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Convergent Synthesis of 2′,3′-Dideoxy-3′-mercapto Nucleosides – Potential Anti-HIV Agents

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Summary. Methyl 3-benzoylthio-5-O-*tert*-butyldiphenylsilyl-2,3-dideoxy-*β-D-erythro*-pentofuranoside (**4**) and its corresponding α anomer **5** were synthesized in four steps from 2-deoxy-*D*-ribose and used as substrates for the synthesis of nucleosides by condensation with silylated thymidine and N^6-isobutyryladenine. The nucleosides were deprotected by treatment with Bu_4NF in *THF* followed by reaction with MeONa in MeOH to give 3′-deoxy-3′-mercaptothymidine (**8**), 2′,3′-dideoxy-3′-mercaptoadenosine (**15**) and its corresponding α anomer **16**. In the latter reactions it was important to use degassed solvents to minimize formation of the corresponding disulfides of purine nucleosides. Using Bu_4NF, without subsequent reaction with MeONa in the deprotection reaction, resulted in intermolecular transesterification reactions.

Keywords. Adenosine, 2′,3′-dideoxy-3′-mercapto; Thymidine, 3′-deoxy-3′-mercapto; Human immunodeficiency virus; Herpes simplex virus.

Konvergente Synthese von 2′,3′-Dideoxy-3′-mercapto-nucleosiden – Potentielle Anti-HIV Wirkstoffe

Zusammenfassung. Methyl-3-benzoylthio-5-O-*tert*-butyldiphenylsilyl-2,3-dideoxy-*β-D-erythro*-pentofuransoid (**4**) und sein entsprechendes α-Anomeres wurden in vier Stufen, ausgehend von 2-Deoxy-*D*-ribose, hergestellt und als Substrat für die Synthese von Nucleosiden durch Kondensation mit silyliertem Thymidin und N^6-Isobutyryladenin verwendet. Die Nucleoside wurden durch Behandeln mit Bu_4NF in *THF* und anschließende Reaktion mit MeONa in MeOH zu 3′-Deoxy-3′-mercaptothymidin (**8**), 2′,3′-Dideoxy-3′-mercaptoadenosin (**15**) und seinem entsprechenden α-Anomeren **16** entschützt. Bei letzterer Reaktion war die Verwendung von entgasten Lösungsmitteln wesentlich, um die Bildung der entsprechenden Disulfide der Purinnucleoside hintanzuhalten. Die Verwendung von Bu_4NF ohne anschließende Reaktion mit MeONa bei der Abspaltung der Schutzgruppen führte zu intermolekularen Umesterungen.

Introduction

Since the human immunodeficiency virus (HIV) was found to be the causative agent of AIDS [1, 2], the interest in 2′,3′-nucleosides has been spurred by the selectivity

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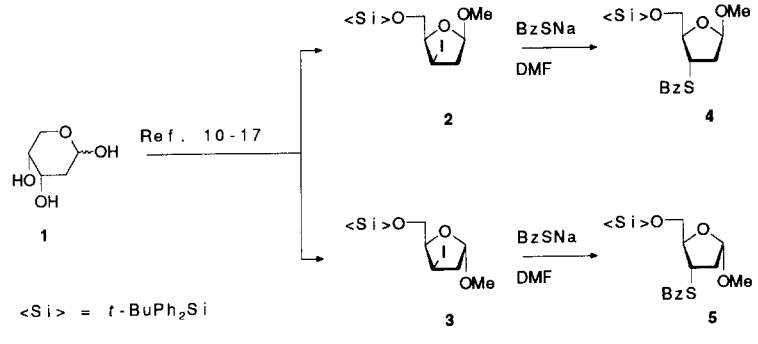
with which 3′-azido-3′-deoxythymidine (*AZT*) inhibits the replication of HIV [3–5]. The 2′-3′-dideoxy nucleosides compete with natural substrates during the reverse transcriptase and/or cause chain termination subsequent to incorporation into the *DNA* [6]. We found it interesting to synthesize various novel 2′,3′-deoxy nucleosides with a substituent in the 3′-position different from azido, yet retaining some of the characteristics of this group. The mercapto group was a substituent of particular interest, since its steric bulk is comparable to that of the azido group (as expressed by their molar refractivity values: SH 0.39; N_3 0.46) [7]. In addition, this substituent is electronically similar to azido (polar F values: SH 0.28; N_3 0.30) [7]. The mercapto group is indeed of interest as reported in a recent paper by *Yuzhakov et al.* [8] who found that 3′-mercapto-3′-deoxythymidine suppresses HIV viruses as efficiently as *AZT*. We can now report that we have been unable to confirm its activity against HIV after preparing this compound by an independent route in our laboratory. We have previously found that 2′,3′-dideoxy-3′-mercaptocytidine showed protection against HIV-1 in MT-4 cells with $ED_{50} = 20\,\mu M$ [9]. This paper describes the convergent syntheses of 2′,3′-dideoxy-3′-mercapto-*β-D-erythro*-pentofuranosyl nucleosides with thymidine and adenine as the nucleobases.

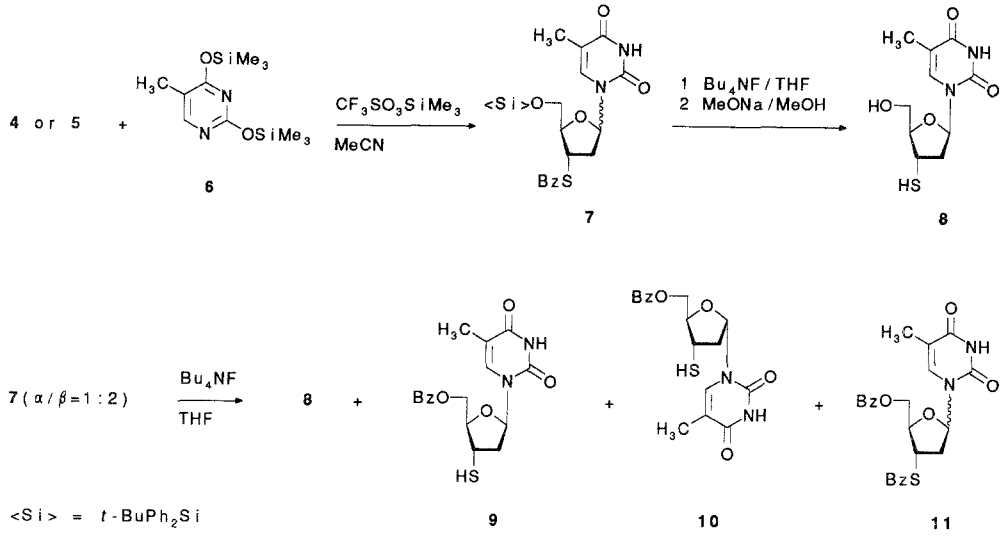
Results and Discussion

The conversion of 2-deoxy-*D*-ribose **1** to methyl 5-O-*tert*-butyldiphenylsilyl-3-iodo-2,3-dideoxy-*β-D-erythro*-pentofuranoside **2** and its α-anomer **3** has been described thoroughly in the literature. Their synthesis starts with a glycosidation of **1** with hydrochloric acid in methanol with concomitant ring contraction to a pentofuranoside [10–15] which is selectively protected at the primary hydroxy group. Treatment with *tert*-butyldiphenylchlorosilane in N,N-dimethylformamide (*DMF*) in the presence of imidazole [16, 17] afford methyl 5-O-*tert*-butyldiphenylsilyl-2-deoxy-*D-erythro*-pentofuranoside, which was treated with methyl iodide in the presence of triphenylphosphine and diethyl azodicarboxylate (*DEAD*) in dry toluene [18, 19] to afford the iodides **2** and **3** [17]. The benzoylthio group was introduced into the 3-position by reaction with sodium thiobenzoate in dry *DMF* to give **4** and its α anomer **5** in 78–80% yield, following a procedure that has been devised be *Cosstick* and *Vyle* [20].

Silylation of the nucleobases in order to obtain **6** and **12** was accomplished according to standared procedures [21, 22] by refluxing the nucleobases in



Scheme 1

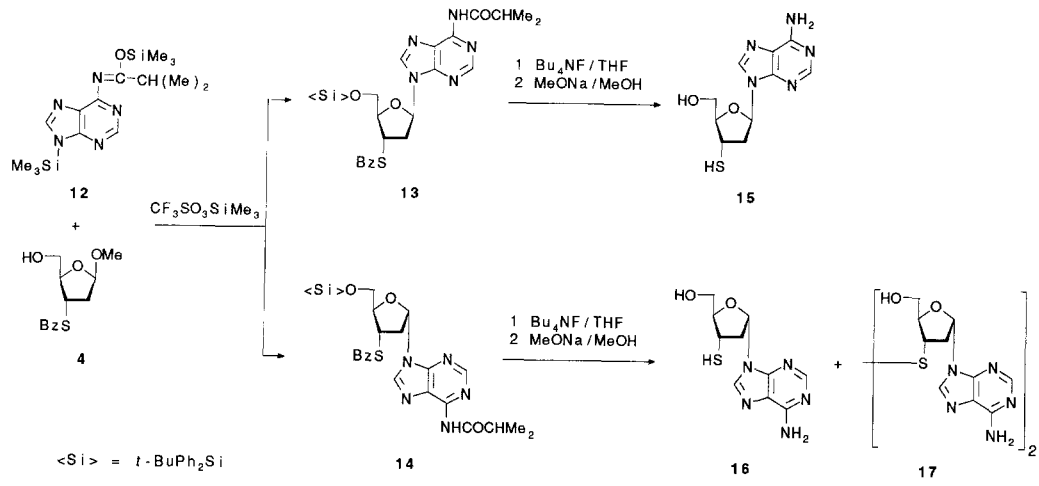


Scheme 2

1,1,1,3,3,3-hexamethyldisilazane (*HMDS*) in the presence of catalytic amounts of ammonium sulfate. Condensation of the β-anomeric thiobenzoate **4** and silylated thymine **6** was performed according to the *Friedel–Crafts* catalyzed [23] silyl *Hilbert–Johnson*-reaction modified by *Vorbrüggen et al.* [22]. The reaction was performed in dry acetonitrile in the presence of trimethylsilyl trifluoromethanesulfonate (*TMS* triflate) and **7** was produced in 85% yield ($\alpha/\beta = 1:2$). On the other hand, condensation of the α-anomeric thiobenzonate **5** and the silylated nucleobase **6** under similar conditions produced **7** in 83% yield ($\alpha/\beta = 1:5$). The more favorable α/β ratio obtained in the anomeric mixture of nucleosides, when starting from the α methyl glycoside **5**, is rather difficult to explain, since the mechanism of condensation of methyl glycosides with nucleobases is very complex as it was reported by *Jørgensen et al.* [24]. The protected nucleoside **7** ($\alpha/\beta = 1:5$) was deblocked through treatment with tetrabutylammonium fluoride (Bu_4NF) in tetrahydrofuran (*THF*), followed by reaction with sodium methoxide in methanol and subsequent neutralization by hydrochloric acid in methanol. 71% yield of **8** was obtained when the deblocking reaction was performed under nitrogen to prevent oxidation of the deprotected product to the corresponding disulfide by atmospheric oxygen [9, 25]. When the protected nucleoside **7** ($\alpha/\beta = 1:2$) was deblocked through treatment with Bu_4NF in *THF* under nitrogen without subsequent addition of sodium methoxide, intermolecular transfer of benzoyl groups seemed to take place and the products **8**, **9**, **10** and **11** were isolated in 8–18% yields after separation by reversed phase chromatography.

Condensation of the thiobenzoate **4** with the silylated adenine derivative **12** produced **13** and **14** in 15–18% yields. The protected nucleosides **13** and **14** were again deblocked by treatment with tetrabutylammonium fluoride in *THF*, followed by addition of sodium methoxide in methanol.

It is important to use degassed solvents in order to minimize disulfide formation, but even then the disulfide **17** was formed in 12% yield together with the α nucleoside **16** in 15% yield when **14** was



Scheme 3

deblocked. Under similar conditions it was possible to avoid disulfide formation during deblocking of the β anomer **13** and free nucleoside **15** was obtained in 46% yield.

The configuration of **4** was deduced from NOE spectra: on irradiation of the 1-H resonance, an NOE enhancement (6%) was observed for the 2α-H resonance at 2.08 ppm. On irradiation of the 2β-H resonance at 2.59 ppm a strong enhancement (9%) was observed for the 3-H resonance which also showed a strong enhancement (5%) on irradiation of 5-H. Minor discrepancies were observed between our ^{1}H NMR spectrum of 3′-deoxy-3′-mercaptothymidine (**8**) and the one previously reported for the same compound [8]. We certainly have isolated a 3′-mercapto derivative and not the corresponding disulfide as revealed by the SH resonance found as a doublet at 1.78 ppm which couples with 3′-H (3.54 ppm) as confirmed by the HH-COSY experiment. In the ^{13}C NMR spectrum, the C-3′ resonance of **8** was found at 42.64 and not at the typical value ($\sim$46 ppm) of the corresponding disulfide [9]. Typically for a β anomer we observed strong NOE enhancements for the 3′-H (10%) and 1′-H (11%) resonance of **8** upon specific irradiation of 2′β-H and 2′α-H, respectively. The assignment of the configuration of the products **9**, **10** and **15–17** was accomplished by comparison with **8** and with the corresponding 2′,3′-dideoxy-3′-mercapto-β-*D-erythro*-pentofuranosyl nucleosides and their disulfides that previously have been synthesized [9]. The chemical shifts of 5′-H of 4′-H (in particular of the latter) indicate the configuration of C-1′; if the 4′-H is *syn* to the base moiety, it will appear at a lower field than if it is *anti* to the base moiety due to a larger deshielding. The same relationship holds for 5′-H [26, 27]. These considerations add up to the α-anomer having 4′-H at a lower field and 5′-H a higher field than is the case for the β anomer.

We were unable to confirm the previously reported [8] against HIV-1 in MT-4 cells when 3′-deoxy-3-mercapto thymidine (**8**) was tested at 100 μM. The corresponding 2′,3′-dideoxy-3′-mercaptoadenosine (**15**) also was devoid of any activity at 100 μM against HIV-1 in MT-4 cells. MT-4 cells were incubated with virus, washed and added in a proportion of 1:10 to uninfected MT-cells which had

been preincubated in test compared containing culture medium (RPM 1640 containing 10% FCS) for 2 h. The MT-4 cells were maintained in culture medium likewise containing the test compound. Expression of HIV in culture medium was quantiated by HIV antigen detection ELISA.

Experimental

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC 250 FT spectrometer or a Varian UNITY 500 spectrometer. IR spectra were recorded with a Perkin–Elmer 1720 spectrometer. Mass spectra (MS) were recorded using electron ionization (EI) on a Varian 311A spectrometer and fast atom bombardment (FAB) on a Kratos MS-50 spectrometer. The silica gel (0.040–0.063 mm) used for column chromatography was purchased from Merck.

Methyl 3-Benzoylthio-5-O-tert-butyldiphenylsilyl-2,3-dideoxy-β-D-erythro-pentofuranoside (**4**; $C_{29}H_{34}O_4SSi$)

A solution of methyl 5-*O-tert*-butyldiphenylsilyl-3-iodo-2,3-dideoxy-β-*D-threo*-pentofuranoside **2** (3.80 g, 7.6 mmol) and sodium thiobenzoate (4.50 g, 28 mmol) in anhydrous *DMF* (60 ml) was stirred at 75 °C for 5 h. After cooling to r.t., CH_2Cl_2 (300 ml) was added and the mixture was washed with saturated aqueous $NaHCO_3$ (2 × 300 ml) with saturated aqueous NaCl (2 × 200 ml). The organic phase was dried (Na_2SO_4) and evaporated to dryness to yield a yellow residue which was purified on a silica gel column with petroleum ether (65–70 °C)/Et_2O (9:1, v/v) to give 3.1 g (80%) of **4** as a pale yellow oil. IR (KBr), $\nu = 1667\ cm^{-1}$ (C=O); MS. *m/z* (%) = 449 (M^+–Me_3C, 36); ^1H NMR ($CDCl_3$/*TMS*, 250 MHz): $\delta = 1.06$ (9H, s, 3 CH_3), 2.08 (1H, ddd, $J = 4.6$, 8.6, 14.2 Hz, 2'α-H), 2.59 (1H, ddd, $J = 1.2$, 7.5, 13.1 Hz, 2'β-H), 3.31 (3H, s, OCH_3), 3.79–3.90 (2H, m, 5'-H), 4.14–4.19 (1H, m, 4'-H), 4.26 (1H, td, $J = 7.4$, 9.0 Hz, 3'-H), 5.09 (1H, dd, $J = 1.0$, 4.0 Hz, 1'-H), 7.32–7.94 (15 Hz, m, H_{arom}); ^{13}C NMR ($CDCl_3$/*TMS*, 62.9 MHz): $\delta = 19.19$ (C–Si), 26.68 (CH_3), 40.44, 40.73 (C-2', C-3'), 54.61 (OCH_3), 65.66 (C-5'), 84.46 (C-4'), 104.86 (C-1'), 127.11, 127.49, 127.52, 128.47, 129.46, 133.29, 135.51, 135.54 (C_{arom}), 190.46 (C = O).

Methyl 3-Benzoylthio-5-O-tert-butyldiphenylsilyl-2,3-dideoxy-α-D-erythro-pentofuranoside (**5**; $C_{29}H_{34}O_4SSi$)

The anomer **5** was prepared as described for **4**. The mixture was chromatographed on silica gel with petroleum ether (65–70 °C)/Et_2O (9:1, v/v) to yield 3.0 g (78%) of **5** as a pale yellow oil. IR (KBr), $\nu = 1661\ cm^{-1}$ (C=O); MS, *m/z* (%) 449 (M^+–Me_3C, 34); ^1H NMR ($CDCl_3$/*TMS*, 250 MHz): $\delta = 1.07$ (9H, s, 3 CH_3), 2.03 (1H, ddd, $J = 1.2$, 3.7, 13.9 Hz, 2'α-H), 2.75 (1H, ddd, $J = 4.8$, 9.3, 14.00 Hz, 2'β-H), 3.39 (3H, s, OCH_3), 3.89 (2H, t, $J = 3.8$ Hz, 5'-H), 4.17 (1H, td, $J = 3.5$, 5.5 Hz, 4'-H), 4.22–4.28 (1H, m, 3'-H), 5.16 (1H, dd, $J = 1.1$, 5.0 Hz, 1'-H), 7.35–7.94 (15H, m, H_{arom}); ^{13}C NMR ($CDCl_3$/*TMS*, 62.9 MHz): $\delta = 19.19$ (C–Si), 26.73 (CH_3), 40.10, 40.31 (C-2', C-3'), 54.67 (OCH_3), 64.78 (C–5'), 84.80 (C–4'), 104.99 (C–1'), 127.14, 127.53, 127.56, 128.45, 129.50, 129.53, 133.24, 135.59 (C_{arom}), 191.50 (C=O).

1-(3-Benzoylthio-5-tert-butyldiphenylsilyl-2,3-dideoxy-D-erythro-pentofuranosyl)thymine (**7**; $C_{33}H_{36}N_2O_5SSi$)

The silylated thymine (**6**, 4 mmol) was dissolved in anhydrous MeCN (20 ml) and the benzoylthio derivative **4** (1.0 g, 2 mmol) dissolved in anhydrous MeCN (10 ml) was added. The mixture was cooled to −50 °C and $CF_3SO_3SiMe_3$ (0.6 ml, 3 mmol) dissolved in anhydrous MeCN (5 ml) was added dropwise with stirring. The mixture was stirred for 2 h at −30 °C and then overnight at −10 °C. The mixture was diluted with CH_2Cl_2 (200 ml), washed with cold saturated aqueous $NaHCO_3$ (200 ml)

and water (2 × 100 ml) and dried over Na_2SO_4. After evaporation to dryness, the residue was chromatographed on silica gel with petroleum ether (65–70 °C)/Et_2O (7:3, v/v) to yield 1.02 g (85%) of **7** as a white foam ($\alpha/\beta = 1:2$). FAB MS (MeOH + 3-nitrobenzylalcohol), m/z (%) = 601 ($M + H^+$).

Preparation of **7** *starting from* **5**

Using the benzoylthio derivative **5** instead of **4**, the same procedure as above was followed for the preparation of **7**. The mixture was chromatographed on silica gel with petroleum ether (65–70 °C)/Et_2O (7:3, v/v) to give 1.0 g (83%) of **7** as white foam ($\alpha/\beta = 1:5$).

3′-Deoxy-3′-mercaptothymidine (**8**; $C_{10}H_{14}N_2O_4S$ (HRMS))

A solution of **7** (0.7 g, 1.1 mmol, α/β 1:5) in *THF* (15 ml) and 1*M* Bu_4NF/*THF* (2 ml, 2 mmol) was stirred under N_2. After complete reaction (30 min), the solvent was removed *in vacuo*. The residue was dissolved in MeOH (10 ml) and NaOMe [prepared from Na (0.05 g, 2.2 mmol)] in MeOH (10 ml) was added dropwise at r.t. under N_2 and stirring was continued for 4 h. The solution was neutralized ($pH = 5$) by addition of HCl in MeOH. The solvent was evaporated and the crude material was purified by column chromatography on silica gel with 1–5% MeOH in $CHCl_3$ to give **8** as a white foam, yield 0.20 g (70%). ^{1}H NMR ($CDCl_3$/*TMS*, 250 MHz): $\delta = 1.78$ (1H, d, $J = 7.8$ Hz, SH) 1.87 (3H, s, CH_3), 2.29–2.42 (1H, m, 2′α-H), 2.53–2.62 (1H, ddd, $J = 3.1$, 8.0, 14.0 Hz, 2′β-H), 3.54 (1H, quint., $J = 8.6$, 3′-H), 3.84 (1H, m, 4′-H), 3.91 (1H, dd, $J = 2.5$, 12.4 Hz, 5′-H), 4.06 (1H, dd, $J = 2.0$, 12.4 Hz, 5′-H), 5.30 (1H, s, 5′-OH), 6.14 (1H, dd, $J = 3.1$, 7.4 Hz, 1′-H), 7.59 (1H, s, 6-H), 9.61 (1H, s, NH); ^{13}C NMR ($CDCl_3$/*TMS*, 62.9 MHz): $\delta = 12.33$ (CH_3), 33.58 (C-2′), 42.64 (C-3′), 59.70 (C-5′), 84.77, 88.77 (C-1′ and C-4′), 110.56 (C-5), 136.42 (C-6), 150.35 (C-2), 164.08 (C-4).

5′-O-Benzoyl-3′-deoxy-3′-mercaptothymidine (**9**), *1-(5-O-Benzoyl-2,3-dideoxy-3-mercapto-α-D-erythro-pentofuranosyl)thymine* (**10**) *and 1-(5-O-benzoyl-3-benzoylthio-2,3-dideoxy-D-erythro-pentofuranosyl)thymine* (**11**):

A solution of **7** (1.1 g, 1.8 mmol, α/β 1:2) in *THF* (20 ml) and 1*M* Bu_4NF/*THF* (3.1 ml, 3.1 mmol) was stirred under N_2. After complete reaction (30 min), the solvent was removed *in vacuo*. The crude material was purified by column chromatography on silica gel with 1–5% MeOH in $CHCl_3$ to give a colourless oil. The oil was further purified on HPLC with 25% EtOH in water on a reversed phase column (RP-18, 15 μ*M*, 300A) to give the products **8** (13%), **9**, **10** and **11**.

Compound **9**: Yield, 60 mg (9%) as a white foam; FAB MS (*DMSO* + 1% AcOH + 3-nitrobenzylalcohol), m/z (%) = 363 ($M + H^+$); ^{1}H NMR ($CDCl_3$/*TMS*, 250 MHz): $\delta = 1.65$ (3H, s, CH_3), 2.35–2.48 (1H, m, 2′α-H), 2.55–2.65 (1H, m, 2′β-H), 3.43 (1H, q, $J = 8.9$ Hz, 3′-H), 4.10 (1H, m, 4′-H), 4.67 (1H, dd, $J = 3.6$, 12.6 Hz, 5′-H), 4.76 (1H, dd, $J = 2.4$, 12.6 Hz, 5′-H), 6.15 (1H, dd, $J = 3.3$, 7.2 Hz, 1′-H), 7.25–8.06 (6H, m, 6-H and H_{arom}), 9.46 (1H, broad s, NH); ^{13}C NMR ($CDCl_3$/*TMS*, 62.9 MHz): $\delta = 12.13$ (CH_3), 34.69 (C-2′),42.45 (C-3′), 61.96 (C-5′), 84.61, 86.29 (C-1′ and C-4′), 110.83 (C-5), 128.52, 129.39, 129.46, 133.46 (C_{arom}), 134.80 (C-6), 150.20 (C-2), 163.76 (C-4), 166.01 (C–O).

Compound **10**: Yield, 50 mg (8%) as a white foam; FAB MS (*DMSO* + 1% AcOH + 3-nitrobenzyl-alcohol), m/z (%) = 363 ($M + H^+$); ^{1}H NMR ($CDCl_3$/*TMS*, 250 MHz): $\delta = 1.95$ (3H, s, CH_3), 2.05–2.14 (1H, m, 2′β-H), 2.97–3.43 (1H, td, $J = 6.7$, 13.3 Hz, 2′α-H), 3.41 (1H, q, $J = 9.2$ Hz, 3′-H), 4.41 (1H, dd, $J = 3.6$, 8.2 Hz, 4′-H), 4.51 (1H, dd, $J = 4.4$, 12.3 Hz, 5′-H), 4.65 (1H, dd, $J = 2.5$, 12.1 Hz, 5′-H), 6.08 (1H, t, $J = 6.7$ Hz, 1′-H), 7.24–8.07 (6H, m, 6-H and H_{arom}), 9.50 (1H, broad s, NH); ^{13}C NMR ($CDCl_3$/*TMS*, 62.9 MHz): $\delta = 12.47$ (CH_3), 36.36 (C-2′), 42.95 (C-3′), 62.98 (C-5′), 86.03, 86.19 (C-1′ and C-4′), 111.12 (C-5), 128.38, 129.29, 129.58, 133.25 (C_{arom}), 135.21 (C-6) 150.33 (C-2), 163.86 (C-4), 166.09 (C=O).

Compound **11**: Yield, 150 mg (18%) as a white foam ($\alpha/\beta = 1:3$); FAB MS ($CHCl_3$ + 1% AcOH + 3-nitrobenzyalcohol); m/z (%) = 467 ($M + H^+$); ^{1}H NMR ($CDCl_3$/*TMS*, 250 MHz): $\delta = 1.66$ (3H, s,

CH_3, β), 1.96 (3H, s, CH_3, α), 2.33 (1H, m, 2'β-H, α), 2.62 (2H, m, 2'-H, β), 3.10 (1H, m, 2'α-H, α), 4.25–4.83 (4H, m, 3'-H, 4'-H, 5'-H, $\alpha + \beta$), 6.20 (1H, t, $J = 5.9$ Hz, 1'-H, α), 6.27 (1H, *t*, $J = 6.1$ Hz, 1'-H, β), 7.26–8.10 (11H, m, 6-H and H_{arom}), 8.83 (1H, broad s, NH); ^{13}C NMR ($CDCl_3$/*TMS*, 62.9 MHz): $\delta = 12.11$, 12.50 (CH_3), 38.35, 38.64 (C-2'), 40.01, 40.84 (C-3'), 63.59, 64.66 (C-5'), 83.02, 84.09 (C-4'), 84.84, 87.00 (C-1'), 111.00, 111.24 (C-5), 127.30, 128.41, 128.57, 128.74, 129.52, 129.63, 133.20, 133.40, 133.99, 134.60, 135.30, 136.01 (C_{arom} and C-6), 150.07 (C-2), 163.36 (C-4), 166.01 (C=O), 190.10 (S–C=O).

3'-Benzoylthio-5'-O-tert-butyldiphenylsilyl-2',3'-didcoxy-N^6-isobutyryladenosine (**13**) *and 9-(3-Benzoylthio-5-O-tert-butyldiphenylsilyl-2,3-dideoxy-α-D-erythro-pentofuranosyl)-6-isobutyrylaminopurine* (**14**):

A mixture of adenine (0.82 g, 4 mmol), ammonium sulfate (0.02 mmol) and 1,1,1,3,3,3-hexamethyldisilazane (30 ml) was refluxed overnight. The clear solution obtained was cooled and the solvent was evaporated *in vacuo* to give the silylated compound **12** as an oil. A solution of the sugar **4** (1.36 g, 2.7 mmol) in anhydrous MeCN (10 ml) was added a stirred solution of the silylated 6-isobutrylaminopurine (**12**, 4 mmol) in anhydrous MeCN (20 ml) and the mixture was cooled to -50 °C. A solution of $CF_3SO_3SiMe_3$ (0.6 ml, 3 mmol) in anhydrous MeCN (5 ml) was added dropwise during five minutes at -50 °C and the mixture was stirred at -30 °C for 2 h and then overnight at -10 °C. The mixture was diluted with CH_2Cl_2 (200 ml), washed with cold saturated aqueous $NaHCO_3$ (200 ml), water (2×100 ml) and dried over $NaSO_4$. After evaporation to dryness, the residue was chromatographed on silica gel with petroleum ether (65–70 °C)/Et_2O (7:3, v/v) to obtain **13** and **14**.

Compound **13** ($C_{37}H_{41}N_5O_4SSi$ (HRMS)): Yield, 280 mg (15%) as a pale yellow foam; FAB MS ($CHCl_3$ + 3-nitrobenzylalcohol), *m/z* (%) = 680 ($M + H^+$) ^{1}H NMR ($CDCl_3$/*TMS*, 250 MHz): $\delta = 1.06$ (9H, s, $(CH_3)_3C$), 1.31 (6H, d, $J = 6.8$ Hz, $(CH_3)_2CH$), 2.70 (1H, td, $J = 7.2$, 14.3 Hz, 2'-H), 3.11–3.39 (2H, m, 2'-H and CHCO), 3.91 (1H, dd, $J = 3.6$, 11.7 Hz, 5'-H), 4.07 (1H, dd, $J = 2.8$, 11.7 Hz, 5'-H), 4.25 (1H, m, 4'-H), 4.59 (1H, m, 3'-H), 6.50 (1H, m, 1'-H), 7.22–7.94 (15 H, m, H_{arom}), 8.40, 8.71 (2H, 2s, 2-H and 8-H), 8.83 (1H, s, NH), ^{13}C NMR ($CDCl_3$/*TMS*, 62.9 MHz): $\delta = 19.06$ (C–Si and $(CH_3)_2$ CH), 26.76 ($(CH_3)_3$ C), 35.90 (CH), 39.76, 39.81 (C-2' and C-3'), 63.25 (C-5'), 84.27 (C-4'), 85.12 (C-1'), 122.80 (C-5), 127.20, 127.60, 127.66, 128.61, 128.66, 133.72 (C_{arom}), 140.74 (C-8), 149.26 (C-4), 152.33 (C-6), 152.46 (C-2), 176.12 (NHCO), 190.40 (S–C=O).

Compound [**14**] ($C_{37}H_{41}N_5O_4SSi \cdot 0.5\ H_2O$): Yield, 320 mg (18%) as a pale yellow foam; FAB MS ($CDCl_3$ + 3-nitrobenzylalcohol), *m/z* (%) = 680 ($M + H^+$); ^{1}H NMR ($CDCl_3$/*TMS*, 250 MHz): $\delta =$ 1.11 (9H, s, $(CH_3)_3C$), 1.32 (6H, d, $J = 6.7$ Hz, $(CH_3)_2CH$), 2.88 (1H, dt, $J = 14.2$, 4.6 Hz, 2'-H), 3.20–3.76 (2H, m, 2'-H and CH), 3.97 (2H, d, $J = 2.5$ Hz, 5'-H), 4.49 (1H, m, 4'-H), 4.47 (1H, m, 3'-H), 6.49 (1H, dd, $J = 4.0$, 6.4 Hz, 1'-H), 7.34–7.86 (15H, m, H_{arom}), 8.26, 8.72 (2H, 2s, 2-H and 8-H), 9.02 (1H, s, NH); ^{13}C NMR ($CDCl_3$/*TMS*, 62.9 MHz): $\delta = 19.05$ ($(CH_3)_2CH$), 19.11 (C–Si), 26.72 ($(CH_3)_3C$), 35.85 (CH), 39.18 (C-2'), 40.63 (C-3'), 64.43 (C-5'), 86.12 (C-4'), 86.94 (C-1'), 122.79 (C-5), 127.12, 127.62, 128.56, 129.67, 132.78, 133.68, 135.44 (C_{arom}), 140.94 (C-8), 149.25 (C-4), 150.77 (C-6), 152.28 (C-2), 176.15 (NHCO), 190.49 (S–C=O).

2',3'-Dideoxy-3'-mercaptodenosine (**15**; $C_{10}H_{13}N_5O_2S$ (HRMS))

A solution of **13** (280 mg, 0.41 mmol) in degassed *THF* (10 ml) and degassed 1*M* Bu_4NF/*THF* (1.0 ml, 1.0 mmol) was stirred under N_2. After complete reaction (30 min), the solvent was removed *in vacuo*. The residue was dissolved in degassed MeOH (10 ml). NaOMe (54 mg, 1.0 mmol) in degassed MeOH (10 ml) was added dropwise at r.t. and stirring was continued for 2 h and was followed by neutralization (*pH* = 5) by addition of HCl in MeOH. The solvent was evaporated and the crude material was purified by column chromatography on silica gel with 5–10% MeOH in CH_3COOEt to give compound **15**. Yield, 50 mg (46%); m.p., 195–197 °C; ^{1}H NMR (*DMSO*/*TMS*, 500 MHz): $\delta = 2.43$–2.52 (1H, m, 2'-H), 2.88 (1H, ddd, $J = 3.3$, 7.5, 13.4 Hz, 2'-H), 3.05 (1H, s, SH), 3.62 (1H, m, 3'-H), 3.67–3.78 (2H, m, 5'-H),

Table 1

			C	H	N
Microanalyses					
4	$C_{29}H_{34}O_4SSi$	calc.	68.74	6.76	
	(506.7)	found	68.74	6.82	
5	$C_{29}H_{34}O_4SSi$	calc.	68.74	6.76	
	(506.7)	found	68.89	6.98	
7	$C_{33}H_{36}N_2O_5SSi$	calc.	65.97	6.04	4.66
	(600.8)	found	66.37	6.39	4.52
14	$C_{37}H_{41}N_5O_4SSi \cdot 0.5\ H_2O$	calc.	64.53	6.00	10.17
		found	64.32	6.07	9.96
		calc.	found		
HRMS					
8	$C_{10}H_{14}N_2O_4S$	258.0674	258.0641		
13	$C_{37}H_{41}N_5O_4SSi$	679.2648	679.2662		
15	$C_{10}H_{13}N_5O_2S$	267.0790	267.0795		
16	$C_{10}H_{13}N_5O_2S$	267.0790	267.0795		

3.85 (1H, m, 4'-H), 5.08 (1H, t, $J = 5.6$ Hz, 5'-OH), 6.34 (1H, dd, $J = 3.2$, 7.3 Hz, 1'-H), 7.24 (2H, s, NH_2), 8.15, 8.36 (2H, 2s, 2-H and 8-H); ^{13}C NMR (*DMSO/TMS*, 125 MHz): $\delta = 34.64$ (C-2'), 41.63 (C-3'), 60.11 (C-5'), 82.77, 88.99 (C-1' and C-4'), 119.01 (C-5), 139.12 (C-8), 148.69 (C-4), 152.38 (C-2), 155.95 (C-6).

6-Amino-9-(2,3-dideoxy-3-mercapto-α-D-erythro-pentofuranosyl)purine (**16**) *and its disulfide* (**17**)

The same procedure as for preparation of **15** was used. The crude material was purified by column chromatography on silica gel with 5–10% MeOH in CH_3COOEt to give the compounds **16** and **17**.

Compound **16** ($C_{10}H_{13}N_5O_2S$ (HRMS)): Yield, 20 mg (15%) as a pale yellow foam; ^{1}H NMR (CD_3OD/TMS, 500 MHz): $\delta = 2.86$ (1H, m, 2'-H). 3.20 (1H, m, 2'-H), 3,57 (1H, m, 3'-H), 3.85 (1H, dd, $J = 4.1$, 12.4 Hz, 5'-H), 4.00 (1H, dd, $J = 2.5$, 11.5 Hz, 5'-H), 4.41 (1H, ddd, $J = 2.6$, 4.1, 11.0 Hz, 4'-H), 6.43 (1H, t, $J = 6.5$ Hz, 1'-H), 8.36, 8.43 (2H, 2s, 2-H and 8-H); ^{13}C NMR (CD_3OD/TMS, 125 MHz): $\delta = 36.74$ (C-2'), 43.29 (C-3'), 61.56 (C-5'), 85.64, 89.97 (C-1' and C-4'), 120.76 (C-5), 141.24 (C-8), 150.40 (C-4), 153.79 (C-2), 157.37 (C-6).

Compound **17**: Yield, 30 mg (11%); ^{1}H NMR (*DMSO/TMS*, 500 MHz): $\delta = 2.85$ (1H, m, 2'-H), 2.95 (1H, td, $J = 6.7$, 14.4 Hz, 2'-H), 3.54 (1H, dd, $J = 4.2$, 12.2 Hz, 5'-H), 3.66–3.74 (2H, m, 3'-H and 5'-H), 4.34 (1H, td, $J = 3.6$, 7.3 Hz, 4'-H), 5.09 (1H, s, 5'-OH), 6.31 (1H, t, $J = 6.3$ Hz, 1'-H), 7.23 (2H, s, NH_2), 8.14, 8.28 (2H, 2s, 2-H and 8-H); ^{13}C NMR (*DMSO/TMS*, 125 MHz): $\delta = 39.43$ (C-2'), 48.02 (C-3'), 61.21 (C-5'), 83.62, 85.22 (C-1' and C-4'), 119.24 (C-5), 139.17 (C-8), 148.95 (C-4), 152.47 (C-2), 155.94 (C-6).

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