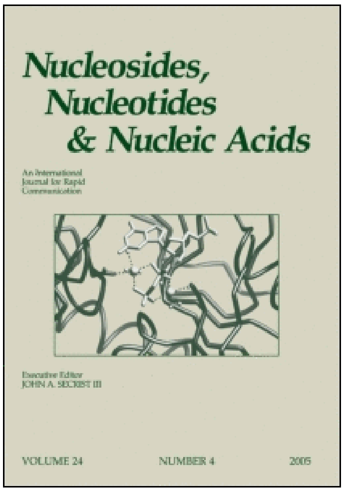

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SYNTHESIS OF BRANCHED-CHAIN AND BICYCLIC THIOSUGAR NUCLEOSIDES

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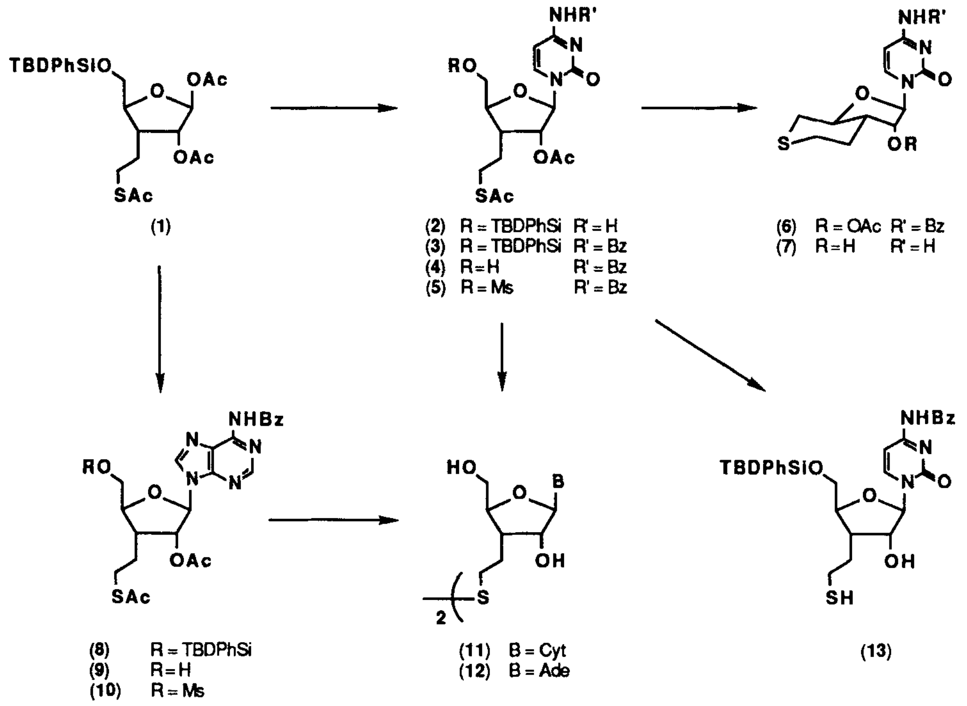
Abstract: The synthesis of strategically protected nucleosides bearing β-mercaptoethyl chains at the α-C-3' position from 1,2-di-O-acetyl-2'-S-acetyl-5-*t*-butyldiphenylsilyl-3-deoxy-3-C-(2'-mercaptoethyl)-α-D-ribofuranose **1** is described. It was found that treatment of the 5-O-methanesulfonyl sugar **19** or nucleoside **5** with either benzylmercaptan or methoxide resulted in rapid cleavage of the thiolester followed by intramolecular cyclization. This was used to prepare the novel *trans*-fused oxathiahydrindane nucleosides **7** and **27** as well as the cAMP analogue **29**.

INTRODUCTION

The last decade has seen an increasing interest in oligonucleotide analogues in which the phosphodiester linkage has been either modified[1] or replaced[2] altogether. In the course of our synthesis of such a system in which a thioether function replaces the phosphate group, nucleosides bearing an α-C-3' β-mercaptoethyl chain were prepared. It was our hope that the oligomers could be grown by successive displacement of the 5'-O-mesyl group of **5** (or the growing chain) by the branch-chain thiol of the next monomer unit. We discovered, however, that this displacement occurs much more slowly than transthiolesterification and intramolecular sulfide formation.

The apparent ease of formation of the *trans*-fused 5,6-ring system was surprising to us since they are generally regarded as being strained. This has been used to explain the difficulties encountered in forming the *trans*-fused dioxahydrindane system of octosyl acid.[3] It may be that a thiane ring can accommodate the *trans*-fusion much better than one containing an oxygen. In this work, we describe the use of this highly efficient intramolecular cyclization in preparing novel bicyclic thiosugar nucleosides.



(1)

(2) R = TBDPhSi R' = H
(3) R = TBDPhSi R' = Bz
(4) R = H R' = Bz
(5) R = Ms R' = Bz

(6) R = OAc R' = Bz
(7) R = H R' = H

(8) R = TBDPhSi
(9) R = H
(10) R = Ms

(11) B = Cyt
(12) B = Ade

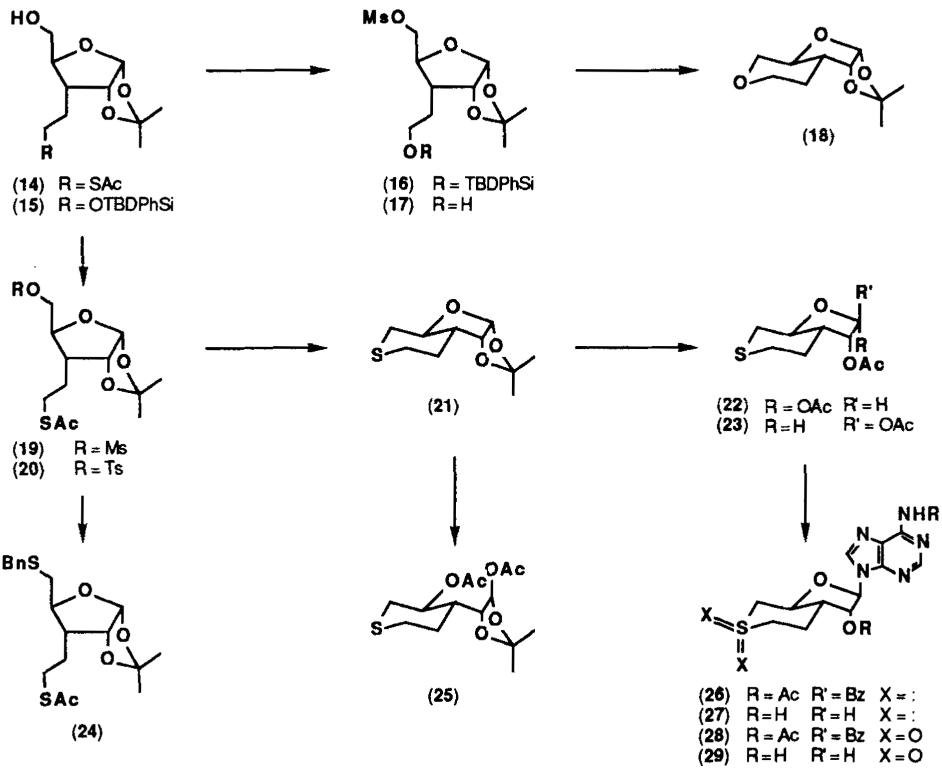
(13)

RESULTS & DISCUSSION

The branched-chain 1,2-di-O-acetyl furanose **1**, prepared[4] from 1,2-O-isopropylidene-α-D-xylofuranose in 32 % overall yield, was subjected to a trimethylsilyl triflate promoted condensation of **1** and *bis*-(trimethylsilyl)cytosine as described[5] by Vorbruggen to afford excellent yields of nucleoside **2**. Subsequent benzoylation of the exocyclic amino group yielded the fully protected monomeric nucleoside unit **3**.

Our coupling strategy hinged on the ability to independently deprotect the 5' and 2" ends of the monomer unit. Treatment of **3** with tetra-*n*-butylammonium fluoride trihydrate in tetrahydrofuran did result in cleavage of the 5'-O-silyl ether accompanied, however, with considerable deacetylation. This was easily overcome by carrying out the reaction in the presence of acetic acid which afforded **4** in 95 % yield. The acetyl groups at the 2' and 2"-positions could be removed using methanolic sodium hydroxide but the surprisingly strong tendency of the resulting 2"-thiol to be oxidized to the symmetrical disulfide necesitated that the conversion be performed in the presence of dithiothreitol to obtain **13**. Having found that the two ends of the monomer could be freed, alcohol **4** was mesylated in 99 % yield in the hope that reaction of mesylate **5** with **13** would result in selective displacement by the primary thiol to give the coupled product.

The analogous branched-chain adenine nucleoside was also prepared. The trimethylsilyl triflate catalyzed Vorbruggen coupling of **1** and *bis*-(trimethylsilyl)-N^6-benzoyl-adenine afforded



(14) R = SAc
(15) R = OTBDPhSi
(16) R = TBDPhSi
(17) R = H
(18)
(19) R = Ms
(20) R = Ts
(21)
(22) R = OAc R' = H
(23) R = H R' = OAc
(24)
(25)
(26) R = Ac R' = Bz X = :
(27) R = H R' = H X = :
(28) R = Ac R' = Bz X = O
(29) R = H R' = H X = O

the purine monomer unit **8** in 90 % yield. Generating the silylated base just prior to each coupling as described[6] was found to be unreliable and time-consuming. Using a stock solution of previously distilled silylated base[7] in dichloroethane proved to be much more convenient.

Both the cytosine and adenine monomers were fully deprotected by desilylation followed by treatment with base. The silyl ether of **8** was cleanly removed, again, by fluoride in the presence of acetic acid. **4** and **9** were deacylated using methanolic hydroxide which afforded the free nucleosides as the symmetrical disulfides **11** and **12**.

Model studies carried out on various 5-O-methanesulfonyl furanoses suggested that sulfide formation at the 5'-position of nucleoside **5** could be cleanly accomplished by the reaction of mesylate and thiol in DMF in the presence of DBU. Under these conditions, treatment of mesylate **5** with benzylmercaptan did indeed afford a single compound. This product, however, was found not to be the anticipated 5'-benzyl sulfide but the thiane nucleoside **6**. The possibility that the compound was a dimeric *bis*-sulfide was eliminated by the mass spectral data and, ultimately, by X-ray analysis of a related nucleoside product. It appeared that the benzyl thiolate preferentially attacked the thiolacetate carbonyl, thus liberating the 2''-thiol, rather than displace the mesyl group. This latter thiolate immediately displaces the mesyl group intramolecularly.

To verify that the thiaoxahydrindane system did indeed arise from transthiolesterification / cyclization, the following was performed. Branched-chain thiosugar **14** was mesylated to **19** which was in turn treated with 1.1 equivalents of benzyl mercaptan. After one hour, the novel tricyclic furanose sugar **21** was isolated as the major product in 85 % yield with only traces of the 5-S-benzyl derivative **24** arising from intermolecular displacement being formed. The isolation of benzyl thiolacetate provided conclusive evidence for the transthiolesterification step.

Another interesting aspect of the thiol-induced cyclization is that it permits the selective cleavage of the thiolester while leaving the 2'-O-acetyl intact. This allowed for the clean conversion of mesylate **5** to **6** in 95 % yield. Subsequent deacylation in methanol saturated with ammonia afforded the novel bicyclic nucleoside **7**. The corresponding adenosine analogue was prepared by a similar route. Treatment of mesylate **10** with methanolic sodium hydroxide resulted in cyclization as well as complete deacylation leading directly to nucleoside **27**.

An obviously more expedient route to these cyclic nucleosides is to form the bicyclic sugar prior to the attachment of the base. Treatment of either the mesylate **19** or tosylate **20** with methanolic sodium hydroxide afforded the crystalline thianylfuranose **21** in quantitative yield.

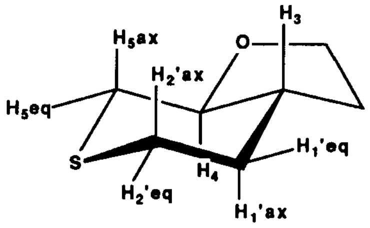
In earlier work, we demonstrated that the acetolytic deacetalation of 1,2-O-isopropylidene furanoses tends to yield acyclic products arising from furanose ring-opening when performed at low temperatures and that this can be prevented by heating. The acetolysis of **21** carried out at 75°C, however, gave only the ring-opened 1-O-acetyl-1,2-O-isopropylidene sugar **25**. The acetonide **21** was eventually hydrolyzed under fairly harsh conditions using acidic resin. Subsequent acetylation of the free sugar yielded the desired 1,2-di-O-acetyl furanoses **22** and **23** as a 1 : 1.56 (α : β) mixture of separable anomers in a combined yield of 87 %.

The trimethylsilyl triflate-catalyzed coupling of **23** and *bis*-(trimethylsilyl)-N^6-benzoyl-adenine cleanly yielded the bicyclic nucleoside **26** in 88 % yield which, upon stirring in methanolic ammonia, afforded the free nucleoside **27**. The oxidation of the sulphur in **26** was performed using the Oxone reagent as described by Trost[8] which gave the desired sulfone **28**. Deacylation in methanolic ammonia afforded the uncharged cAMP analogue **29** in 72 % yield for the two steps.

Detailed analysis of the ^{1}H-NMR spectra of the thiane ring-containing sugars and nucleosides (TABLE 1) shows that the couplings between protons of the thiane ring are remarkably constant over a variety of compounds, indicating that they all exist in very similar conformations. The only exception is the four-bond "W" coupling between the equatorial $H5^{(')}$ and $H2'^{(')}$ protons where the central atom appears to influence it's magnitude. The coupling data are consistant with the thiane ring of the compounds existing in a chair conformation, perhaps best described as $^{3'}C_S$.

When comparing the values of $J_{H3,H4}$ for the uncyclized branched-chain compounds and those containing the cyclic sulfide, one finds little variation. Ranges of 9.7-10.8 Hz and 10.2-11.3

TABLE 1. Coupling Constants (Hertz) for Thiane Ring Protons.



H-H COUPLING	7	27	29	21	22	26	18
H3 - H4	10.8	10.2	11.3	10.3	10.3	10.6	10.3
H4 - H5eq	3.7	3.8	4.1	3.7	3.9	3.6	4.3
H4 - $H5_{ax}$	11.1	10.9	11.4	11.0	10.8	10.8	10.0
$H5_{eq}$ - $H5_{ax}$	-11.9	-12.0	-12.6	-12.0	-12.2	-12.0	-9.8
H3 - $H1'_{eq}$	3.0	3	3.2	3.0	2.8	----	----
H3 - $H1'_{ax}$	11.8	12.0	11.9	12.1	12.0	12.5	----
$H1'_{eq}$ - H1'ax	-13.2	-12.8	-14.0	-13.2	-13.1	-12.5	----
$H1'_{eq}$ - $H2'_{eq}$	3.0	3	3.4	3.0	2.9	----	2.5
$H1'_{eq}$ - $H2'_{ax}$	3.0	3.1	3.4	2.9	2.9	----	----
$H1'_{ax}$ - $H2'_{eq}$	4.0	3.8	4.8	4.1	5.5	4.1	3.5
$H1'_{ax}$ - $H2'_{ax}$	12.3	11.8	12.7	12.1	10.5	12.5	----
$H2'_{eq}$ - $H2'_{ax}$	-13.5	-13.5	-14	-13.6	----	-13	-11.5
$H2'_{eq}$ - $H5_{eq}$	-0.9	-1.1	-2.8	<0.5	<0.5	<0.5	0

Hz are found for the two groups of compounds respectively. This consistency is also observed for $J_{H2,H3}$ where, in both groups, the values are within 4 and 5 Hz. This suggests that in both systems the furanose is puckered such that the C-3$^{(\prime)}$ and C-4$^{(\prime)}$ substituents are pseudo-equatorial and that little conformational change is required in the sugar for cyclization to occur. This may contribute to the rapid sulfide formation observed for **19** and **5**. The X-ray crystallographic structure of **27** (FIGURE 1) confirmed our NMR analyses, clearly showing the thiane ring in the chair conformation fused to an ^3E-puckered ($C_{3'}$ -endo) furanose ring.

Since the branched-chain furanose **15** was available to us from earlier work, the oxygen-analogue **18** was prepared. Sugar **15** was mesylated and the silyl ether cleaved with fluoride to afford the highly unstable alcohol **17**. We expected that this compound might also cyclize spontaneously but found, rather, that it was very prone to hydrolysis. Treatment of **17** with sodium hydride did afford the tricyclic ether **18** in 25 % yield demonstrating that the dioxahydrindane system is also accessible by this route.

EXPERIMENTAL

General Methods

Melting points (m.p.) were determined using an Electrothermal MP apparatus and are uncorrected. Optical rotation measurements were carried out in the indicated solvents employing

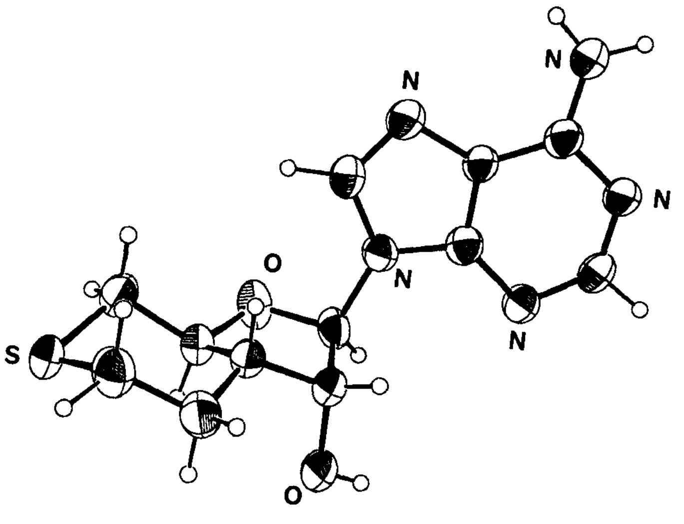


FIGURE 1. X-ray crystallographic structure of nucleoside **27**.

a Jasco DIP-140 digital polarimeter and a 1-dm cell. Low-resolution chemical ionization mass spectra (CI-MS) were obtained on an HP 5980A quadrupole mass spectrometer in the direct-inlet mode. High-resolution CI and FAB mass spectra (HRMS) were obtained on a VG ZAB-HS sector mass spectrometer in the direct-inlet mode. Elemental analyses were performed by Guelph Chemical Laboratories Ltd. (Guelph, Ontario). All compounds were shown to be homogeneous by tlc and to have a purity of >95% by high-field nmr.

^{1}H-nmr spectra were recorded on either Varian XL200 or Varian XL300 spectrometers and the assignments based on homonuclear decoupling and / or COSY experiments. When deuteriochloroform was employed as solvent, internal tetramethylsilane was used as reference. The residual proton signals of deuterated DMSO and methanol (assigned values of δ2.49 and δ3.35 ppm) were used as reference in these solvents. The multiplicities are recorded using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; q^5, quintet; h, hextet; h^7, heptet; o, octet; m, multiplet; m^n, symmetical signal of n lines; br, broad. ^{13}C-nmr spectra were all obtained at 75.4 MHz using a Varian XL300 spectrometer. The $^{13}CDCl_3$, $^{13}CD_3OD$, $^{13}CD_3S(O)CD_3$, and $^{13}CD_2Cl_2$ signals (assigned values of δ77.00; δ49.00; δ39.50 and δ53.80 ppm) were used as reference signals in these solvents. Peak assigments were, in some cases, made with the aid of APT or HETCOR experiments.

Tetrahydrofuran was distilled from sodium benzophenone ketyl. Methylene chloride and 1,2-dichloroethane were distilled from P_2O_5. Toluene was dried over sodium wire. Pyridine was distilled from calcium hydride. *N,N*-Dimethylformamide was dried by shaking with KOH followed by distillation at reduced pressure from BaO. Kieselgel 60 F_{254} plates (0.2 mm thickness) were used for thin-layer chromatography and Kieselgel 60 (Merck 230-400 mesh) was employed for column chromatography.

2'-O-Acetyl-2"-S-acetyl-5'-O-*t*-butyldiphenylsilyl-3'-deoxy-3'-C-(2"-mercapto ethyl)-cytidine (2).

Trimethylsilyl trifluoromethanesulfonate (182 mL, 0.942 mmol) was added dropwise to a stirred solution of triacetate **1** (876 mg, 1.57 mmol) and *bis*-(trimethylsilyl)-cytosine[6] (401 mg, 1.57 mmol) in dry 1,2-dichloroethane (12 mL) and the resulting solution heated to reflux under nitrogen. After 1 h an additional portion of trimethylsilyl trifluoromethanesulfonate (121 µL, 0.628 mmol) was added and the refluxing continued. After an additional 2.5 h the solution was cooled in an ice bath and poured into ice-cold aqueous sodium bicarbonate solution (5 % w/v, 250 mL). The mixture was then shaken vigorously with methylene chloride (225 mL). The resulting emulsion was broken by filtration and the organic phase dried (Na_2SO_4), filtered and the solvent removed *in vacuo* yielding a white foam. Chromatography over silica gel (20 : 1 methylene chloride / methanol, v/v) afforded nucleoside **2** as an amorphous white solid (823 mg, 86% yield): ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.11 ppm (s, 9H, *t*-butyl), 1.30-1.68 (m, 2H, H1"$_{A,B}$), 2.15 (s, 3H, OAc), 2.27 (s, 3H, SAc), 2.40-2.56 (m, 1H, H3'), 2.58-2.76 and 2.88-3.04 (two m, 2H, H2"$_{A,B}$), 3.71 (dd, 1H, H5'$_A$), 3.93 (br d, 1H, H4'), 4.14 (d, 1H, H5'$_B$), 5.35 (d, 1H, H5), 5.56 (d, 1H, H2'), 5.92 (s, 1H, H1'), 7.35-7.74 (m, 10H, phenyls), 8.02 (d, 1H, H6), 8.6 (br. and exchangeable, 1H, NHBz), coupling constants (Hertz): $J_{H1'-H2'} \sim 0$, $J_{H2'-H3'} = 5.0$, $J_{H3'-H4'} = 10.4$, $J_{H4'-H5'A} \sim 0.2$, $J_{H4'-H5'B} \sim 0$, $^2J_{H5'A-H5'B} = -12.0$, $J_{H5-H6} = 7.3$; ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 194.84 ppm (S**C**OMe), 169.14 (O**C**OMe), 165.93 (C4), 155.47 (C2), 140.01 (C6), 135.37; 135.22; 132.50; 132.10; 129.91; 129.74; 127.75; 127.70 (phenyls), 94.72 (C5), 90.01 (C1'), 84.19 (C4'), 77.11 (C2'), 62.09 (C5'), 39.17 (C3'), 30.30 (SCO**Me**), 26.98 (C2"), 26.76 (C**Me**$_3$), 24.66 (C1"), 20.63 (OCO**Me**), 19.02 (**C**Me$_3$); $[\alpha]^{20}_D = +76.8^o$ (c = 1, $CHCl_3$); UV (methanol) λ_{max} 274 nm (ε 7500); HRMS (CI-NH_3), m/e calcd. for $C_{27}H_{30}O_6NSSi$ [MH^+-C_4H_{10}]: 552.1625. found: 552.1626; Anal. calcd. for $C_{31}H_{39}O_6N_3SSi$: C, 61.06; H, 6.44; N, 6.89; S, 5.26. found: C, 61.34; H, 6.58; N, 6.88; S, 5,34.

2'-O-Acetyl-2"-S-acetyl-N^4-benzoyl-5'-O-*t*-butyldiphenylsilyl-3'-deoxy-3'-C-(2"-mercaptoethyl)-cytidine (3).

Benzoyl chloride (234 mL, 2.00 mmol) was added dropwise to an ice-cold solution of nucleoside **2** (814 mg, 1.33 mmol) in dry pyridine (4 mL) and the reaction stirred at room temperature under nitrogen. After stirring for 6 h the reaction was poured into aqueous sodium bicarbonate (5 % w/v, 150 mL), extracted with methylene chloride (2 x 100 mL) and washed with dilute sulphuric acic (1 % w/v, 100 mL) and water / brine (100 mL). The combined organic phases were then dried (Na_2SO_4), filtered, and the solvent removed *in vacuo* yielding a yellow syrup which was chromatographed over silica gel (2 : 1 ethyl acetate / hexanes, v/v) affording nucleoside **3** as a colorless solid (853 mg, 90 % yield). Recrystallization from methanol yielded white needles: m.p. 191^{o}C; ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.15 ppm (s, 9H, *t*-butyl), 1.28-1.72 (m, 2H, H1"$_{A,B}$), 2.21 (s, 3H, OAc), 2.23 (s, 3H, SAc), 2.45-2.74 (m, 2H, H3' and H2"$_B$), 2.89-3.03 (m, 1H, H2"$_A$), 3.70 (A of ABX, 1H, H5'$_A$), 4.00 (br. d, 1H, H4'), 4.24 (B of ABX, 1H, H5'$_B$), 5.65 (d, 1H, H2'), 6.01 (s, 1H, H1'), 7.28-7.91 (m, 16H, phenyls and H5), 8.53 (d, 1H, H6), 8.6 (br and exchangeable, 1H, NHBz), coupling constants (Hertz): $J_{H1'-H2'} \sim 0$, $J_{H2'-H3'} = 4.8$, $J_{H3'-H4'} = 10.4$, $J_{H4'-H5'A} = 1.9$, $J_{H4'-H5'B} < 1$, $^2J_{H5'A-H5'B} = -12.3$, $J_{H5-H6} = 7.6$; ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 195.02 ppm (S**C**OMe), 169.04 (O**C**OMe), 166.70 (C4), 162.30 (N**C**OPh), 154.30 (C2), 144.19 (C6), 135.49; 135.28; 133.14; 132.83; 132.25; 131.98; 130.12; 130.02; 128.72; 127.91 (2C); 127.58 (phenyls), 96.48 (C5), 90.50 (C1'), 84.88 (C4'), 76.86 (C2'), 61.53 (C5'), 38.58 (C3'), 30.40 (SCO**Me**), 27.02 (C2"), 26.86 (C**Me**$_3$), 24.50 (C1"), 20.69 (OCO**Me**), 19.11 (**C**Me$_3$); $[\alpha]^{20}_D = +88.5^o$ (c = 1, $CHCl_3$); UV (methanol) λ_{max} 262 nm (ε 23600) and 304 nm (ε 10600); HRMS (CI-NH_3), m/e calcd. for $C_{34}H_{34}O_7N_3SSi$ [MH^+-C_4H_{10}]: 656.18868. found: 656.18866; Anal. calcd. for $C_{38}H_{43}O_7N_3SSi$: C, 63.93; H, 6.07; N, 5.89; S, 4.49. found: C, 64.23; H, 6.32; N, 5.57; S, 4.41.

2'-O-Acetyl-2"-S-acetyl-N^4-benzoyl-3'-deoxy-3'-C-(2"-mercaptoethyl)-cytidine (4).

A solution of tetra-*n*-butylammonium fluoride trihydrate (198 mg, 0.630 mmol), nucleoside **3** (300 mg, 0.420 mmol) and glacial acetic acid (72 mL, 1.26 mmol) in dry tetrahydrofuran (3.4 mL) was stirred at ambient temperature under nitrogen. After 5 h the solvent was evaporated *in vacuo* and the resulting syrup extracted with methylene chloride (2 x 80 mL) and washed with aqueous sodium bicarbonate solution (5 % w/v, 80 mL) and water (80 mL). The combined organic phases were then dried (Na_2SO_4), filtered and the solvent removed *in vacuo* yielding a yellow foam which was chromatographed over silica gel (25 : 1 methylene chloride / methanol, v/v) affording nucleoside **4** as a colorless solid (189 mg, 95 % yield). Recrystallization from methanol yielded needles: m.p. 163-164^{o}C; ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.45-1.80 ppm (m, 2H, H1"$_{A,B}$), 2.16 (s, 3H, OAc), 2.25 (s, 3H, SAc), 2.62 (h^7, 1H, H3'), 2.65-2.97 (m, 2H, H2"$_{A,B}$), 3.5 (br and exchangeable, 1H, 5'-OH), 3.78 (A of ABX, 1H, H5'$_A$), 4.07 (m, 1H, H4'), 4.14 (B of ABX, 1H, H5'$_B$), 5.64 (d, 1H, H2'), 5.77 (s, 1H, H1'), 7.39-7.88 (two m, 6H, H5 and phenyl), 8.39 (d, 1H, H6), 8.9 (br and exchangeable, 1H, NHBz), coupling constants (Hertz): $J_{H1'-H2'} \sim 0$, $J_{H2'-H3'} = 5.4$, $J_{H3'-H4'}$

~ 11, $J_{H4'-H5'A}$ = 2.1, $J_{H4'-H5'B}$ = 1.4, $^2J_{H5'A-H5'B}$ = -12.6, J_{H5-H6} = 7.4; ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 195.48 ppm (SCOMe), 169.50 (OCOMe), 166.75 (C4), 162.50 (NCOPh), 154.88 (C2), 145.70 (C6), 132.89; 132.78; 128.57; 127.65 (phenyl), 96.92 (C5), 91.84 (C1'), 85.65 (C4'), 77.28 (C2'), 60.17 (C5'), 38.64 (C3'), 30.38 (SCO**Me**), 26.96 (C2"), 24.94 (C1"), 20.67 (OCO**Me**); $[\alpha]^{20}_D$ = +88° (c = 0.5, $CHCl_3$); UV (methanol) λ_{max} 260 nm (ε 20600) and 304 nm (ε 3100); HRMS (CI-NH_3), m/e calcd. for $C_{22}H_{26}O_7N_3S$ [MH^+]: 476.1491. found: 476.1493; Anal. calcd. for $C_{22}H_{25}O_7N_3S$: C, 55.57; H, 5.30; N, 8.84; S, 6.74. found: C, 55.41; H, 5.70; N, 8.96; S, 6.39.

2'-O-Acetyl-2"-S-acetyl-N^4-benzoyl-3'-deoxy-3'-(2"-mercaptoethyl)-5'-O-methanesulfonyl-cytidine (5).

Methanesulfonyl chloride (138 µL, 1.78 mmol) was added dropwise to a cooled (0°C) solution of nucleoside **4** (431 mg, 0.889 mmol) and dry pyridine (324 mL, 4.00 mmol) in dry methylene chloride (6 mL) and the resulting solution stirred at ambient temperature under nitrogen. After 10 h the reaction was diluted with methylene chloride (150 mL), washed with dilute sulphuric acid (1% w/v, 200 mL), aqueous sodium bicarbonate solution (sat., 200 mL) and water (200 mL), and reextracted with methylene chloride (150 mL). The combined organic phases were then dried (Na_2SO_4), filtered and the solvent removed *in vacuo* affording mesylate **5** as a white solid (499 mg, 99 % yield). Recrystallization from methanol yielded colorless crystals: m.p. 174-175°C (dec.); ^{1}H-NMR (DMSO-d_6, 200 MHz) δ 1.61 ppm (q, 2H, H1"$_{A,B}$), 2.16 (s, 3H, OAc), 2.29 (s, 3H, SAc), 2.40 (h^7, 1H, H3'), 2.79 (o, 2H, H2"$_{A,B}$), 3.26 (s, 3H, OMs), 4.16 (dt, 1H, H4'), 4.48 (A of ABX, 1H, H5'$_A$), 4.58 (B of ABX, 1H, H5'$_B$), 5.56 (d, 1H, H2'), 5.78 (s, 1H, H1'), 7.36 (d, 1H, H5), 7.46-8.02 (two m, 5H, phenyl), 8.12 (d, 1H, H6), 11.3 (br and exchangeable, 1H, NHBz), coupling constants (Hertz): $J_{H1'-H2'}$ ~ 0, $J_{H2'-H3'}$ = 5.4, $J_{H3'-H4'}$ = 10.8, $J_{H4'-H5'A}$ = 5.0, $J_{H4'-H5'B}$ = 2.0, $^2J_{H5'A-H5'B}$ = -11.8, J_{H5-H6} = 7.5; ^{13}C-NMR (CD_2Cl_2, 75.4 MHz) δ 195.72 ppm (SCOMe), 169.82 (OCOMe), 167.20 (C4), 162.96 (NCOPh), 154.52 (C2), 144.90 (C6), 133.46; 133.35; 129.28; 128.02 (phenyl), 96.57 (C5), 93.11 (C1'), 82.66 (C4'), 76.78 (C2'), 68.03 (C5'), 40.47 (OMs), 38.09 (C3'), 30.77 (SCO**Me**), 27.28 (C2"), 25.11 (C1"), 20.97 (OCO**Me**); $[\alpha]^{20}_D$ = +105.5° (c = 0.5, CH_2Cl_2); UV (CH_2Cl_2) λ_{max} 262 nm (ε 21800) and 312 nm (ε 9550); HRMS (CI-NH_3), m/e calcd. for $C_{22}H_{24}O_6N_3S$ [MH^+-MsOH]: 458.13858. found 458.13856.

2'-O-Acetyl-2",5'-anhydro-N^6-benzoyl-3'-C-(2"-mercaptoethyl)-cytidine (6).

Benzyl mercaptan (95 mL, 0.809 mmol) and diazabicycloundecene (242 mL, 1.62 mmol) were added successively to a stirring solution of mesylate **5** (407 mg, 0.735 mmol) in dry N,N-dimethylformamide (4.5 mL) and the reaction heated to 45°C under nitrogen. After 1.5 hr the solution was cooled and the solvent removed *in vacuo*. The resulting yellow syrup was extracted with methylene chloride (2 x 75 mL) and washed with saturated aqueous sodium bicarbonate solution (75 mL) and brine (75 mL). The combined organic phases were then dried (Na_2SO_4), filtered and evaporated *in vacuo*. The residue was chromatographed over silica gel (300 : 11 methylene chloride / methanol, v/v) yielding a colorless solid. Recrystallization from methanol afforded the cyclized nucleoside **6** as a colorless powder (291 mg, 95 % yield): m.p. 225°C; ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.49-1.74 ppm (m, 2H, H3' and H1"$_{ax}$), 2.17 (s, 3H, OAc), 2.24-2.33 (m, 1H, H1"$_{eq}$), 2.58-2.66 (m, 2H, H2"$_{eq,ax}$), 2.84 (A of ABX, 1H, H5'$_{ax}$), 3.09 (B of ABX, 1H, H5'$_{eq}$), 4.12 (td, 1H, H4'), 5.49 (d, 1H, H2'), 5.80 (s, 1H, H1'), 7.47-7.92 (two m, 7H; H5,H6 and phenyl), 8.7 (br and exchangeable, 1H, NHBz), coupling constants (Hertz): $J_{H1'-H2'}$ ~ 0, $J_{H2'-H3'}$ = 4.1, $J_{H3'-H4'}$ = 10.0, $J_{H4'-H5'eq}$ = 3.7, $J_{H4'-H5'ax}$ = 11.1, $^2J_{H5'eq-H5'ax}$ = -11.8; ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 169.48 ppm (OCOMe), 166.73 (C4), 162.53 (NCOPh), 154.40 (C2), 143.75 (C6), 133.03; 132.91; 128.81; 127.64 (phenyl), 96.57 (C5), 90.48 (C1'), 80.24 (C4'), 77.92 (C2'), 45.92 (C3'), 32.74 (C5'), 28.03 and 27.92 (C1" and C2"), 20.62 (OCO**Me**); $[\alpha]^{23}_D$ = +47.4° (c = 1.065, $CHCl_3$); UV (methanol) λ_{max} 262 nm (ε 23200) and 304 nm (ε 10200); HRMS (CI-NH_3), m/e calcd. for $C_{20}H_{22}O_5N_3S$ [MH^+]: 416.12798. found: 416.12802.

2",5-Anhydro-3'-deoxy-3'-C-(2"-mercaptoethyl)-cytidine (7).

Nucleoside **6** (291 mg, 0.700 mmol) was suspended in dry methanol (15 mL) and cooled to 0°C. The mixture was then saturated with ammonia gas and allowed to warm to room temperature. After 9 h the resulting homogeneous solution was evaporated *in vacuo* yielding an amorphous white solid. Trituration with acetone resulted in the formation of fine white crystals of nucleoside **7** which were filtered, washed repeatedly with acetone and dried *in vacuo* (160 mg, 84 % yield): m.p. 215°C (darkens); ^{1}H-NMR (CD_3OD, 300 MHz) δ 1.32 ppm (m[15], 1H, H3'), 1.83 (m[12], 1H, H1"$_{ax}$), 2.17 (dq, 1H, H1"$_{eq}$), 2.51-2.70 (m, 2H, H2"$_{eq,ax}$), 2.88 (A of ABX, 1H, H5'$_{ax}$), 2.95 (B of ABX, 1H, H5'$_{eq}$), 4.09 (td, 1H, H4'), 4.10 (d, 1H, H2'), 5.61 (s, 1H, H1'), 5.89 (d, 1H, H5), 7.61 (d, 1H, H6), coupling constants (Hertz): $J_{H1'-H2'}$ ~ 0, $J_{H2'-H3'}$ = 4.4, $J_{H3'-H4'}$ = 10.8, J_{H5-H6} = 7.5 (other coupling constants listed in TABLE 1); ^{13}C-NMR (CD_3OD, 75.4 MHz) δ 167.74 ppm (C4), 158.23 (C2), 141.76 (C6), 95.60 (C5), 93.62 (C1'), 81.47 (C4'), 78.42 (C2'), 47.80 (C3'), 33.61 (C5'), 29.10 and 28.89 (C2" and C1'); $[\alpha]^{20}_D$ = +13.8° (c = 0.5, DMSO); UV (methanol) λ_{max} 276 nm (ε 8400); HRMS (CI-NH_3), m/e calcd. for $C_{11}H_{16}N_3O_3S$ [MH^+]: 270.09124. found: 270.09126; Anal. calcd. for $C_{11}H_{15}N_3O_3S$: C, 49.06; H, 5.61; N, 15.60; S, 11.90. found: C, 49.30; H, 5.59; N, 15.85; S, 12.06.

3'-Deoxy-3'-C-(2"-mercaptoethyl)-cytidine disulfide (11).

Alcohol **4** (140 mg, 0.294 mmol) was dissolved with heating into degassed methanol (0.25 mL) and methanolic sodium hydroxide (1.0 N, 0.55 mL) then added. After 21 h of stirring at ambient temperature under argon the solution was evaporated *in vacuo* and the resulting solid recrystallized from methanol / water affording disulfide **9** as a colorless crystalline solid (62 mg, 73 % yield): m.p. 246°C (dec.); ^{1}H-NMR (DMSO-d_6, 200 MHz) δ 5.04 ppm (t, 1H, 5'-OH, J = 5 Hz), 5.6 (br, 1H, 2'-OH), 6.98 (s, 2H, -NH_2) (DMSO-d_6 / D_2O) δ 1.49-1.67 and 1.70-1.88 ppm (two m, 2H, H1"$_{A,B}$), 2.07 (h[7], 1H, H3'), 2.56-2.84 (m, 2H, H2"$_{A,B}$), 3.54 (A of ABX, 1H, H5'$_A$), 3.70 (B of ABX, 1H, H5'$_B$), 3.85 (dt, 1H, H4'), 3.98 (d, 1H, H2'), 5.60 (s, 1H, H1'), 5.68 (d, 1H, H5), 8.05 (d, 1H, H6), coupling constants (Hertz): $J_{H1'-H2'}$ ~ 0, $J_{H2'-H3'}$ = 4.6, $J_{H3'-H4'}$ = 11.6, $J_{H4'-H5'A}$ = 2, $J_{H4'-H5'B}$ = 3, $^2J_{H5'A-H5'B}$ = -12.3, J_{H5-H6} = 7.5; ^{13}C-NMR (DMSO-d_6, 300 MHz) δ 165.64 ppm (C4), 155.10 (C2), 140.81 (C6), 92.69 and 91.92 (C1' and C5), 84.60 (C4'), 75.30 (C2'), 59.82 (C5'), 38.66 (C3'), 35.56 (C2"), 23.88 (C1"); $[\alpha]^{22}_D$ = +104° (c = 0.270, DMSO); λ_{max} (methanol) 274 nm (ε 18400); HRMS (FAB-glycerol), m/e calcd. for $C_{22}H_{33}O_8N_6S_2$ [MH^+]: 573.1801, found: 573.1800; Anal. calcd. for $C_{22}H_{33}O_8N_6S_2$: C, 46.14; H, 5.63; N, 14.68; S, 11.20. found: C, 46.08; H, 5.73; N, 14.26; S, 11.05.

2'-O-Acetyl-2"-S-acetyl-N^6-benzoyl-5'-O-*t*-butyldiphenylsilyl-3'-deoxy-3'-C-(2"-mercaptoethyl)-adenosine (8).

Chlorotrimethylsilane (86 μL, 0.678 mmol) was added to a suspension of N^6-benzoyladenine[9] (213 mg, 0.890 mmol) in hexamethyldisilazane (6 mL) and the mixture refluxed under nitrogen. After 15 h the clear solution was evaporated *in vacuo* (0.02 mm Hg, 50°C) yielding a thick yellow syrup which was dissolved in dry 1,2-dichloroethane (2 mL). To this solution was added a solution of triacetate **1** (474 mg, 0.848 mmol) in dry 1,2-dichloroethane (5 mL) followed by trimethylsilyl trifluoromethanesulfonate (25 μL, 0.128 mmol). The resulting solution was then refluxed under nitrogen. After 15 h the reaction was cooled in ice, poured into ice-cold aqueous sodium bicarbonate solution (5 % w/v, 150 mL) and the product extracted with methylene chloride (150 mL). The organic phase was then dried (Na_2SO_4), filtered and the solvent removed *in vacuo* yielding a brown foam. Chromatography over silica gel (1 : 1 ethyl acetate / hexanes, v/v) afforded nucleoside **8** as an amorphous white solid (563 mg, 90 % yield). (It was found that a more convenient method is to use a stock solution of *bis*-(trimethylsilyl)-N^6-benzoyladenine in 1,2-dichloroethane rather than to generate the silylated base *in situ*.): ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.04 ppm (s, 9H, *t*-butyl), 1.72-1.93 and 1.48-1.67 (two m, 2H, H1"$_{A,B}$), 2.24 (s, 3H, OAc), 2.30 (s, 3H, SAc), 2.67-2.82 (m, 1H, H2"$_A$), 2.89-3.09 (m, 2H, H3' and H2"$_B$), 3.74 (A of ABX, 1H, H5'$_A$), 4.01-4.14 (overlapping B of ABX and dt, 2H, H5'$_B$ and H4'), 5.88 (d, 1H, H2'), 6.15 (d, 1H, H1'), 7.30-8.04 (two m, 15H, phenyls), 8.35 (s,1H, H8), 8.81 (s, 1H, H2), 9.0 (br and exchangeable, 1H, N**H**Bz), coupling constants (Hertz): $J_{H1'-H2'}$ = 1.0, $J_{H2'-H3'}$ = 5.3, $J_{H3'-H4'}$ = 10.8, $J_{H4'-H5'A}$ = 3.4, $J_{H4'-H5'B}$ = 2.7, $^2J_{H5'A-H5'B}$ = -11.9; ^{13}C-NMR ($CDCl_3$, 300 MHz) δ 195.24 ppm (S**C**OMe), 170.01 (O**C**OMe), 164.46 (N**C**OPh), 152.82 (C6), 151.00 (C2), 149.46 (C4), 141.45 (C8), 135.56; 135.42; 133.79; 132.65; 132.50; 129.97; 129.85; 128.81; 127.78 (phenyls), 123.16 (C5), 89.12 (C1'), 85.10 (C4'), 77.42 (C2'), 62.86 (C5'), 40.00 (C3'), 30.57 (SCO**Me**), 27.09 (C2"), 26.82 (C**Me**$_3$), 25.13 (C1"), 20.78 (OCO**Me**), 19.11 (**C**Me$_3$); $[\alpha]^{20}_D$ = +14.1° (c =

1.6, CHCl$_3$); λ_{max} (methanol) 282 nm (ε 19000); HRMS (CI-NH$_3$), m/e calcd. for $C_{35}H_{34}O_6N_5SSi$ [MH$^+$-C_4H_{10}]: 680.1999. found: 680.1998.

2'-O-Acetyl-2"-S-acetyl-N^6-benzoyl-3'-deoxy-3'-C-(2"-mercaptoethyl)-adenosine (9).

The desilylation of **8** was carried out in a manner identical to that described for the preparation of nucleoside **4** above. The 5'-alcohol **9** was thus obtained as a colorless solid in 97 % yield: ^{1}H-NMR (CDCl$_3$, 200 MHz) δ 1.60-1.98 (m, 2H, H1"$_{A,B}$), 2.23 (s, 3H, OAc), 2.31 (s, 3H, SAc), 2.72-3.13 (m, 3H, H3' and H2"$_{A,B}$), 3.72 (dd, 1H, H5'$_A$), 4.09-4.18 (m, 2H, H4' and H5'$_B$), 5.0 (br and exchangeable, 1H, 5'-OH), 5.52 (d, 1H, H2'), 6.07 (d, 1H, H1'), 7.46-8.06 (two m, 5H, phenyl), 8.26 (s, 1H, H8), 8.75 (s, 1H, H2), 9.3 (br and exchangeable, 1H, NHBz), coupling constants (Hertz): ^{13}C-NMR (CDCl$_3$, 75.4 MHz) δ 195.31 ppm (SCOMe), 170.37 (OCOMe), 164.78 (NCOPh), 152.30 (C6), 150.72 (C2), 149.66 (C4), 142.00 (C8), 133.49; 132.63; 128.63; 127.87 (phenyl), 123.27 (C5), 90.31 (C1'), 85.95 (C4'), 78.54 (C2'), 60.82 (C5'), 39.01 (C3'), 30.49 (SCO**Me**), 26.83 (C2"), 25.33 (C1"), 20.66 (OCO**Me**); $[\alpha]^{21}_D$ = -27.6° (c = 0.5, CHCl$_3$); UV (methanol) λ_{max} 282 nm (ε 19300) and 232 nm (ε 16200); HRMS (CI-NH$_3$), m/e calcd. for $C_{23}H_{26}O_6N_5S$ [MH$^+$]: 500.1604. found 500.1606.

3'-Deoxy-3'-C-(2"-mercaptoethyl)-adenosine disulfide (12).

Nucleoside **9** was deacylated as described for **11** above. Thus, disulfide **12** was obtained as a white crystalline solid in 81 % yield after recrystallization from methanol: m.p. 237-239°C (dec.); ^{1}H-NMR (DMSO-d_6, 200 MHz) δ 5.12 (t, 1H, 5'-OH, J = 5.3 Hz), 5.79 (d, 1H, 2'-OH, J = 5.3 Hz), 7.21 (s, 2H, -NH$_2$), (DMSO-d_6 / D$_2$O) 1.56-1.74 and 1.79-1.99 (two m, 2H, H1"$_{A,B}$), 2.40 (h^7, 1H, H3'), 2.56 (dd, 1H, H5'$_A$), 2.60-2.87 (m, 2H, H2"$_{A,B}$), 3.77 (dd, 1H, H5'$_B$), 3.94 (dt, 1H, H4'), 4.39 (d, 1H, H2'), 5.92 (d, 1H, H1'), 8.14 (s, 1H, H8), 8.40 (s, 1H, H2), coupling constants (Hertz): $J_{H1'-H2'}$ = 1.1, $J_{H2'-H3'}$ = 4.4, $J_{H3'-H4'}$ = 9.5, $J_{H4'-H5'A}$ = 3.7, $J_{H4'-H5'B}$ = 2.3, $^2J_{H5'A-H5'B}$ = -12.4; ^{13}C-NMR (DMSO-d_6, 75.4 MHz) δ 155.96 (C6), 152.39 (C2), 148.65 (C4), 138.65 (C8), 119.01 (C5), 90.43 (C1'), 84.86 (C4'), 75.15 (C2'), 60.75 (C5'), 39.87 (C3'), 35.64 (C2"), 24.49 (C1"); $[\alpha]^{22}_D$ = -31° (c = 0.259, DMSO); UV (1N NaOH) λ_{max} 262 (ε 15200); HRMS (FAB-glycerol), m/e calcd. for $C_{24}H_{33}O_6N_{10}S_2$ [MH$^+$]: 621.2026. found: 621.2024, m/e calcd. for $C_{24}H_{32}O_6N_{10}S_2Na$ [M+Na$^+$]: 643.18454. found: 643.18457; Anal. calcd. for $C_{24}H_{32}O_6N_{10}S_2 \cdot CH_4O$: C, 46.00; H,5.56; N, 21.46; S, 9.82. found: C, 45.87; H, 5.13; N, 21.67; S, 9.63.

2'-S-Acetyl-3-deoxy-1,2-O-isopropylidene-3-C-(2'-mercaptoethyl)-5-O-methanesulphonyl-α-D-ribofuranose (19).

Alcohol **14** was mesylated and worked up as described for the preparation of nucleoside **5** above which afforded **19** as a clear, colorless syrup in quantitative yield: ^{1}H-NMR (CDCl$_3$, 200 MHz) δ 1.34 and 1.51 ppm (two s, 6H, C**Me$_2$**), 1.48-1.68 (m, 1H, H1'$_A$), 1.88-2.13 (m, 2H, H3 and H1'$_B$), 2.36 (s, 3H, SAc), 2.96-3.14 (m, 2H, H2"$_{A,B}$), 3.07 (s, 3H, OMs), 4.02 (o, 1H, H4), 4.24 (A of ABX, 1H, H5$_A$), 4.43 (B of ABX, 1H, H5$_B$), 4.70 (apparent t, 1H, H2), 5.81 (d, 1H, H1), coupling constants (Hertz): J_{H1-H2} = 3.7, J_{H2-H3} = 4.1, J_{H3-H4} = 9.7, J_{H4-H5A} = 4.5, J_{H4-H5B} = 2.2, $^2J_{H5A-H5B}$ = -11.7; ^{13}C-NMR (CDCl$_3$, 75.4 MHz) δ 195.20 ppm (SCOMe), 111.64 (CMe$_2$), 104.63 (C1), 80.06 and 78.60 (C2 and C4), 68.37 (C5), 43.21 (C3), 37.22 (OMs), 30.31 (SCO**Me**), 26.62 and 26.42 (C1' and C2'), 26.02 and 24.38 (C**Me$_2$**); $[\alpha]^{20}_D$ = +74.4° (c = 2, CHCl$_3$); HRMS (CI-NH$_3$), m/e calcd. for $C_{13}H_{26}O_7S_2N$ [M+NH$_4^+$]: 372.11507. found: 372.11511.

2'-S-Acetyl-3-deoxy-1,2-isopropylidene-3-C-(2'-mercaptoethyl)-5-O-*p*-toluenesulfonyl-α-D-ribofuranose (20).

A solution of *p*-toluenesulfonyl chloride (3.72 g, 19.5 mmol) and alcohol **14** (3.60 g, 13.0 mmol) in dry pyridine (20 mL) was stirred at ambient temperature under nitrogen. After 20 h the reaction mixture was poured into ice water (200 mL), extracted with ethyl ether (2 x 200 mL), and washed with aqueous hydrochloric acid (2% v/v, 200 mL), saturated aqueous sodium bicarbonate solution (200 mL) and water (200 mL). The combined ether layers were then dried (MgSO$_4$), filtered and the solvent removed *in vacuo* yielding a yellow syrup. The crude product was chromatographed over silica gel (3 : 1 ethyl acetate / hexanes, v/v) affording tosylate **20** as a clear, colorless syrup (5.57 g, 99 % yield): ^{1}H-NMR (CDCl$_3$, 200 MHz) δ 1.31 and 1.45 (two s, 6H, C**Me**$_2$), 1.41-1.58 (m, 1H, H1'$_A$), 1.80-2.10 (m, 2H, H3 and H1'$_B$), 2.36 (s, 3H, SAc), 2.45 (s, 3H, TsCH$_3$), 2.84-3.07 (m, 2H, H2'$_{A,B}$), 3.90 (ddd, 1H, H4), 4.05 (A of ABX, 1H, H5$_A$), 4.21 (B of ABX, 1H, H5$_B$), 4.63 (apparent t, 1H, H2), 5.69 (d, 1H, H1), 7.35 and 7.80 (two d, 4H, aromatic H's, J = 8.4 Hz), coupling constants (Hertz): $J_{H1\text{-}H2}$ = 3.6, $J_{H2\text{-}H3}$ = 4.3, $J_{H3\text{-}H4}$ = 9.8, $J_{H4\text{-}H5A}$ = 3.9, $J_{H4\text{-}H5B}$ = 2.6, $^{2}J_{H5A\text{-}H5B}$ = -11.2; ^{13}C-NMR (CDCl$_3$, 75.4 MHz) δ 195.08 ppm (SCOMe), 144.66; 132.34; 129.58; 127.61 (aromatic C's), 111.46 (CMe$_2$), 104.51 (C1), 80.44 and 78.35 (C2 and C4), 68.34 (C5), 43.22 (C3), 30.25 (SCO**Me**), 26.36; 26.57; 25.98; 24.28 (C1',C2' and C**Me**$_2$), 21.26 (TsCH$_3$); [α]$^{20}_D$ = +58.6° (c = 1, CHCl$_3$); HRMS (CI-NH$_3$), m/e calcd. for C$_{19}$H$_{30}$O$_7$S$_2$N [M+NH$_4^+$]: 448.14637. found: 448.14634.

2',5-Anhydro-3-deoxy-1,2-O-isopropylidene-3-C-(2'-mercaptoethyl)-α-D-ribofuranose (21).

Method A: Benzyl mercaptan (19 µL, 0.155 mmol) and diazabicycloundecene (42 µL, 0.282 mmol) were successively added to a stirred solution of mesylate **19** (50 mg, 0.141 mmol) in dry N,N-dimethylformamide (0.8 mL) and the reaction heated to 40°C under nitrogen. After 1 h the reaction was extracted with methylene chloride (3 x 25 mL) and washed with dilute sulphuric acid (1% w/v, 25 mL), saturated aqueous sodium bicarbonate solution (25 mL) and water (2 x 25 mL). The combined organic phases were then dried (MgSO$_4$), filtered and the solvent removed *in vacuo* yielding a clear, colorless oil. Chromatography over silica gel afforded three products: cyclized sulfide **21** as a crystalline solid (26 mg, 85 % yield): m.p. 91-92°C; ^{1}H-NMR (CDCl$_3$, 300 MHz) δ 1.26 ppm (m[15], 1H, H3), 1.33 and 1.54 (two s, 6H, C**Me**$_2$), 1.90 (m[16], 1H, H1'$_{ax}$), 2.26 (dq, 1H, H1'$_{eq}$), 2.54-2.70 (m, 2H, H2'$_{A,B}$), 2.67 (A of ABX, 1H, H5$_{ax}$), 2.91 (B of ABX, 1H, H5$_{eq}$), 3.39 (td, 1H, H4), 4.60 (apparent t, 1H, H2), 5.77 (d, 1H, H1), coupling constants (Hertz): $J_{H1\text{-}H2}$ = 3.6, $J_{H2\text{-}H3}$ = 4.1, $J_{H3\text{-}H4}$ = 10.3 (other coupling constants given in TABLE 1); ^{13}C-NMR (CDCl$_3$, 75.4 MHz) δ 111.77 ppm (CMe$_2$), 103.76 (C1), 80.88 and 76.84 (C2 and C4), 49.29 (C3), 32.26 (C5), 28.37 and 27.55 (C1' and C2'), 26.23 and 26.00 (C**Me**$_2$); [α]$^{20}_D$ = +20.5° (c = 1, CHCl$_3$); HRMS (CI-NH$_3$), m/e calcd. for C$_{10}$H$_{17}$O$_3$S [MH$^+$]: 217.0898. found: 217.0899; Anal. calcd. for C$_{10}$H$_{16}$O$_3$S: C, 55.53; H, 7.46; S, 14.82. found: C, 55.39; H, 7.26; S, 14.78; the 5-S-benzyl sugar **24** as a clear, colorless oil (2 mg, 3.7 % yield): ^{1}H-NMR (CDCl$_3$, 200 MHz) δ 1.32 and 1.48 ppm (two s, 6H, C**Me**$_2$), 1.35-1.55 (m, 1H, H1'$_A$), 1.75-2.06 (m, 2H, H3 and H1'$_B$), 2.34 (s, 3H, SAc), 2.48 (A of ABX, 1H, H5$_A$), 2.76 (B of ABX, 1H, H5$_B$), 2.91-3.02 (m, 2H, H2'$_{A,B}$), 3.79 (s, 2H, CH$_2$Ph), 3.94 (h[7], 1H, H4), 4.64 (apparent t, 1H, H2), 5.80 (d,1H, H1), 7.20-7.35 (m, 5H, phenyl), coupling constants (Hertz): $J_{H1\text{-}H2}$ = 3.8, $J_{H2\text{-}H3}$ = 4.2, $J_{H3\text{-}H4}$ = 9.4, $J_{H4\text{-}H5A}$ = 5.8, $J_{H4\text{-}H5B}$ = 3.2, $^{2}J_{H5A\text{-}H5B}$ = -14.3; ^{13}C-NMR (CDCl$_3$, 75.4 MHz) δ 195.67 ppm (SCOMe), 138.38; 129.08; 128.44; 126.97 (phenyl), 111.57 (CMe$_2$), 104.81 (C1), 81.20 and 80.61 (C2 and C4), 46.66 (C3), 37.22 (CH$_2$Ph), 33.08 (C5), 30.65 (SCO**Me**), 27.18 and 26.38 (C1' and C2'), 26.38 and 24.75 (C**Me**$_2$); HRMS (CI-NH$_3$), m/e calcd. for C$_{19}$H$_{27}$O$_4$S$_2$ [MH$^+$]: 383.1351. found: 383.1350; and benzyl thiolacetate (17 mg) whose ^{1}H-NMR spectrum was identical to that of a commercial sample.

Method B: A solution of methanolic sodium hydroxide (1.0 N, 14.5 mL) was added to a stirred solution of tosylate **20** in methanol (50 mL) and the reaction stirred at ambient temperature. After 4 h glacial acetic acid (0.43 mL, 5.8 mmol) was added to the solution and the solvent was removed *in vacuo*. The residue was then extracted with methylene chloride (2 x 250 mL) and washed with saturated aqueous sodium bicarbonate solution (300 mL) and water (300 mL). The combined organic extracts were dried (MgSO$_4$), filtered and the solvent evaporated *in vacuo* affording a colorless syrup. Crystalline sulfide **21** was obtained upon standing in a dessicator (2.53 g, quantitative).

Acetolysis of (21) to 1,4-Di-O-acetyl-2',5-anhydro-3-deoxy-1,2-O-isopropylidene-3-C-(2'-mercaptoethyl)-D-ribofuranose (25).

Anhydrous *d,l*-camphorsulfonic acid (622 mg, 2.68 mmol) was added to a stirred solution of **21** (290 mg, 1.34 mmol) in glacial acetic acid (16 mL) containing acetic anhydride (3.2 mL) and the resulting solution stirred at 60°C under nitrogen. After 4 h the reaction was cooled in ice, slowly poured into a solution of sodium carbonate (45 g) in water (250 mL) and the resulting suspension swirled intermittently over 0.5 h. The product was then extracted with ethyl ether (2 x 200 mL) and washed with saturated aqueous sodium bicarbonate solution (250 mL) and water (250 mL). The combined ether layers were then dried ($MgSO_4$), filtered and the solvent removed *in vacuo* yielding a yellow syrup. Chromatography over silica gel (4 : 1 hexanes / ethyl acetate, v/v) afforded the unstable *aldehydo*-sugar **25** as a clear, slightly yellow syrup (278 mg, 65 % yield): ^1H-NMR ($CDCl_3$, 200 MHz) δ 1.43 and 1.46 ppm (two s, 6H, CMe_2), 1.71-1.92 (m, 1H, $H1'_{ax}$), 1.98-2.12 (m, 1H, H3), 2.07 and 2.08 (two s, 6H, OAc's), 2.23 (dq, 1H, $H1'_{eq}$), 2.50-2.62 (m, 2H, $H2''_{eq,ax}$), 2.56 (A of ABX, 1H, $H5_{ax}$), 2.82 (B of ABX, 1H, $H5_{eq}$), 4.15 (dd, 1H, H2), 4.96 (td, 1H, H4), 6.28 (d,1H, H1), coupling constants (Hertz): $J_{H1\text{-}H2}$ = 2.3, $J_{H2\text{-}H3}$ = 2.7, $J_{H3\text{-}H4}$ = 10.3, $J_{H4\text{-}H5eq}$ = 4.1, $J_{H4\text{-}H5ax}$ = 10.3, $^2J_{H5eq\text{-}H5ax}$ = -12.7; ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 170.36 and 169.81 ppm (OCOMe), 112.12 (CMe_2), 97.40 (C1), 83.56 (C2), 71.71 (C4), 42.27 (C3), 31.65 and 31.33 (C5 and C2'), 27.62 (C1'), 26.31 and 25.70 (**CMe$_2$**), 21.13 and 20.94 (**OCOMe**); No furthur characterization was possible for this compound due to its instability.

1,2-Di-O-Acetyl-2',5-anhydro-3-deoxy-3-C-(2'-mercaptoethyl)-D-ribofuranoses (22) and (23).

Amberlite 1R-50(H) resin was added to a stirred suspension of acetonide **21** (439 mg, 2.03 mmol) in water (4 mL) and the mixture was heated to 65°C in an oil bath. After 3 h the resin was filtered out of the homogeneous solution and washed thoroughly with methanol. Repeated coevaporation with toluene afforded a white solid (359 mg) which was dissolved in dry methylene chloride (10 mL) containing dry pyridine (821 µL, 10.2 mmol) and N,N-dimethylaminopyridine (~0.2 mmol). Acetic anhydride (766 µL, 8.12 mmol) was then added dropwise and the reaction stirred at ambient temperature under nitrogen. After 45 min the reaction was diluted with methylene chloride (150 mL), washed with dilute hydrochloric acid solution (1.5 % v/v, 200 mL) and water (200 mL), and reextracted with methylene chloride (150 mL). The combined organic phases were dried ($MgSO_4$), filtered and the solvent removed *in vacuo* yielding a white solid. Chromatography over silica gel (4.5 : 1 hexanes / ethyl acetate, v/v) afforded two products: α-acetate **22** as a clear, colorless oil (150 mg, 34 % yield): ^1H-NMR ($CDCl_3$, 200 MHz) δ 1.53 ppm (m^{15}, 1H, H3), 1.77 (m^{16}, 1H, $H1'_{ax}$), 2.02 and 2.08 (two s, 6H, OAc's), 2.13 (dq, 1H, $H1'_{eq}$), 2.47-2.65 (m, 2H, $H2'_{eq,ax}$), 2.61 (A of ABX, 1H, $H5_{ax}$), 2.88 (B of ABX, 1H, $H5_{eq}$), 4.08 (td, 1H, H4), 5.37 (apparent t, 1H, H2), 6.24 (d, 1H, H1), coupling constants (Hertz): $J_{H1\text{-}H2}$ = 4.3, $J_{H2\text{-}H3}$ = 5.2, $J_{H3\text{-}H4}$ = 10.3, (other coupling constants given in TABLE 1); ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 169.74 and 169.26 ppm (OCOMe), 94.56 (C1), 78.53 (C4), 72.86 (C2), 47.53 (C3), 32.32 (C5), 27.78 and 27.15 (C1' and C2'), 20.60 and 20.19 (**OCOMe**); $[\alpha]^{20}_D$ = +93.3° (c = 2, $CHCl_3$); HRMS (CI-NH_3), m/e calcd. for $C_9H_{13}O_3S$ [MH^+-AcOH]: 201.0585. found: 201.0584.; and β-diacetate **23** as colorless crystals (282 mg, 53 % yield): m.p. 125-126°C; ^1H-NMR ($CDCl_3$, 200 MHz) δ 1.59-1.82 ppm (m, 2H, H3 and $H1'_{ax}$), 2.08 and 2.12 (two s, 6H, OAc's), 2.27 (dq, 1H, $H1'_{eq}$), 2.52-2.75 (m, 2H, $H2'_{eq,ax}$), 2.72 (A of ABX, 1H, $H5_{ax}$), 2.98 (B of ABX showing an additional fine splitting, 1H, $H5_{eq}$), 4.06 (td, 1H, H4), 5.19 (d, 1H, H2), 5.99 (s, 1H, H1), coupling constants (Hertz): $J_{H1\text{-}H2}$ ~ 0, $J_{H2\text{-}H3}$ = 3.7, $J_{H3\text{-}H4}$ = 10.3, $J_{H4\text{-}H5eq}$ = 3.9, $J_{H4\text{-}H5ax}$ = 10.9, $^2J_{H5eq\text{-}H5ax}$ = -12.0, $^4J_{H2eq\text{-}H5eq}$ = -0.7; ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 169.93 and 169.30 ppm (OCOMe), 97.67 (C1), 80.31 (C4), 77.81 (C2), 45.40 (C3), 33.63 (C5), 28.21 and 27.70 (C1' and C2'), 21.04 and 20.62 (**OCOMe**); $[\alpha]^{20}_D$ = -126° (c = 1, $CHCl_3$); HRMS (CI-NH_3), m/e calcd. for $C_9H_{13}O_3S$ [MH^+-AcOH]: 201.0585. found: 201.0584; Anal. calcd. for $C_{11}H_{16}O_5S$: C, 50.76; H, 6.20; S, 12.32. found: C, 50.78; H, 6.12; S, 12.00.

2'-O-Acetyl-2",5'-anhydro-N^6-benzoyl-3'-deoxy-3'-C-(2"-mercaptoethyl)-adenosine (26).

Diacetate **23** (1.15g, 4.41 mmol) was dissolved in a stock solution of *bis*-(trimethylsilyl)-N^6-benzoyladenine in 1,2-dichloroethane (0.339 M solution, 14.3 mL, 4.86 mmol) to which was slowly added trimethylsilyl trifluoromethanesulfonate (170 µL, 0.882 mmol). After refluxing under a nitrogen atmosphere for 50 min the reaction was cooled in ice, diluted with methylene chloride (500 mL) and shaken vigorously with saturated aqueous sodium bicarbonate solution (500 mL). The organic layer was then dried (Na_2SO_4), filtered and the solvent removed *in vacuo*. Chromatography of the crude product over silica gel (25 : 1 methylene chloride / methanol, v/v) afforded nucleoside **26** as a colorless solid (1.72 g, 88 % yield). Recrystallization from methanol yielded colorless needles: m.p. 192-193°C (dec.); ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.82 ppm (qd, 1H, $H1''_{ax}$), 2.19 (s, 3H, OAc), 2.28-2.45 (m, 2H, H3' and $H1''_{eq}$), 2.58-2.85 (m, 2H, $H2''_{eq,ax}$), 2.88 (A of ABX, 1H, $H5'_{ax}$), 3.01 (B of ABX, 1H, $H5'_{eq}$), 4.12 (td, 1H, H4'), 5.68 (d,1H, H2'), 5.96 (d, 1H, H1'), 7.47-8.05 (two m, 5H, phenyl), 8.06 (s, 1H, H8), 8.79 (s, 1H, H2), 9.2 (br and exchangeable, 1H, NHBz), coupling constants (Hertz): $J_{H1'-H2'}$ = 0.8, $J_{H2'-H3'}$ = 5.0, $J_{H3'-H4'}$ = 10.6, (other coupling constants given in TABLE 1); ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 170.16 ppm (OCOMe), 164.73 (NCOPh), 152.67 (C6), 151.07 (C2), 149.66 (C4), 141.65 (C8), 133.53; 132.70; 128.74; 127.87 (phenyl), 123.49 (C5), 88.66 (C1'), 80.20 (C4'), 78.56 (C2'), 46.14 (C3'), 32.72 (C5'), 28.17 and 27.70 (C1" and C2"), 20.65 (OCOMe); $[\alpha]^{20}_D$ = -71.9° (c = 1.1, $CHCl_3$); UV (methanol) λ_{max} 282 nm (ε 20700) and sh. 234 nm (ε 14300); HRMS (CI-NH_3), m/e calcd. for $C_{21}H_{22}O_4N_5S$ [MH^+]: 440.13925. found: 440.13924; Anal. calcd. for $C_{21}H_{21}O_4N_5S$: C, 57.39; H, 4.82; N, 15.94; S, 7.29. found: C, 57.77; H, 5.06; N, 16.23; S, 7.07.

Oxidation of (26) to cyclic sulfone (28).

To an ice-cold solution of nucleoside **26** (500 mg. 1.14 mmol) in methanol (5 mL) was added a solution of Oxone reagent (1.05 g, 3.41 mmol) in water (5 mL) and the resulting suspension allowed to warm to room temperature with vigorous stirring. After 4 h the reaction was diluted with water (100 mL), extracted with chloroform (3 x 100 mL), and washed with water (100 mL) and brine (100 mL). The combined organic layers were dried (Na_2SO_4), filtered and the solvent removed *in vacuo* yielding a white solid. This material was chromatographed over silica gel (25 : 1 methylene chloride / methanol, v/v) affording sulfone **26** as a colorless glass (484 mg, 90 % yield): ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.92-2.20 ppm (m, 1H, $H1''_{ax}$), 2.17 (s, 3H, OAc), 2.25-2.38 (m, 1H, $H1''_{eq}$), 3.03-3.38 (m, 3H, H3' and $H2''_{eq,ax}$), 3.44 (A of ABX, 1H, $H5'_{ax}$), 3.67 (dt (B of ABX with an additional coupling), 1H, $H5'_{eq}$), 4.36 (td, 1H, H4'), 5.67 (d, 1H, H2'), 6.03 (s, 1H, H1'), 7.41-8.05 (two m, 5H, phenyl), 8.15 (s, 1H, H8), 8.75 (s, 1H, H2), 9.3 (br and exchangeable, 1H, NHBz), coupling constant (Hertz): $J_{H1'-H2'}$ ~ 0, $J_{H2'-H3'}$ = 5.4, $J_{H3'-H4'}$ = 11.4, $J_{H4'-H5'eq}$ = 3.9, $J_{H4'-H5'ax}$ = 12.2, $^2J_{H5'eq-H5'ax}$ = -12.2, $^4J_{H2''eq-H5'eq}$ = -2.7; ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 170.13 (OCOMe), 164.91 ppm (NCOPh), 152.37 (C6), 150.99 (C2), 149.71 (C4), 142.36 (C8), 133.11; 132.68; 128.58; 127.84 (phenyl), 123.62 (C5), 90.86 (C1'), 77.12 and 76,92 (C2' and C4'), 56.69 (C5'), 50.90 (C2"), 44.66 (C3'), 20.48 (OCOMe), 18.44 (C1"); $[\alpha]^{22}_D$ = -43.2° (c = 1, $CDCl_3$); UV (methanol) λ_{max} 280 nm (ε 16000) and sh. 234 nm (ε 10100); HRMS (CI-NH_3), m/e calcd. for $C_{21}H_{22}O_6N_5S$ [MH^+]: 472.1291. found: 472.1292.

Adenosyl 2",5'-cyclic sulfone (29).

An ice-cold solution of nucleoside **28** (215 mg, 0.456 mmol) in anhydrous methanol (9 mL) was saturated with ammonia gas and allowed to warm to room temperature. After 24 h the reaction was briefly heated to boiling and allowed to cool. The resulting fine crystalline solid (100 mg) was then filtered and washed repeatedly with cold methanol. Concentration of the filtrate resulted in the precipitation of additional nucleoside **29** (combined 118 mg, 80 % yield): m.p. 252°C (darkens); ^{1}H-NMR (DMSO-d_6, 300 MHz) δ 4.42 ppm (t, 1H, H2'), 5.84 (d, 1H, 2'-OH, J = 4.5 Hz), 7.12 (s, 2H, -NH_2), (DMSO-d_6 / D_2O) δ 1.81 (dtd, 1H, $H1''_{ax}$), 2.11 (dq, 1H, $H1''_{eq}$), 2.36 (m[11], 1H, H3'), 3.10-3.26 (m, 1H, $H2''_{eq,ax}$), 3.36 (apparent dt (A of ABX with an additional large coupling), 1H, $H5'_{eq}$), 3.50 (apparent t (B of ABX), 1H, $H5'_{ax}$), 4.17 (td, 1H, H4'), 4.41 (d, 1H, H2'), 5.97 (s, 1H, H1'), 8.15 and 8.20 (two s, 2H, H2 and H8), coupling constants (Hertz): $J_{H1'-H2'}$ ~ 0, $J_{H2'-H3'}$ = 4.6, $J_{H3'-H4'}$ = 11.3, (other coupling constants given in TABLE 1); ^{13}C-NMR ($CDCl_3$, 75.4 MHz) δ 156.04 (C6), 153.13 (C2), 149.08 (C4), 139.41 (C8), 119.02 (C5), 91.99 (C1'), 76.80 and 75.24 (C2' and C4'), 56.51 (C5'), 50.82 (C2"), 45.52 (C3'), 18.44 (C1"); $[\alpha]^{20}_D$ = -68.2° (c = 0.5, DMSO); UV (methanol) λ_{max} 262 nm (ε 12100); HRMS (CI-NH_3), m/e calcd. for $C_{12}H_{16}O_4N_5S$ [MH^+]: 326.0923. found: 326.0924; Anal. calcd. for $C_{12}H_{15}O_4N_5S$: C, 44.30; H, 4.65; N, 21.53; S, 9.85. found: C, 44.21; H, 4.93; N, 21.25; S, 9.68.

2",5'-Anhydro-3'-deoxy-3'-C-(2"-mercaptoethyl)-adenosine (27).

Method A: Alcohol **9** (150 mg, 0.300 mmol) was mesylated in a manner identical to that described for the preparation of **5** above. Mesylate **10** was obtained as an amorphous white solid in 96 % yield: ^{1}H-NMR (CDCl$_3$, 200 MHz) δ 1.63-1.84 and 1.87-2.08 (two m, 2H, H1"$_{A,B}$), 2.26 (s, 3H, OAc), 2.33 (s, 3H, SAc), 2.75-3.18 (m, 3H, H3' and H2"$_{A,B}$), 2.96 (s, 3H, OMs), 4.31 (dq, 1H, H4'), 4.49 (A of ABX, 1H, H5'$_A$), 4.54 (B of ABX, 1H, H5'$_B$), 5.85 (d, 1H, H2'), 6.11 (s, 1H, H1'), 7.47-8.06 (two m, 5H, phenyl), 8.18 (s, 1H, H8), 8.80 (s, 1H, H2), 9.2 (br and exchangeable, 1H, NHBz), coupling constants (Hertz): $J_{H1'-H2'}$ ~ 0, $J_{H2'-H3'}$ = 5.4, $J_{H3'-H4'}$ = 10.1, $J_{H4'-H5'A}$ = 4.7, $J_{H4'-H5'B}$ = 2.5, $^2J_{H5'A-H5'B}$ = -11.8; ^{13}C-NMR (CDCl$_3$, 75.4 MHz) δ 195.42 ppm (SCOMe), 170.07 (OCOMe), 164.92 (NCOPh), 151.78 (C6), 151.05 (C2), 149.14 (C4), 142.16 (C8), 132.98; 132.93; 128.76; 128.11 (phenyl), 122.48 (C5), 89.93 (C1'), 82.53 (C4'), 77.06 (C2'), 67.95 (C5'), 40.75 (C3'), 37.63 (OMs), 30.54 (SCO**Me**), 26.77 (C2"), 25.15 (C1"), 20.67 (OCO**Me**). Mesylate **10** was then dissolved in methanol (2 mL) to which was then added methanolic sodium hydroxide (1.0 N, 480 μL). After stirring for 16 h at ambient temperature the resulting solid was filtered. Reduction of the filtrate volume to 0.5 mL resulted in the precipitation of additional product. The combined solids were then recrystallized from methanol affording nucleoside **27** as colorless needles (51 mg, 58 % yield from **9**): m.p. 237-239°C (dec.); ^{1}H-NMR (CD$_3$OD, 300 MHz) δ 1.75-1.97 ppm (m, 2H, H3' and H1"$_{ax}$), 2.23 (dq, 1H, H1"$_{eq}$), 2.58 (dddd, 1H, H2"$_{eq}$), 2.72 (ddd, 1H, H2"$_{ax}$), 2.88 (A of ABX, 1H, H5'$_{ax}$), 2.94 (B of ABX, 1H, H5'$_{eq}$), 4.13 (td, 1H, H4'), 4.43 (d, 1H, H2'), 5.91 (s, 1H, H1'), 8.12 and 8.20 (two s, 2H, H2 and H8), coupling constants (Hertz): $J_{H1'-H2'}$ ~ 0, $J_{H2'-H3'}$ = 4.3, $J_{H3'-H4'}$ = 10.2, (other coupling constants given in TABLE 1); ^{13}C-NMR (CD$_3$OD, 75.4 MHz) δ 157.39 ppm (C6), 153.91 (C2), 150.07 (C4), 140.32 (C8), 120.67 (C5), 92.15 (C1'), 81.43 (C4'), 78.39 (C2'), 48.51 (C3'), 33.80 (C5'), 29.16 and 28.86 (C2' and C1'); $[\alpha]^{20}_D$ = -115° (c = 1, DMSO); UV (methanol) λ_{max} 262 nm (ε 13700); HRMS (CI-NH$_3$), m/e calcd. for $C_{12}H_{16}O_2N_5S$ [MH$^+$]: 294.10247. found: 293.10251.

Method B: An ice-cold solution of nucleoside **26** (300 mg, 0.683 mmol) in dry methanol (8 mL) was saturated with ammonia gas and allowed to warm to room temperature. After 30 h the reaction was briefly heated to boiling and then allowed to cool, resulting in the formation of fine white crystals which were filtered and washed repeatedly with cold methanol (107 mg). The filtrate was evaporated *in vacuo* to a yellow solid which was washed repeatedly with acetone. Recrystallization of the resulting white powder from methanol / water afforded an additional 48 mg of nucleoside **27** as colorless needles (combined 155 mg, 77 % yield).

2'-O-*t*-butyldiphenylsilyl-3-deoxy-3-C-(2"-hydroxyethyl)-1,2-O-isopropylidene-5-O-methanesulfonyl-α-D-ribofuranose (16).

Alcohol **15** was mesylated in a manner identical to that described for the preparation of **5** above. Chromatography of the crude product over silica gel (3 : 1 hexanes / ethyl acetate, v/v) afforded mesylate **16** as a clear, colorless syrup (260 mg, 93 % yield): ^{1}H-NMR (CDCl$_3$, 200 MHz) δ 1.07 ppm (s, 9H, *t*-butyl), 1.26 and 1.47 (two s, 6H, C**Me$_2$**), 1.41-1.65 and 1.75-1.92 (two m, 2H, H1'$_{A,B}$), 2.17 (tt, 1H, H3), 3.03 (s, 3H, OMs), 3.70-3.90 (m, 2H, H2'$_{A,B}$), 4.02 (ddd, 1H, H4), 4.20 (A of ABX, 1H, H5$_A$), 4.41 (dd, 1H, H2), 4.43 (B of ABX, 1H, H5$_B$), 5.73 (d, 1H, H1), 7.38-7.72 (m, 10H, phenyls), coupling constants (Hertz): J_{H1-H2} = 3.6, J_{H2-H3} = 4.3, J_{H3-H4} = 10.5, J_{H4-H5A} = 5.0, J_{H4-H5B} = 2.2, $^2J_{H5A-H5B}$ = -11.7; ^{13}C-NMR (CDCl$_3$, 75.4 MHz) δ 135.52; 135.48; 133.53; 133.49; 129.68; 127.66 ppm (phenyls), 111.71 (**C**Me$_2$), 104.90 (C1), 80.62 and 79.11 (C2 and C4), 68.79 (C5), 61.76 (C2'), 41.61 (C3), 37.54 (OMs), 27.36 (C1'), 26.83 (C**Me$_3$**), 26.70 and 26.18 (C**Me$_2$**), 19.08 (**C**Me$_2$); $[\alpha]^{20}_D$ = +35.0° (c = 2.5, CHCl$_3$); HRMS (CI-NH$_3$), m/e calcd. for $C_{27}H_{42}O_7NSSi$ [M+NH$_4^+$]: 552.2451. found: 552.2452.

3-Deoxy-3-C-(2'-hydroxyethyl)-1,2-O-isopropylidene-5-O-methanesulfonyl-α-D-ribofuranose (17).

A solution of tetra-*n*-butylammonium fluoride trihydrate (95 mg, 0.30 mmol) and mesylate **16** (107 mg, 0.200 mmol) in dry tetrahydrofuran (1.0 mL) was stirred at ambient temperature under nitrogen. After 1 h the solvent was removed *in vacuo* and the resulting solid extracted with methylene chloride (2 x 30 mL) and washed with water (30 mL) and brine (30 mL). The combined organic phases were then dried (MgSO$_4$), filtered and evaporated *in vacuo* yielding a colorless syrup. This material was chromatographed over silica gel (3 : 1 ethyl acetate / hexanes, v/v) affording the unstable alcohol **17** as a clear, colorless syrup (49 mg, 83 % yield): ^{1}H-NMR (CDCl$_3$, 200 MHz) δ 1.34 and 1.51 ppm (two s, 6H, C**Me$_2$**), 1.58-1.74 and 1.81-1.98 (two m, 2H, H1'$_{A,B}$), 2.0 (br and exchangeable, 1H, 2'-OH), 2.18 (tt, 1H, H3), 3.08 (s, 3H, OMs), 3.68-3.86 (m, 2H, H2'$_{A,B}$), 4.07 (ddd, 1H, H4), 4.30 (A of ABX, 1H, H5$_A$), 4.48 (B of ABX, 1H, H5$_B$), 4.73 (apparent t, 1H, H2), 5.82 (d, 1H, H1), coupling constants (Hertz): $J_{H1\text{-}H2}$ = 3.6, $J_{H2\text{-}H3}$ = 4.6, $J_{H3\text{-}H4}$ = 10.4, $J_{H4\text{-}H5A}$ = 4.4, $J_{H4\text{-}H5B}$ = 2.2, $^2J_{H5A\text{-}H5B}$ = -11.7; ^{13}C-NMR (CDCl$_3$, 75.4 MHz) δ 111.86 ppm (**C**Me$_2$), 104.84 (C1), 80.86 and 79.16 (C2 and C4), 68.59 (C5), 60.58 (C2'), 41.55 (C3), 37.54 (OMs), 27.46 (C1'), 26.66 and 26.23 (C**Me$_2$**); No furthur characterization was possible for this compound due to its instability.

2',5-Anhydro-3-deoxy-3-C-(2'-hydroxyethyl)-1,2-O-isopropylidene-α-D-ribofuranose (18).

To a stirred suspension of sodium hydride (60 % oil disp., 14 mg) in dry tetrahydrofuran (0.3 mL) cooled to 0°C was slowly added a solution of mesylate **17** (45 mg, 0.152 mmol) in dry tetrahydrofuran (1.5 mL). After 20 h of stirring at ambient temperature the solvent was removed *in vacuo* and the resulting syrup was extracted with methylene chloride (2 x 20 mL) and washed with aqueous sodium bicarbonate solution (5 % w/v, 25 mL) and water (25 mL). The combined organic phases were then dried (MgSO$_4$), filtered and evaporated *in vacuo* to a colorless syrup which was chromatographed over silica gel (2 : 1 hexanes / ethyl acetate, v/v) affording cyclic ether **18** as a crystalline solid (7 mg, 23 % yield): m.p. 101°C; ^{1}H-NMR (CDCl$_3$, 200 MHz) δ 1.34 and 1.53 ppm (two s, 6H, C**Me$_2$**), 1.36-1.51 (m, 1H, H3), 1.72-1.97 (m, 2H, H1'$_{eq,ax}$), 3.22-3.38 (m, 1H, H2'$_{ax}$), 3.30 (apparent t, 1H, H5$_{ax}$), 3.70 (td, 1H, H4), 4.04 (ddd, 1H, H2'$_{eq}$), 4.28 (dd, 1H, H5$_{eq}$), 4.66 (apparent t, 1H, H2), 5.84 (d,1H, H1), coupling constants (Hertz): $J_{H1\text{-}H2}$ = 3.5, $J_{H2\text{-}H3}$ = 3.9, $J_{H3\text{-}H4}$ = 10.3, (other coupling constants given in TABLE 1); ^{13}C-NMR (CDCl$_3$, 75.4 MHz); δ 112.04 ppm (**C**Me$_2$), 105.63 (C1), 79,92 (C2), 74.05 (C4), 70.73 (C5), 67.46 (C2'), 48.20 (C3), 26.14 and 26.00 (C**Me$_2$**), 25.75 (C1'); HRMS (CI-NH$_3$), m/e calcd. for $C_{10}H_{17}O_4$ [MH$^+$]: 201.112684. found: 201.112680.

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