, rt, 30 min; (ii) KCN, MeOH, rt; (iii) H₂, 10% Pd/C, EtOH, water; (iv) H₂, 10% Pd/C, EtOH, EtOAc; (v) NH₃, MeOH; (vi) DMF, rt; (vii) DMF, filtration at 95 °C; (viii) 2 eq. cyclohexa-1,3-diene, DMF, 90 °C, 30 min.

Ene reaction with cyclohexene. Ene reactions with nitroso compounds are limited to reactive derivatives such as nitroso-carbonyl compounds,²¹ *p*-nitro nitrosobenzene²² or pentafluoronitrosobenzene.²³ Also, **4** showed reactivity and with excess of cyclohexadiene the anticipated hydroxylamine **21** was formed in moderate yield, as a 1 : 1 mixture of diastereomers (Scheme 5). This reaction probably proceeds *via* an aziridine *N*-oxide intermediate, followed by hydrogen abstraction.²¹ An aziridine *N*-oxide is also suggested as one of the possible intermediates in the rearrangement described in the next paragraph [structure **25** (Scheme 5)].

Addition reactions with furans. Rather unexpected were the addition reactions of **4** with furan and 2-methylfuran (Scheme 5). Only a few reactions of nitroso compounds with furans are known in the literature. *N*-Aclylnitroso compounds react in general in a 4 + 2 fashion with the furan system, but in this example the furan ring acts as the dienophile.²⁴ An intramolecular addition process of a nitrosoarene to the 2- and 5-position of the furan ring has been reported,²⁵ but the actual cycloadducts were never observed and merely rearranged, and ring-opened products were isolated. From

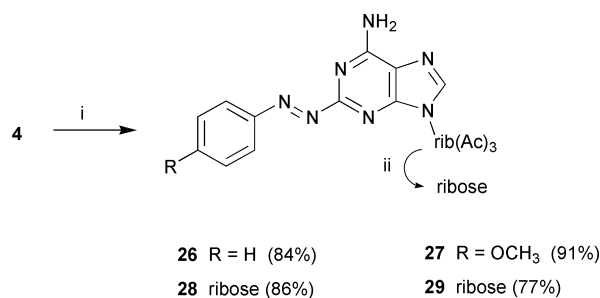


Scheme 5 Reagents and conditions: (i) 5 eq. cyclohexene, DCM–MeOH 18 h, rt; (ii) 5 eq. furan or 2-methylfuran, DCM, 18 h, rt.

our room-temperature reactions of nitrosoadenosine **4** with excess of furan or 2-methylfuran the moderately stable α , β -unsaturated nitrones **22** and **23** were obtained. To monitor the formation of primary adducts such as **24** or **25** in this reaction, the process was repeated in an NMR tube. 4 + 2 Addition products (**24**) or ‘ene’ intermediates (**25**) were not observed, however. From this NMR experiment we obtained an explanation for the *E*-geometry of the double bond in **22** and **23** (J = 16.1 and 16.3 Hz respectively). The originally formed *Z*-alkenes *Z*-**22** and *Z*-**23** (J = 11.6 Hz) were observed but completely isomerised to the *E*-alkenes *E*-**22** and *E*-**23** during the reaction.

Mills coupling with aniline. 2-Phenyldiazo-substituted purine nucleosides such as **28** and **29** (Scheme 6) have not been reported before in the literature. Classical diazonium coupling with phenyldiazonium salts cannot be used since the purine 2-position is not suitable for electrophilic substitution. The alternative route *via* 2-diazonium purines is also impossible since these compounds, as most heterocyclic diazonium salts, are not stable.

Mills coupling between nitrosoaromatics and anilines is a complementary method for the preparation of azo compounds.²⁶ Acetic acid-catalyzed condensation of **4** with 2 eq. of aniline or *p*-anisidine produced the expected diazo compounds **26** and **27** in 84 and 91% yield, respectively. After deprotection with aq. ammonia in methanol the orange coloured *E*-form of 2-phenylazoadenosine **28** and 2-(4-methoxyphenylazo)-adenosine **29** were obtained. When quickly dissolved in D₂O, the ¹H NMR spectrum of **28** showed only the *E*-form; however, during storage in daylight *E*-**28** was transformed into a mixture of *Z* and *E* isomers. After storage for *ca.* 6 h a photo-stationary phase was reached with *Z* : *E* = 41 : 59. Irradiation of this D₂O



isomerisation of **28**

	Z	E
solid state	0	100
daylight (D ₂ O)	41	59
350 nm (D ₂ O)	79	21

Scheme 6 Reagents and conditions: (i) ArNH₂, CH₃CN–HOAc 5 : 1; rt, 5 h; (ii) NH₃, MeOH.

sample at 350 nm produced predominantly the *Z*-isomer (*Z* : *E* = 79 : 21) and this mixture returned to the stationary state of 41 : 59 after 4–6 h in daylight.

Conclusions

In summary, 2-nitrosoadenosine, and in particular its triacetate, are made readily available from inosine and are presented as versatile precursors for a large number of new, 2-substituted adenosine derivatives. Biological applications of 2-nitrosoadenosine and its derivatives will be described elsewhere.

Experimental

General

All reagents and solvents were used as commercially available, unless indicated otherwise. Flash chromatography refers to purification using the indicated eluents and Janssen Chimica silica gel 60 (0.030–0.075 mm). Mps were measured with a Leitz melting point microscope and are uncorrected. Elemental analyses were performed by Kolbe, Mülheim a. d. Ruhr, Germany. IR spectra were obtained from CHCl₃ solutions unless indicated otherwise, using a Bruker IFS 28 FT-spectrophotometer, and wavenumbers are reported in cm⁻¹. Proton nuclear magnetic resonance (¹H NMR) spectra and carbon nuclear magnetic resonance (¹³C NMR; APT) spectra were determined in CDCl₃ at 300 K using a Bruker ARX 400 (400 MHz, 100 MHz respectively) spectrometer, unless indicated otherwise. *J*-values are given in Hz. Mass spectra and accurate mass measurements were performed on a JEOL JMS-SX/SX 102 A Tandem Mass Spectrometer using Fast Atom Bombardment (FAB) or Electron Impact (EI). A resolving power of 10 000 (10% valley definition) for high-resolution electron impact or FAB mass spectrometry was used.

6-Chloro-2-nitro-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-9*H*-purine **6** ¹

In the synthesis of 6-chloro-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-9*H*-purine ^{27,28} the work-up of the chlorination reaction was slightly modified: the residue obtained after evaporation of the POCl₃ was poured into a stirred mixture of ice and water. This reversed quenching procedure gave the quantitative yield the authors claimed.

A nitrating mixture was prepared at 0 °C by adding TFAA (6.34 mL, 45 mmol) to a solution of tetrabutylammonium nitrate (TBAN, 13.7 g, 45 mmol) in dry DCM (75 mL) during *ca.* 2 min. After being stirred for 10 min this solution was added *via* syringe to an ice-cold solution of 6-chloro-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-9*H*-purine (12.39 g, 30 mmol) in

DCM (75 mL). The reaction was quenched after 3 h at 0 °C by pouring the reaction mixture into a stirred mixture of saturated aq. NaHCO₃ (200 mL), water (200 mL) and diethyl ether (*ca.* 250 mL). The water layer was extracted with a 2 : 1 mixture of diethyl ether and DCM, the combined organic layers were washed successively with dilute aq. NaHCO₃ (2 × 30 mL) and water (30 mL), and dried over Na₂SO₄ (sometimes crystallisation of the product occurs during the extraction procedure). The pale yellow product was obtained by trituration with methanol (9.75 g, 71%). An analytical sample was obtained by recrystallisation from EtOAc, mp 170–172 °C (Found: C, 42.02; H, 3.46; N, 15.22. Calc. for C₁₆H₁₆ClN₅O₉: C, 41.98; H, 3.52; N, 15.30%); $\nu_{\max}/\text{cm}^{-1}$ (KBr) 3131, 1771, 1745, 1734, 1589, 1560 and 1331; δ_{H} 8.58 (1H, s, 8-H), 6.30 (1H, d, *J* 5.3, 1'-H), 5.76 (1H, dd, *J* 5.3 and 5.3, 2'-H), 5.57 (1H, m, 3'-H), 4.52 (1H, m, 4'-H), 4.44 (2H, m, 5'-H₂), 2.16, 2.09 and 2.06 (all 3H, s, acetates); δ_{C} 170.0, 169.4, 169.4, 153.1, 152.7, 151.3, 147.0, 134.8, 87.13, 81.16, 73.53, 70.53, 62.82, 20.56, 20.35 and 20.14; *m/z* (FAB⁺) 458 (7%), 259 (100) and 242 (31) (Found: M⁺ + 1, 458.0712. C₁₆H₁₇ClN₅O₉ requires *m/z* 458.0719).

6-Azido-2-nitro-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-9*H*-purine **2**

Sodium azide (0.65 g, 10 mmol) was added to a solution of **6** (4.58 g, 10 mmol) in DMF (40 mL) at –18 °C (bath temperature). After stirring for 1 h at this temperature, stirring was continued at 0 °C for 2 h. Water (40 mL) was slowly added, resulting in crystallisation of the product. The mixture was kept for 4 h at 0 °C and filtered. The azide was washed with water (3 times) and with 1 : 1 water–methanol (3 times) and dried *in vacuo* (P₂O₅) (4.26 g, 92%). A pure sample was obtained by recrystallisation from EtOAc, mp 164–166 °C (Found: C, 41.48; H, 3.49; N, 24.02. C₁₆H₁₆N₈O₉ requires C, 41.39; H, 3.47; N, 24.13%); $\nu_{\max}/\text{cm}^{-1}$ (KBr) 2165, 2143, 1746, 1602, 1557 and 1435; δ_{H} 8.39 (1H, s, 8-H), 6.28 (1H, d, *J* 5.5, 1'-H), 5.76 (1H, dd, *J* 5.3 and 5.3, 2'-H), 5.58 (1H, m, 3'-H), 4.52 (1H, m, 4'-H), 4.46 (2H, m, 5'-H₂), 2.16, 2.12 and 2.09 (all 3H, s, acetates); δ_{C} 170.4, 169.8, 169.4, 155.0, 153.9, 152.2, 145.0, 127.1, 87.3, 81.7, 73.5, 71.4, 63.2, 20.6, 20.4 and 20.2; *m/z* (FAB⁺) 456 (M⁺ + 1, 3%) and 259 (100) (Found: M⁺ + 1, 456.1089. C₁₆H₁₇N₈O₉ requires *m/z*, 456.1088).

2',3',5'-Tri-*O*-acetyl-2-nitrosoadenosine **4** and its dimer **5**

A suspension of **2** (1.39 g, 3 mmol) and Pd/C (10%; 0.150 g) in a mixture of EtOAc (50 mL) and EtOH (25 mL) was stirred at 45–50 °C (bath temperature) under hydrogen (1 atm). After 3 h the catalyst was removed by filtration and the mixture was evaporated to leave a glass. The resulting 2',3',5'-tri-*O*-acetyl-2-(hydroxyamino)adenosine **3** was used in the next step without purification, δ_{H} 9.2 (1H, br, NHOH), 8.4 (1H, br, NHOH), 7.71 (1H, s, 8-H), 6.45 (2H, br, NH₂), 6.06 (1H, d, *J* 4.1, 1'-H), 5.98 (1H, dd, *J* 4.1 and 5.3, 2'-H), 5.78 (1H, m, 3'-H), 4.39 (3H, m, 4'-H, 5'-H₂), 2.10, 2.05, 2.02 (all 3H, s, acetates).

To a vigorously stirred solution of crude compound **3** (3 mmol) in EtOAc (50 mL) at 0 °C was added an ice-cold solution of sodium periodate (0.77 g, 3.6 mmol) in 30 mL of water. After 15 min the mixture was warmed to room temperature and stirring was continued for 1 h. The precipitated product was dissolved by adding methanol and additional EtOAc. The layers were separated and the organic layer was dried (Na₂SO₄) and the solvent evaporated off. Trituration with methanol and cooling in ice produced pure **4** (0.792 g, 63% from **2**) as a yellow solid, mp 158–159 °C (Found: C, 45.36; H, 4.41; N, 19.82. C₁₆H₁₈N₆O₈ requires C, 45.50; H, 4.30; N, 19.90%); λ_{\max}/nm (1,4-dioxane) 248, 371; $\nu_{\max}/\text{cm}^{-1}$ (KBr) 1750, 1641, 1600, 1483, 1371 and 1329; δ_{H} (monomer **4**, obtained from mixtures with its dimer **5**) 8.28 (1H, s, 8-H), 6.5–6.9 (2H, br, NH₂), 6.43 (1H, d, *J* 5.6, 1'-H), 5.89 (1H, t, *J* 5.6, 2'-H), 5.69 (1H, dd, *J* 5.3 and 5.6, 3'-H), 4.6–4.4 (3H, m, 4'-H and 5'-H₂),

2.19, 2.14 and 2.09 (all 3H, s, acetates); δ_{H} (dimer **5**, obtained from mixtures with its monomer **4**) 8.08 (1H, s, 8-H), 6.34 (1H, d, J 6.5, 1'-H), 6.04 (2H, br s, NH₂), 5.58 (1H, dd, J 5.8 and 6.5, 2'-H), 5.45 (1H, dd, J 2.4 and 5.8, 3'-H), 4.6–4.4 (3H, m, 4'-H and 5'-H₂), 2.22, 2.17 and 2.14 (all 3H, s, acetates).

2-(Hydroxyamino)adenosine 6

Aq. ammonia (25%; 3 mL) was added to a solution of **3** (0.20 g, 0.47 mmol) in methanol (3 mL) and the resulting solution was stirred at rt for 16 h. The mixture was evaporated and the residue was coevaporated twice with ethanol. Trituration with a small amount of ethanol produced **6** (0.114 g, 81%) as a solid, mp 185–195 °C; δ_{H} (d₆-DMSO) 8.56 (1H, br, NHOH), 8.27 (1H, br, NHOH), 8.03 (1H, s, 2-H), 6.96 (2H, br, NH₂), 5.80 (1H, d, J 6.8, 1'-H), 5.39 (1H, d, J 6.1, OH), 5.20 (1H, d, J 5.0, OH), 5.14 (1H, d, J 5.6, OH), 4.59 (1H, dd, J 6.8 and 5.3, 2'-H), 4.18 (1H, m, 3'-H), 3.98 (1H, m, 4'-H), 3.60 (2H, m, 5'-H₂); δ_{C} (d₆-DMSO) 162.8, 156.2, 155.9, 151.0, 137.1, 114.8, 86.9, 85.7, 73.2, 70.8 and 64.9; m/z (FAB⁺) 299 (M⁺ + 1, 22%), 217 (62), 154 (100) and 136 (87) (Found: M⁺ + 1, 299.1103). C₁₀H₁₅N₆O₅ requires m/z 299.1104).

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-2-nitroadenosine 9

A solution of 2-nitroadenosine **8** (0.106 g, 0.5 mmol), TBDMS-Cl (0.377 g, 2.5 mmol) and imidazole (0.198 g, 3.0 mmol) in DMF (3 mL) was stirred for 42 h at room temperature. Extractive work-up using water and diethyl ether followed by trituration with methanol produced **9** (0.271 g, 83%); mp 92–96 °C; $\nu_{\text{max}}/\text{cm}^{-1}$ (KBr) 1490, 1345; δ_{H} 8.45 (s, 1H, 8-H), 7.39 (br, s, 2H, NH₂), 5.99 (d, 1H, J 4.2, H-1'), 4.66 (dd, 1H, J 4.2, 4.3, 2'-H), 4.33 (m, 1H, 3'-H), 4.18 (m, 1H, 4'-H), 4.15 (m, 1H, 5'-H^a), 3.83 (m, 1H, 5'-H^b), 0.15, 0.14, 0.09, 0.08, 0.01, -0.10 (6 s, SiCH₃); δ_{C} 152.4, 152.1, 151.1, 148.0, 134.8, 89.6, 85.6, 76.2, 71.1, 61.8, 25.7, 25.4, 18.4, 17.9, -4.10, -4.58, -4.59, -4.76, -5.13 and -5.28.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-2-nitrosoadenosine 10

A mixture of **9** (0.171 g, 0.261 mmol) and 10% Pd/C (10 mg) in EtOAc (10 mL) was stirred at 45–50 °C (bath temperature) under hydrogen (1 atm). After 3 h the catalyst was removed by filtration and the resulting solution was cooled to 0 °C. An ice-cold solution of sodium periodate (0.075 g, 0.35 mmol) in 30 mL of water was added and the mixture was stirred vigorously for 30 min. Separation of the layers, drying of the organic layer (Na₂SO₄), and trituration of the residue obtained after evaporation produced **10** (0.116 g, 69%) as a yellow solid: mp >180 °C (decomp.); δ_{H} (mixture of monomer and dimer, selected signals): 8.61 (s, 1H, 8-H monomer), 8.31 (s, 1H, 8-H dimer), 6.32 (d, J 4.3, 1'-H monomer), 5.72 (d, J 4.1, 1'-H dimer).

2',3',5'-Tri-*O*-acetyl-2-(2-oxa-3-azabicyclo[2.2.1]hept-5-en-3-yl)adenosine 11

Cyclopentadiene (30 μL , 0.5 mmol) was added to a suspension of **4** (0.085 g, 0.2 mmol) in DCM (2 mL). After stirring of the mixture for 30 min the volatiles were removed by evaporation, yielding pure **11** (quantitative) as a glass (inseparable 1 : 1 mixture of isomers). The ¹H NMR spectrum could not be resolved except for the signals for 8-H, δ_{H} 7.70 and 7.64; δ_{C} 170.5, 170.4, 169.5, 169.42, 169.4, 169.3, 162.7, 155.7, 155.6, 150.3, 150.2, 136.0, 135.4, 133.2, 132.9, 116.2, 116.0, 87.39, 86.82, 83.39, 83.37, 79.50, 79.48, 73.10, 72.85, 70.19, 70.17, 65.93, 65.92, 63.15, 62.70, 48.16, 48.02, 20.62, 20.55, 20.43, 20.39 and 20.38.

2-(2-Oxa-3-azabicyclo[2.2.1]hept-5-en-3-yl)adenosine 12

Direct preparation *via* **11**: a suspension of **4** (0.844 g, 2.0 mmol) in methanol (25 mL) was stirred with cyclopentadiene (0.248 mL, 3 mmol) for 1 h until a clear solution of **11** (1 : 1 mixture of

isomers) was obtained. KCN (26 mg, 0.40 mmol) was added and after *ca.* 1 h crystallisation started. This KCN-catalysed deprotection was in general complete after 6 h, but filtration of the product at this stage of the reaction gave much lower yields of the crystalline isomer and the filtrate consisted mainly of the second isomer. When stirring was continued for 48 h **12** was obtained as a single isomer by filtration (0.633 g, 87%), mp >200 °C (decomp.) (Found: C, 49.66; H, 4.95; N, 23.08. C₁₅H₁₈N₆O₅ requires C, 49.72; H, 5.01; N, 23.19%); δ_{H} (d₆-DMSO) 8.09 (1H, s, 8-H), 7.16 (2H, s, NH₂), 6.36 (1H, m, 5''-H or 6''-H), 6.24 (1H, m, 6''-H or 5''-H), 5.76 (1H, d, J 5.6, 1'-H), 5.40 (1H, d, J 6.2, 2'-OH), 5.36 (1H, m, 1''-H or 4''-H), 5.20 (1H, m, 4''-H or 1''-H), 5.15 (1H, d, J 4.5, 3'-OH), 5.02 (1H, dd, J 7.0 and 4.8, 5'-OH), 4.67 (1H, m, 2'-H), 4.17 (1H, m, 3'-H), 3.93 (1H, m, 4'-H), 3.64 (1H, m, 5'-H^a), 3.55 (1H, m, 5'-H^b), 1.93 (1H, d, J 8.3, 7''-H^a), 1.71 (1H, d, J 8.3, 7''-H^b); m/z (FAB⁺) 363 (M⁺ + 1, 4%), 307 (33), 289 (27), 154 (100) and 136 (96) (Found: M⁺ + 1, 363.1413). C₁₅H₁₉N₆O₅ requires m/z , 363.1317).

When this NMR sample was heated for a short time at 50 °C complete isomerisation occurred and a 1 : 1 mixture of two isomers **12** was formed. From the second isomer only two proton signals were observed separately at 500 MHz (d₆-DMSO): δ_{H} 5.06 (1H, m, 5'-OH) and 4.61 (1H, m, 2'-H).

2-Nitrosoadenosine 7

A vigorous stream of N₂ was led through a solution of **12** (0.2 g, 0.55 mmol) in anhydrous DMF (8 mL) at 95 °C (bath temperature). After 15 min the solvent was evaporated off and the residue was crystallised from water (*ca.* 3 mL) to give **7** (0.072 g) as a yellow crystalline solid. The filtrate was evaporated, and the residue was thermolyzed in DMF (3 mL) as described before to give a combined yield of 0.094 mg of *title compound* **7** (58%), mp >250 °C (decomp.) (Found: C, 40.40; H, 4.10; N, 28.21. C₁₀H₁₂N₆O₅ requires C, 40.54; H, 4.08; N, 28.37%); $\lambda_{\text{max}}/\text{nm}$ (H₂O) 247, 311, 400; $\nu_{\text{max}}/\text{cm}^{-1}$ (KBr) 1655, 1597, 1492, 1365 and 1330; δ_{H} monomer (d₆-DMSO; 70 °C, 1 mg in 0.6 mL; monomer : dimer = 1 : 1) 8.68 (1H, s, 2-H), 7.7 (2H, s, NH₂), 6.05 (1H, d, J 5.6, 1'-H), 5.33 (1H, d, J 5.6, OH), 4.99 (1H, m, OH), 4.87 (1H, m, OH), 4.67 (1H, m, 2'-H), 4.24 (1H, m, 3'-H), 4.02 (1H, m, 4'-H), 3.62–3.75 (2H, m, 5'-H₂); δ_{H} dimer 8.43 (1H, s, 8-H), 7.8 (2H, br, NH₂), 5.64 (1H, d, J 5.6, 1'-H), 5.54 (1H, d, J 6.1, OH), 5.17 (1H, m, OH), 5.10 (1H, m, OH), 4.32 (1H, m, 2'-H), 4.09 (1H, m, 3'-H), 3.88 (1H, m, 4'-H), 3.65–3.55 (2H, m, 5'-H₂); distinct ¹³C NMR spectra of **4** or **5** could not be obtained; with FAB techniques the M⁺ or M⁺ + 1 ion could not be detected.

2-(*cis*-3-Hydroxycyclopentylamino)adenosine 13

A suspension of **12** (0.048 g, 0.13 mmol) and 10% Pd/C (10 mg) in a mixture of ethanol (3 mL) and water (2 mL) was stirred under 1 atm hydrogen for 24 h. Chromatography on silica, and elution with EtOAc–MeOH 4 : 1, gave **13** (0.035 g, 74%) as a white solid, mp 131–151 °C; δ_{H} (d₆-DMSO) 7.90 (1H, s, 8-H), 6.72 (2H, s, NH₂), 6.01 (1H, d, J 8.2, NH), 5.72 (1H, d, J 6.0, 1'-H), 5.37 (1H, br, OH), 5.13 (1H, br, OH), 4.64 (1H, m, 2'-H), 4.60 (1H, br, OH), 4.21 (1H, br, OH), 4.13 (2H, m), 3.90 (1H, m, 4'-H), 3.5–3.7 (2H, m, 5'-H₂), 2.10 (1H, m), 1.90 (1H, m), 1.65–1.75 (3H, m), 1.44 (1H, m); m/z (FAB⁺) 367 (M⁺ + 1, 55%), 235 (25), 154 (100) and 136 (96) (Found: M⁺ + 1, 367.1735). C₁₅H₂₃N₆O₅ requires m/z , 367.1722).

2',3',5'-Tri-*O*-acetyl-2-(*cis*-4-hydroxycyclohexylamino)adenosine 15

Cyclohexa-1,3-diene (19 μL , 0.2 mmol) was added to a suspension of **4** (0.042 g, 0.1 mmol) in DCM (2 mL). After stirring of the mixture for 30 min the volatiles were removed by evaporation, leaving pure 2',3',5'-tri-*O*-acetyl-2-(2-oxa-3-azabicyclo-

[2.2.2]oct-5-en-3-yl)adenosine **14** (quantitative) as a glass (inseparable 1 : 1 mixture of isomers). The ^1H NMR spectrum of this mixture could not be resolved except for the signals for 8-H: δ_{H} 7.67 and 7.62; δ_{C} 170.4, 170.3, 169.4, 169.33, 169.3, 169.25, 162.8, 162.6, 155.7, 155.6, 150.4, 150.2, 132.8, 132.3, 131.6, 131.3, 126.2, 124.1, 115.9, 115.7, 87.30, 86.98, 79.47, 73.11, 72.86, 70.37, 70.14, 70.08, 63.06, 62.76, 51.06, 50.99, 24.05, 23.96, 21.89, 20.56, 20.51, 20.45, 20.39 and 20.34.

A suspension of **14** (50 mg, 0.1 mmol) and 10% Pd/C (10 mg) in a mixture of ethanol (2 mL) and EtOAc (2 mL) was stirred under 1 atm hydrogen for 16 h. Filtration and evaporation of the mixture gave pure **15** (0.046 mg, 92%) as a glass: δ_{H} 7.58 (1H, s, 8-H), 5.9–6.2 (2H, br, NH₂), 6.06 (1H, m), 5.88 (1H, m), 5.73 (1H, m), 5.5 (1H, br, N-H), 4.42 (1H, m, 5'-H^a), 4.35 (1H, m, 4'-H), 4.25 (1H, m, 5'-H^b), 2.09, 2.07 and 2.02 (all 3H, s, acetates), 1.6–1.8 (8H, m); δ_{C} 170.4, 169.3, 169.25, 157.7, 155.0, 151.4, 113.9, 110.5, 110.45, 87.00, 79.29, 72.65, 70.25, 66.97, 63.13, 47.49, 30.96, 27.54, 27.43, 20.53, 20.37 and 20.32.

2-(*cis*-4-Hydroxycyclohexylamino)adenosine **16**

The acetates were removed from **15** (49 mg, 0.1 mmol) with aq. ammonia (25%; 3 mL) and methanol (3 mL) as described for **6**. Trituration with diethyl ether produced **16** (32 mg, 84%) as a white solid; mp 135–138 °C; δ_{H} (d₆-DMSO) 7.89 (1H, s, 8-H), 6.69 (2H, s, NH₂), 5.85 (1H, d, *J* 6.7, NH), 5.72 (1H, d, *J* 6.0, 1'-H), 5.4–5.0 (3H, m, 3 × OH), 4.63 (1H, m, 2'-H), 4.3 (2H, m, 2 × OH), 4.16 (1H, m, 3'-H), 3.5–3.9 (6H, m), 1.5–1.7 (8H, m); *m/z* (FAB⁺) 381 (M⁺ + 1, 15%), 307 (13), 217 (20), 154 (100) and 136 (92) (Found: M⁺ + 1, 381.1848. C₁₆H₂₅N₆O₅ requires *m/z*, 381.1847).

2',3',5'-Tri-*O*-acetyl-2-(4,5-dimethyl-3,6-dihydro-1,2-oxazin-2-yl)adenosine **17**

2,3-Dimethylbuta-1,3-diene (20 μL, 0.2 mmol) was added to a suspension of **4** (0.042 g, 0.1 mmol) in DCM (2 mL). After 30 min at rt the reaction mixture was evaporated and the residue was purified by chromatography using 2% methanol in EtOAc as eluent, to yield **17** (21 mg, 42%); mp 190–194 °C; δ_{H} 7.66 (1H, s, 8-H), 6.02 (1H, m, 2'-H), 5.96 (1H, d, *J* 3.8, 1'-H), 5.91 (2H, s, NH₂), 5.83 (1H, m, 3'-H), 4.44 (1H, dd, *J* 6.1 and 12.0, 5'-H^a), 4.35 (1H, m, 4'-H), 4.33 (2H, m, 3'-H₂ or 6'-H₂), 4.27 (1H, dd, *J* 6.1 and 12.0, 5'-H^b), 4.18 (2H, m, 6'-H₂ or 3'-H₂), 2.11, 2.09 and 2.02 (all 3H, s, acetates), 1.72 (3H, br s, CH₃), 1.58 (3H, br s, CH₃).

2-(4,5-Dimethyl-3,6-dihydro-1,2-oxazin-2-yl)adenosine **18**

The acetates were removed from **17** (21 mg, 0.042 mmol) with aq. ammonia (25%; 2 mL) and methanol (2 mL) as described for **6**. Trituration with diethyl ether produced **18** (15 mg, 95%) as a white solid; δ_{H} (d₆-DMSO) 8.11 (1H, s, 8-H), 7.20 (2H, s, NH₂), 5.79 (1H, d, *J* 6.5, 1'-H), 5.5–5.0 (3H, m, 3 × OH), 4.64 (1H, m), 4.23 (2H, m), 4.15 (1H, m), 4.08 (2H, m), 3.94 (1H, m), 3.5–3.7 (2H, m, 5'-H), 1.70 (3H, br s, CH₃), 1.57 (3H, br s, CH₃); *m/z* (FAB⁺) 381 (M⁺ + 1, 8%), 154 (100) and 136 (92) (Found: M⁺ + 1, 379.1727. C₁₆H₂₃N₆O₅ requires *m/z*, 379.1715).

Cyclopentadiene-coupled resin **19**

Merrifield resin (1 g; 1.35 mmol g⁻¹) was stirred for 18 h with lithium cyclopentadienide (0.486 g, 6.75 mmol) in DMF (10 mL). The resin was filtered off and washed repeatedly with both DMF–water 9 : 1 and MeOH to remove lithium salts, and finally with DCM and MeOH to give resin **19** (0.59 mmol g⁻¹, as was determined by coupling to excess of **4**; see the next procedure).

Diels–Alder reaction of **4** with **19**

Resin **19** (0.75 g, 0.45 mmol; 0.59 mmol g⁻¹) was stirred with

4 (0.169 g, 0.4 mmol) for 30 min in DCM (10 mL) at rt. The resin was washed, filtered off, and dried *in vacuo* to give **20** (0.91 g, 0.44 mmol g⁻¹): ν_{max} /cm⁻¹ (KBr) 1754, 1620, 1600 and 1580.

Reaction of **20** with cyclohexadiene

Resin **20** (0.130 g; 0.59 mmol g⁻¹) was stirred with cyclohexa-1,3-diene (0.05 mL) in DMF (2 mL) at 90 °C for 30 min. The resin was filtered off, and washed successively with DMF and diethyl ether. Evaporation of solvents produced pure **14** (27 mg, 93%) as a glass.

Ene reaction of **4** with cyclohexene to give adduct **21**

A solution of **4** (0.063 g, 0.15 mmol) in a mixture of DCM (10 mL) and MeOH (10 mL) was stirred with cyclohexene (0.152 mL, 1.5 mmol) for 18 h. Chromatography of the reaction mixture (EtOAc–MeOH 98 : 2) gave **21** (0.018 g, 24%) as a 1 : 1 mixture of isomers; δ_{H} 7.70 (0.5H, s, 8-H), 7.69 (0.5H, s, 8-H), 6.0–5.9 (3H, m, 1'-H, CH=CH), 5.83 (1H, m, 2'-H), 5.67 (1H, m, 3'-H), 5.59 (2H, br s, NH₂), 5.15 (1H, m, CH N), 4.4–4.25 (3H, m, 4'-H, 5'-H₂), 2.2–1.6 (6H, m), 2.13, 2.11 and 2.06 (all 3H, s, acetates).

Reaction of **4** with furan to give adduct **22**

A solution of **4** (3 mg) and furan (5 μL) was stirred in CDCl₃ (0.5 mL) for 24 h. ^1H NMR after 3 h showed starting material **4** and a mixture of (*Z*)-**22** and (*E*)-**22** in proportions 1 : 1 : 2. After 18 h only the *E*-isomer of **22** was present: ν_{max} /cm⁻¹ 1747, 1644, 1593 and 1373; δ_{H} 9.81 (1H, d, *J* 8.0, CH=O), 9.19 (1H, d, *J* 10.1, CH=N), 8.05 (1H, s, 8-H), 7.93 (1H, dd, *J* 10.1 and 16.1, CH=CCO), 6.90 (1H, dd, *J* 8.0 and 16.1, C=CHCO), 6.2 (2H, br s, NH₂), 6.14 (1H, d, *J* 3.5, 1'-H), 6.01 (1H, m, 2'-H), 5.87 (1H, m, 3'-H), 4.2–4.4 (3H, m, 4'-H and 5'-H), 2.17, 2.14 and 2.02 (all 3H, s, acetates); (*Z*)-**22**: 10.23 (1H, d, *J* 6.0, CH=O), 9.81 (1H, d, *J* 11.6, CH=N), 7.81 (1H, dd, *J* 11.6 and 11.0, CH=CCO), C=CHCO not observed.

Reaction of **4** with 2-methylfuran to give adduct **23**

A solution of **4** (3 mg) and 2-methylfuran (5 μL) was stirred in DCM (1.5 mL) for 3 h at rt. The volatiles were removed *in vacuo* at 20 °C, leaving almost pure **23** as a glass: ν_{max} /cm⁻¹ 1748, 1720, 1645, 1595 and 1373; δ_{H} 9.03 (1H, d, *J* 9.8, CH=N), 8.04 (1H, s, 8-H), 7.86 (1H, dd, *J* 9.8 and 16.3, CH=CCO), 6.99 (1H, d, *J* 16.3, C=CHCO), 6.5 (2H, br s, NH₂), 6.12 (1H, d, *J* 3.8, 1'-H), 6.00 (1H, m, 2'-H), 5.76 (1H, m, 3'-H), 4.2–4.4 (3H, m, 4'-H and 5'-H₂), 2.44 (3H, s), 2.16, 2.13 and 2.02 (all 3H, s, acetates); (*Z*)-**23** (recorded after 50 min reaction time, using CDCl₃ as solvent): 9.91 (1H, d, *J* 10.6, CH=N).

2',3',5'-Tri-*O*-acetyl-2-phenylazoadenosine **26**

A mixture of **4** (0.063 g, 0.15 mmol), aniline (18.6 mL, 0.2 mmol) and acetic acid (0.1 mL) was stirred in acetonitrile (1.5 mL). After *ca.* 10 min the starting material had dissolved and from this yellow solution the product started to precipitate. The mixture was stirred at rt for 5 h, cooled in ice, and filtered, producing **26** (0.063 g, 84%) as an orange solid; mp 108–112 °C; ν_{max} /cm⁻¹ (KBr) 1751, 1638 and 1593; δ_{H} 8.10 (1H, s, 8-H), 8.09 (2H, d, *J* 4.6, ArH_{ortho}), 7.5–7.6 (3H, m, ArH_{meta+para}), 6.43 (1H, d, *J* 5.8, 1'-H), 5.9 (2H, br s, NH₂), 5.84 (1H, m, 2'-H), 5.66 (1H, m, 3'-H), 4.4–4.5 (3H, m, 4'-H and 5'-H₂), 2.16, 2.15 and 2.07 (all 3H, s, acetates).

2',3',5'-Tri-*O*-acetyl-2-(4-methoxyphenylazo)adenosine **27**

Condensation of **4** (0.042 g, 0.1 mmol) with *p*-anisidine (0.013 g, 0.11 mmol) was performed as described for **26**. Chromatography (EtOAc–MeOH 95 : 5) yielded **27** (0.048 g,

91%) as an orange glass: $\nu_{\max}/\text{cm}^{-1}$ 1751, 1640 and 1583; δ_{H} 8.11 (1H, s, 8-H), 8.09 (2H, d, *J* 6.1, ArH_{ortho}), 7.02 (2H, d, *J* 6.1, ArH_{meta}), 6.44 (1H, d, *J* 5.9, 1'-H), 6.26 (2H, br s, NH₂), 5.81 (1H, m, 2'-H), 5.63 (1H, m, 3'-H), 4.4–4.5 (3H, m, 4'-H and 5'-H₂), 3.90 (3H, s, CH₃OAr), 2.15, 2.14 and 2.06 (all 3H, s, acetates).

2-(Phenylazo)adenosine 28

Triacetate **26** (0.050 g, 0.1 mmol) was stirred with methanol (2 mL) and aq. ammonia (25%; 2 mL) for 5 h. Evaporation of the mixture, coevaporation with methanol (3 mL), and trituration with methanol gave **28** (0.032 g, 86%) as an orange solid, mp 215–218 °C (Found: C, 51.63; H, 4.73; N, 26.24. C₁₆H₁₇N₇O₄ requires C, 51.75; H, 4.61; N, 26.40%); $\nu_{\max}/\text{cm}^{-1}$ (KBr) 1647 and 1597; δ_{H} (d₆-DMSO) **28** (*E*-isomer) 8.51 (1H, s, 8-H), 7.95 (2H, m, ArH_{ortho}), 7.8 (2H, br s, NH₂), 7.65 (3H, m, ArH_{meta+para}), 5.96 (1H, d, *J* 6.6, 1'-H), 5.5 (1H, d, *J* 6.3, OH), 5.2 (2H, m, 2 × OH), 4.66 (1H, m 2'-H), 4.17 (1H, m 3'-H), 4.00 (1H, m 4'-H), 3.70 (1H, m 5'-H^a), 3.48 (1H, m, 5'-H)^b; **28** (*Z*-isomer, selected signals) 8.32 (1H, s, 8-H), 7.65 (2H, br s, NH₂), 7.33 (2H, t, *J* 7.3, ArH_{meta}), 7.23 (1H, t, *J* 7.3, ArH_{para}), 6.94 (2H, d, *J* 7.3, ArH_{ortho}), 5.72 (1H, d, *J* 5.8, 1'-H); *m/z* (FAB⁺) 372 (M⁺ + 1, 10%), 307 (13), 217 (29), 154 (100) and 136 (95) (Found: M⁺ + 1, 372.1438. C₁₆H₁₈N₇O₄ requires *m/z*, 372.1420).

2-(4-Methoxyphenylazo)adenosine 29

Deprotection of **27** as described for **26** gave **29** (77%) as an orange solid; mp 140–143 °C (Found: C, 51.03; H, 4.84; N, 24.28. C₁₇H₁₉N₇O₅ requires C, 50.87; H, 4.77; N, 24.43%); $\nu_{\max}/\text{cm}^{-1}$ (KBr) 3332, 3188, 1668, 1640, 1601, 1581, 1504, 1367 and 1335; δ_{H} (d₆-DMSO) **29** (*E*-isomer) 8.48 (1H, s, 8-H), 7.96 (2H, d, *J* 8.8, ArH_{ortho}), 7.72 (2H, br s, NH₂), 7.18 (2H, d, *J* 8.8, ArH_{meta}), 5.95 (1H, d, *J* 6.3, 1'-H), 5.5 (1H, br, OH), 5.22 (2H, br, 2 × OH), 4.66 (1H, m, 2'-H), 4.17 (1H, m, 3'-H), 3.99 (1H, m, 4'-H), 3.91 (3H, s, CH₃OAr), 3.6–3.7 (2H, m, 5'-H₂); **29** (*Z*-isomer, selected signals) 8.35 (1H, s, 8-H), 7.7 (2H, br, NH₂), 7.00 (2H, d, *J* 8.8, ArH), 6.89 (2H, d, *J* 8.8, ArH), 5.76 (1H, d, *J* 5.8, 1'-H), 3.74 (3H, s, CH₃OAr); *m/z* (FAB⁺) 402 (M⁺ + 1, 6%), 154 (100) and 136 (92) (Found: M⁺ + 1, 401.3783. C₁₇H₂₀N₇O₅ requires *m/z*, 401.3769).

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