PREPARATION OF CHLORO AND SULFANYL DERIVATIVES OF 1-(2-DEOXY-4-*C*-HYDROXYMETHYL-α-L-*threo*-PENTOFURANOSYL)URACIL

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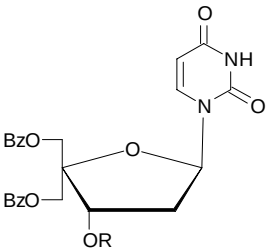
3′-Chloro and 3′-acetylsulfanyl derivatives of 1-(2-deoxy-4-*C*-hydroxymethyl-α-L-*threo*-pentofuranosyl)uracil were prepared by reaction of 2,3′-anhydro-1-{5′-*O*-benzoyl-4′-*C*-[(benzoyloxy)methyl]-2′-deoxy-α-L-*erythro*-pentofuranosyl}uracil (**3**) with hydrogen chloride and thioacetic acid, respectively. The reaction with hydrogen chloride gave a mixture of N-1 and N-3 substituted uracil derivatives **12** and **14**. Reaction of 1-{3-*O*-benzoyl-4-*C*-[(benzoyloxy)methyl]-2-deoxy-α-L-*threo*-pentofuranosyl}uracil (**7**) with thionyl chloride and subsequent debenzoylation afforded 1-(4-*C*-chloromethyl-2-deoxy-β-D-*erythro*-pentofuranosyl)uracil (**19**). Nucleophilic substitution with lithium thioacetate, followed by deacylation, converted 1-{3-*O*-benzoyl-4-*C*-[(benzoyloxy)methyl]-2-deoxy-5-*O*-*p*-toluenesulfonyl-α-L-*threo*-pentofuranosyl}uracil (**9**) into 1-(2-deoxy-4-*C*-sulfanylmethyl-β-D-*erythro*-pentofuranosyl)uracil (**21**). The obtained thiols were oxidized with iodine or air to give 1,1′-[disulfandiylbis(2,3-dideoxy-4-hydroxymethyl-α-L-*threo*-pentofuranose-3,1-diyl]di(pyrimidine-2,4-(1*H*,3*H*)-dione) (**17**) and 1,1′-[disulfandiylbis(2,5-dideoxy-4-hydroxymethyl-α-L-*threo*-pentofuranose-5,1-diyl]di(pyrimidine-2,4(1*H*,3*H*)-dione) (**22**). Reaction of 1-{3-acetylsulfanyl-5-*O*-methanesulfonyl-4-*C*-[(benzoyloxy)methyl]-2,3-dideoxy-α-L-*threo*-pentofuranosyl)}uracil (**24**) with methanolic sodium methoxide afforded 1-(3,5-anhydro-2,3-dideoxy-4-*C*-hydroxymethyl-3-sulfanyl-α-L-*threo*-pentofuranosyl)uracil (**25**). The same reagent was used in the preparation of 1-(3,5-anhydro-2-deoxy-4-*C*-hydroxymethyl-α-L-*threo*-pentofuranosyl)uracil (**26**) from 1-{4-*C*-[(benzoyloxy)methyl]-2-deoxy-5-*O*-*p*-toluenesulfonyl-α-L-*threo*-pentofuranosyl}uracil (**8**). From the series of 4′-substituted 2′-deoxyuridine derivatives, synthesized in this study, solely the 4′-chloromethyl derivative **19** and the oxetane derivative 26 exhibited an appreciable activity against HIV-1 and HIV-2.

Key words: 2′-Deoxy-4′-*C*-hydroxymethyluridine derivatives; Antivirals.

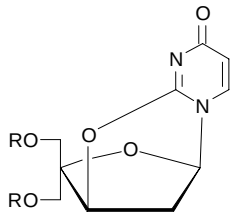
The present work is a part of the synthetic program aimed at preparation and structure–antiviral activity studies of 2′-deoxy-4′-*C*-substituted nucleoside analogues. The biological activity essentially depends on the character of substitution at the positions 4′-C and 3′-C. Antiviral activity has been found for analogues bearing an electron-withdrawing group in position 4′-C and a hydroxyl group in position 3′ (see refs[1–4]). However, also 1-(3,5-anhydro-2-deoxy-4-*C*-hydroxymethyl-α-L-*threo*-pentofuranosyl)thymine

shows significant activity[4]. On the other hand, 3′,5′-alkylidene derivatives of 1-(2-deoxy-4-*C*- hydroxymethyl-α-L-*threo*-pentofuranosyl)uracil have no antiviral activity[5].

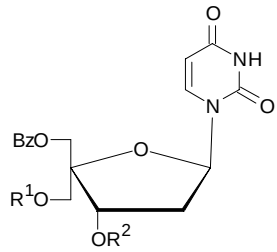
The aim of this study has been to synthesize derivatives of 1-(2-deoxy-4-*C*-hydroxymethyl-α-L-*threo*-pentofuranosyl) uracil, substituted with chlorine or a sulfanyl group in position 3′ or 5′, and also 1-(3,5-anhydro-2,3-dideoxy-4-*C*-hydroxymethyl-3-sulfanyl-α-L-*threo*-pentofuranosyl)uracil, and to study whether they exhibit antiretroviral activity. For the preparation of 3′-substituted derivatives cleavage of the 2,3′-anhydro bond appeared the method of choice whereas the 5′-substituted derivatives were obtained by nucleophilic substitution of suitably protected derivatives of 2′-deoxy-4′-*C*-hydroxymethyluridine. Mesylation of the dibenzoyl derivative **1** (ref.[5]) afforded the mesyl derivative **2** which on reaction with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in acetonitrile afforded 2,3′-anhydronucleoside **3**. In accord with literature data[6], the 2,3′-anhydro bond is formed less readily than the 2,2′-anhydro bond. Whereas 2′-deoxy-4′-*C*-hydroxymethyl-2′,3′-*O*-sulfinyluridine reacted with DBU in acetonitrile after 12 h at room temperature[5], the mesyl derivative **2** gave the corresponding 2,3′-anhydro derivative only after 26 h at 50 °C. The free anhydronucleoside **4** was obtained by debenzoylation with methanolic ammonia.



	R
1	H
2	Ms



	R
3	Bz
4	H

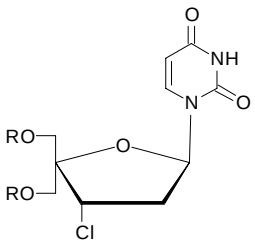


	R^1	R^2
5	H	H
6	Tr	Bz
7	H	Bz
8	Ts	H
9	Ts	Bz
10	Ms	Ms

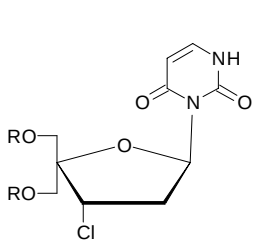
Ts = *p*-toluenesulfonyl
Tr = triphenylmethyl
Ms = methanesulfonyl

Under these conditions, 2,2′-anhydronucleosides usually afford isocytosine derivatives[7]. In our case no isocytosine derivatives were observed. Tritylation and subsequent benzoylation of monobenzoyl derivative **5** (ref.[5]) gave dibenzoyl trityl derivative **6** which was converted into the dibenzoyl derivative **7** by treatment with 80% acetic acid. Reaction of the compound **5** with an equivalent of *p*-toluenesulfonyl chloride gave tosyl derivative **8** which on benzoylation afforded dibenzoyl tosyl derivative **9**. Dimesyl derivative **10** was obtained by mesylation of compound **5**.

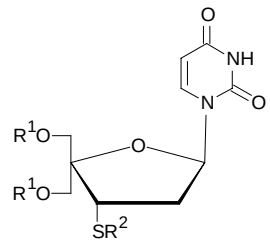
The 3′-chloro derivative **11** was prepared in 45% yield by cleavage of the 2,3′-anhydro bond in nucleoside **3** with 1 M HCl in dimethylformamide at 100 °C. As a by-product we isolated the N-3 derivative **13** in 33% yield. This N-1 to N-3 migration has already been described for cleavage of some 2,2′-anhydronucleosides with hydrogen chloride



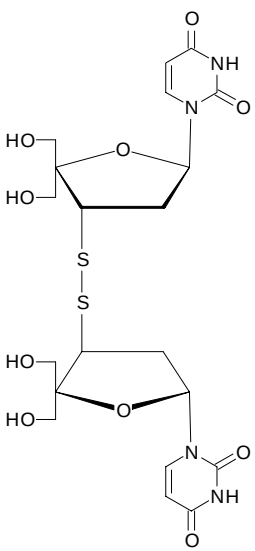
	R
11	Bz
12	H



	R
13	Bz
14	H



	R^1	R^2
15	Bz	Ac
16	H	H



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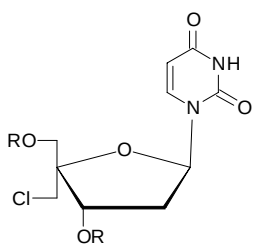
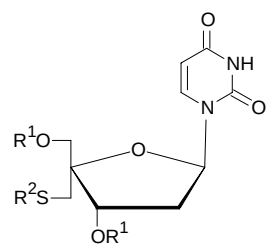
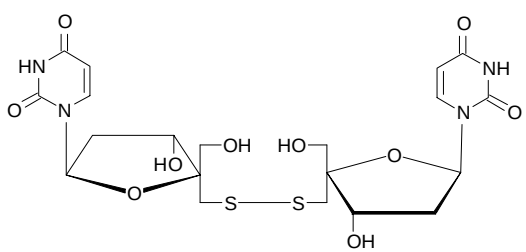


	R
18	Bz
19	H



	R^1	R^2
20	Bz	Ac
21	H	H



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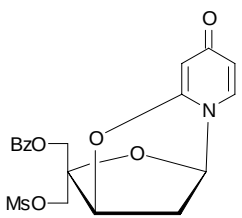
and of 2,3′-anhydronucleosides with azide (see ref.[8] and references therein). Infrared spectrum of the chloro derivative **11** exhibits an NH band at 3 390 cm^{-1} whereas in the spectrum of the N-3 isomer **13** this band is located at 3 422 cm^{-1}, in agreement with the literature data[9] (3 390 cm^{-1} for N-3 and 3 422 cm^{-1} for N-1 isomer). The free nucleo-

sides **12** and **14** were obtained by methanolysis of the respective compounds **11** and **13** with 0.1 M methanolic sodium methoxide. In the UV spectrum, the N-3 derivative **14** exhibits a significant bathochromic shift of the maximum from 264 nm at pH 7 to 294 nm at pH 12 with simultaneous increase in intensity from ε = 7 550 to 10 550, characteristic of N-3 substituted uracil derivatives[9,10].

The 3′-deoxy-3′-sulfanyl derivative was prepared by a procedure described for the synthesis of 2′-deoxy-2′-sulfanyluridine[11]. Acetylsulfanyl derivative **15** was obtained in 50% yield by cleavage of the 2,3′-anhydro bond in nucleoside **3** with thioacetic acid in hexamethylphosphoric triamide (HMPTA) at 110 °C. Debenzoylation of compound **15** with methanolic sodium methoxide in an argon atmosphere afforded the sulfanyl derivative **16**.

Disulfide **17** was prepared by oxidation of compound **16** with iodine. 5′-Chloro-5′-deoxy derivative **18** was obtained in 35% yield by reaction of dibenzoyl derivative **7** with thionyl chloride in HMPTA at 80 °C. In this case, the nucleophilic substitution proceeded very sluggishly, in contrast to the isomeric 1-(2-deoxy-4-*C*-hydroxymethyl-3,5-*O*-isopropylidene-β-D-*threo*-pentofuranosyl)thymine which reacts with thionyl chloride in HMPTA already at room temperature in 84% yield[12]. The free chloro compound **19** was obtained by methanolysis with methanolic sodium methoxide. Tosyl derivative **9** was converted into acetylsulfanyl derivative **20** by nucleophilic substitution with lithium thioacetate. The thiol **21** was obtained from **20** by treatment with methanolic sodium methoxide. In the presence of air and with prolonged reaction time, the reaction gave disulfide **22**.



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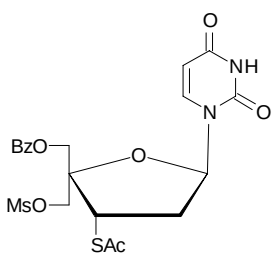

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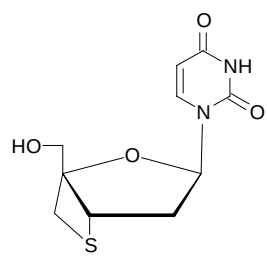

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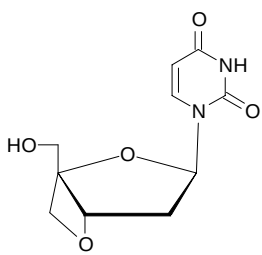

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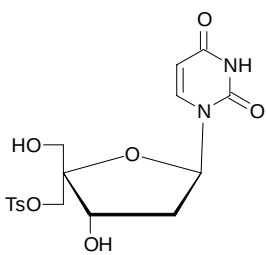

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Reaction of dimesyl derivative **10** with DBU in acetonitrile (50 °C, 20 h) afforded 2,3′-anhydro derivative **23** which was converted into sulfanyl derivative **24** by reaction with thioacetic acid in dioxane at 120 °C. With HMPTA as solvent, the reaction gave a mixture of products and the yield of **24** was low. The sulfanyl derivative **24** reacted with methanolic sodium methoxide to give thietane derivative **25**. Reaction of tosyl derivative **8** with sodium methoxide afforded oxetane derivative **26**. Due to low reactivity of the tosyl group in position 5′, the debenzoylation of the 4′-hydroxy group proceeded much faster and the reaction mixture gave also the tosyl derivative **27**.

Biological Activity

The compounds were evaluated for their inhibitory effect against HSV-1, HSV-2, thymidine kinase (TK)-deficient HSV-1/TK$^-$ and vaccinia virus (VV) replication in E_6SM cells, cytomegalovirus and varicella-zoster virus (TK$^+$ and TK$^-$) replication in HEL cells, Moloney murine sarcoma virus (MSV)-induced transformation of C3H/3T3 cells, and human immunodeficiency virus (HIV-1 and HIV-2)-induced cytopathicity in CEM cells. None of the compounds proved any marked inhibitory effect at subtoxic concentrations on HSV-1 and HSV- 2, VV, CMV, VZV or on MSV-induced transformation of C3H cell cultures. Of the 4′-substituted 2′-deoxyuridine derivatives synthesized in this

TABLE I
Antiretroviral activity of nucleoside analogues

Compound	IC_{50}, μg/ml[a]		
	MSV[b]	HIV-1[c]	HIV-2[c]
4	>40	>100	>100
12	NA	>100	>100
14	>200	>100	>100
16	>40	>100	>100
17	>40	>100	>100
19	173 ± 26	2.75 ± 1.77	2.25 ± 0.35
21	>40	>100	>100
22	>40	>100	>100
25	172 ± 27	>100	>100
26	107 ± 16	2.93 ± 1.85	17.3 ± 4
27	>200	>100	>100

[a] 50% inhibitory concentration, or concentration required to reduce virus plaque formation by 50%. [b] In C3H/3T3 cells. [c] In CEM cells.

study, solely the 4′-chloromethyl derivative **19** and oxetane derivative **26** exhibited appreciable activities against HIV-1 and HIV-2 (Table I).

The activity found for the chloro derivative **19**, is in accord with the assumption that the antiviral activity is exhibited by analogs with an electron-withdrawing group in position 4′-C. The oxetane analog **26** is less active than the earlier described thymine analog[4]. Also in this case, the replacement of thymine by uracil results in reduction of the antiviral activity. Replacement of the oxetane oxygen atom in **26** by sulfur atom in the thietane derivative **25** leads to loss of activity.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Infrared spectra were recorded on a Zeiss UR 20 spectrophotometer (wavenumbers in cm^{-1}) and UV spectra on a Unicam SP 8000 spectrometer. ^1H NMR spektra (δ, ppm; *J*, Hz) were obtained with Varian UNITY 200 and Varian UNITY 500 instruments in hexadeuteriodimethyl sulfoxide with tetramethylsilane as internal standard. Column chromatography was performed on 30–60 μm silica gel (Service Laboratories of this Institute) and thin-layer chromatography (TLC) on Silufol UV 254 foils (Kavalier, Votice). Solvents were evaporated at bath temperature 30–60 °C/2 kPa and compound was dried over phosphorus pentoxide at 13 Pa.

Antiviral Assays

The antiviral assays other than HIV-1, HIV-2 or MLV were based on inhibition of virus-induced cytopathicity in either E_6SM or HEL cell cultures, following previously established procedures [13,14]. Confluent cell cultures in microtiter trays were inoculated with 100 $CCID_{50}$ of virus, 1 $CCID_{50}$ being the virus dose required to infect 50% of the cell cultures. After a 1 h virus adsorption period, the residual virus was removed, and the cell cultures were incubated in the presence of varying concentrations (400, 200, 100,… μg/ml) of the test compounds. Viral cytopathicity was recorded as soon as it reached completion in the control virus-infected cell cultures.

Assays for HIV-1 or HIV-2-induced cytopathicity in CEM T4 lymphocytes were performed under previously described conditions[15]. The anti-MSV activities of the compounds were estimated by transformation assays with MSV-infected murine C3H/3T3 embryo fibroblasts[15].

1-{5-*O*-Benzoyl-4-*C*-[(benzoyloxy)methyl]-3-*O*-methanesulfonyl-α-L-*threo*-pentofuranosyl}uracil (**2**)

Methanesulfonyl chloride (2.8 ml, 36 mmol) was added at 0 °C to a stirred solution of dibenzoyl derivative **1** (4.66 g, 10 mmol) in pyridine (20 ml). The mixture was set aside for 10 min at 0 °C and for 5 h at room temperature. Water (1.5 ml) was added at 0 °C and after 10 min the mixture was concentrated *in vacuo* and the residue was partitioned between ethyl acetate (150 ml) and water (100 ml). The organic phase was washed successively with water (80 ml), 5% hydrochloric acid (to an acid reaction of the washing phase) water (80 ml), 5% sodium hydrogen carbonate solution, dried over magnesium sulfate, and the solvent was evaporated. Chromatography on a column of silica gel (300 g) in ethyl acetate afforded 4.91 g (90%) of mesyl derivative **2** as a solid foam. For $C_{25}H_{24}N_2O_{10}S$ (544.5) calculated: 55.14% C, 4.44% H, 5.14% N, 5.89% S; found: 55.21% C, 4.55% H, 4.95% N, 5.78% S. ^1H NMR spectrum: 2.69–2.98 m, 2 H (2 × H-2′); 3.34 s, 3 H (SO_2CH_3); 4.56 d, 1 H, *J*(a,b) = 11.9 (CHaCH-O); 4.64 s, 2 H (2 × H-5′); 4.67 d, 1 H (CHbH-O); 5.58 d, 1 H, *J*(5,6) = 7.9 (H-5);

5.70 dd, 1 H, *J*(3′,2a′) = 4.7, *J*(3′,2b′) = 6.9 (H-3′); 6.32 t, 1 H, *J*(1′,2a′) = *J*(1′,2b′) = 6.7 (H-1′); 7.50–7.88 m and 7.98–8.02 m, 7 H and 4 H (H-6, H-arom.); 11.43 s, 1 H (H-3).

2,3′-Anhydro-1-{5-*O*-benzoyl-4-*C*-[(benzoyloxy)methyl]-2-deoxy-α-L-*erythro*-pentofuranosyl}-uracil (**3**)

1,8-Diazabicyclo[5.4.0]undec-7-ene (1.5 ml) was added to a solution of mesyl derivative **2** (2.72 g, 5 mmol) in acetonitrile (30 ml) and the solution was heated at 50 °C for 16 h. After dilution with ethyl acetate (200 ml), the mixture was washed with water (3 × 15 ml), dried over magnesium sulfate, and the solvent was evaporated. Crystallization from methanol afforded 1.40 g (63%) of anhydro derivative **3**. Chromatography of the mother liquors on a column of silica gel (80 g) in ethyl acetate–acetone–ethanol–water (19 : 3 : 2 : 1) and subsequent crystallization from methanol gave additional 230 mg (10%) of the product, m.p. 208–210 °C. For $C_{24}H_{20}N_2O_7$ (448.4) calculated: 64.28% C, 4.50% H, 6.25% N; found: 64.22% C, 4.45% H, 6.15% N. ^{1}H NMR spectrum: 2.72 d, 1 H, *J*(2a′,2b′) = 13.4 (H-2a′); 2.90 m, 1 H (H-2b′); 4.44 d, 1 H, *J*(a,b) = 11.9 (CHaH-O); 4.51 d, 2 H (CHbH-O, CHcH-O); 4.58 d, 1 H, *J*(d,c) = 11.9 (CHdH-O); 5.63 bs, 1 H (H-3′); 5.80 d, *J*(5, 6) = 7.6 (H-5); 6.04 d, 1 H, *J*(1′,2b′) = 3.4 (H-1′); 7.44–7.54 m, 7.62–7.71 m and 7.88–8.01 m, 4 H, 3 H and 4 H (H-6, H-arom.).

2,3′-Anhydro-1-(2-deoxy-4-*C*-hydroxymethyl-α-L-*erythro*-pentofuranosyl)uracil (**4**)

A suspension of anhydronucleoside **3** (224 mg, 0.5 mmol) in methanolic ammonia (5 ml) was stirred until it dissolved and the solution was allowed to stand at room temperature for 2 days. The solvent was evaporated and the residue was codistilled with methanol and mixed with ether. The solidified product was filtered, washed with ether, and dissolved in warm water (0.2 ml), and warm ethanol (3 ml) was added. The crystalline free anhydro derivative **4** (92 mg, 77%) was collected, m.p. 207–209 °C. For $C_{10}H_{12}N_2O_5$ (240.2) calculated: 50.00% C, 5.04% H, 11.66% N; found: 49.78% C, 4.94% H, 11.54% N. ^{1}H NMR spectrum: 2.47 d, 1 H, *J*(2a′,2b′) = 13.1 (H-2a′); 2.70 m, 1 H (H-2b′); 3.29–3.62 m, 4 H (2 × H- 5′, CH_2O); 4.97–5.04 m, 2 H (2 × OH); 5.11 bs, 1 H (H-3′); 5.78 d, 1 H, *J*(5,6) = 7.3 (H-5); 5.87 d, 1 H, *J*(1′,2b′) = 3.3 (H-1′); 7.67 d, 1 H (H-6).

1-{3-*O*-Benzoyl-4-*C*-[(benzoyloxy)methyl]-2-deoxy-5-*O*-triphenylmethyl-α-L-*threo*-pentofuranosyl}-uracil (**6**)

A solution of benzoyl derivative **5** (725 mg, 2 mmol) and trityl chloride (697 mg, 2.5 mmol) in pyridine (10 ml) was heated for 1 h at 100 °C. After cooling to room temperature, a solution of benzoyl chloride (0.35 ml, 3 mmol) in pyridine (4 ml) was added under stirring during 2 h. The mixture was set aside for 2 h at room temperature, water (0.5 ml) was added and the reaction mixture was evaporated. The residue was partitioned between water (40 ml) and ethyl acetate (80 ml), the organic layer was separated, washed successively with 5% hydrochloric acid untill an acid reaction of the washings, water (40 ml), 5% sodium hydrogen carbonate solution, dried and the solvent was evaporated. Column chromatography on silica gel (150 g) in toluene–ethyl acetate (3 : 2) afforded 1.25 g (89%) of trityl derivative **6** as an amorphous foam. For $C_{43}H_{33}N_2O_8$ (705.7) calculated: 73.18% C, 4.71% H, 3.97% N; found: 73.38% C, 4.92% H, 3.78% N. ^{1}H NMR spectrum: 2.61 ddd, 1 H, *J*(2a′,1′) = 6.7, *J*(2a′,2b′) = 14.2, *J*(2a′,3′) = 4.9 (H-2a′); 2.83 ddd, 1 H, *J*(2b′,1′) = 7.0, *J*(2b′,3′) = 7.3 (H-2b′); 3.30 d, 1 H, *J*(5a′, 5b′) = 9.5 (H-5a′); 3.47 d, 1 H (H-5b′); 4.59 d, 1 H, *J*(a,b) = 11.0 (CHaH-O); 4.69 d, 1 H (CHbH-O); 5.63 d, 1 H, *J*(5,6) = 8.2 (H-5); 5.84 dd, 1 H (H-3′); 6.40 t, 1 H (H-1′); 7.15–7.73 m, 25 H (H-arom.); 7.83 d, 1 H (H-6); 11.43 s, 1 H (H-3).

1-{3-*O*-Benzoyl-4-*C*-[(benzoyloxy)methyl]-2-deoxy-α-L-*threo*-pentofuranosyl}uracil (**7**)

A solution of trityl derivative **6** (1.06 g, 1.5 mmol) in 80% aqueous acetic acid (6 ml) was boiled for 15 min, cooled and set aside at 4 °C overnight. The crystalline triphenylmethanol was filtered off, washed with 80% aqueous acetic acid, the combined filtrates were concentrated (2 ml) and the deposited crystals were collected and washed with ether. Yield 511 mg (73%) of dibenzoyl derivative **7**, m.p. 161–163 °C. For $C_{24}H_{22}N_2O_8$ (466.4) calculated: 61.80% C, 4.75% H, 6.01% N; found: 61.90% C, 4.69% H, 6.13% N. ^{1}H NMR spectrum: 2.56–2.81 m, 2 H (2 × H-2′); 3.72–3.91 m, 2 H (2 × H-5′); 4.50 d, 1 H, *J*(a,b) = 11.4 (CHaH-O); 4.54 d, 1 H (CHbH-O); 5.14 t, 1 H, *J*(OH,5′) = 5.3 (5′-OH); 5.56 d, 1 H, *J*(5,6) = 7.9 (H-5); 5.82 dd, 1 H, *J*(3′,2a′) = 5.2, *J*(3′,2b′) = 7.0 (H-3′); 6.34 t, 1 H, *J*(1′,2a′) = 6.4, *J*(1′,2b′) = 6.7 (H-1′); 7.43–7.75 m and 7.92–8.06 m, 7 H and 4 H (H-6, H-arom.); 11.38 s, 1 H (H-3).

1-{4-*C*-[(Benzoyloxy)methyl]-2-deoxy-5-*O*-*p*-toluenesulfonyl-α-L-*threo*-pentofuranosyl}uracil (**8**)

Benzoyl derivative **5** (725 mg, 2 mmol) was dissolved in pyridine. The solvent was evaporated, the residue was dissolved in pyridine (12 ml), and a solution of *p*-toluenesulfonyl chloride (570 mg, 3 mmol) was added dropwise during 5 h. Water (0.2 ml) was added and after 20 min the solution was concentrated. The residue was partitioned between water (20 ml) and ethyl acetate (50 ml). The organic phase was separated, washed with water (2 × 10 ml), dried over magnesium sulfate and the solvent was evaporated. Crystallization from methanol gave 870 mg (84%) of tosyl derivative **8**, m.p. 123–125 °C. For $C_{24}H_{24}N_2O_9S$ (516.5) calculated: 55.81% C, 4.68% H, 5.42% N, 6.21% S; found: 55.91% C, 4.63% H, 5.37% N, 5.96% S. ^{1}H NMR spectrum: 2.18 ddd, 1 H, *J*(2a′,1′) = 6.2, *J*(2a′,2b′) = 13.9, *J*(2a′,3′) = 3.1 (H-2a′); 2.24 s, 3 H (CH_3); 2.43 ddd, 1 H, *J*(2b′,1′) = 7.7, *J*(2b′,3′) = 6.5 (H-2b′); 4.18–4.35 m, 4 H (2 × H-5′, CH_2O); 4.47 m, 1 H (H-3′); 5.57 d, 1 H, *J*(5,6) = 8.2 (H-5); 5.75 d, 1 H, *J*(OH,3′) = 4.9 (3′-OH); 6.17 dd, 1 H (H-1′); 7.29 d and 7.47–7.83 m, 2 H and 8 H (H-6, H-arom.); 11.36 s, 1 H (H-3).

1-{3-*O*-Benzoyl-4-*C*-[(benzoyloxy)methyl]-2-deoxy-5-*O*-*p*-toluenesulfonyl-α-L-*threo*-pentofuranosyl}-uracil (**9**)

A solution of benzoyl chloride (0.4 ml, 3.4 mmol) in pyridine (4 ml) was added dropwise during 3 h to a stirred solution of tosyl derivative **8** (1.55 g, 3 mmol) in pyridine (6 ml). Water (0.1 ml) was added and after 15 min the pyridine was evaporated. The residue was partitioned between water (10 ml) and ethyl acetate (50 ml). The organic layer was separated, washed successively with water (10 ml), 5% hydrochloric acid (10 ml), water (10 ml), and 5% aqueous sodium hydrogen carbonate, then dried over magnesium sulfate, and the solvent was evaporated. Crystallization from propan-2-ol afforded 1.45 g (78%) of dibenzoyl derivative **9**, m.p. 201–203 °C. Chromatography of the mother liquors on a column of silica gel in ethyl acetate–toluene (3 : 2), followed by crystallization from propan-2-ol gave further 150 mg (8%) of the product. For $C_{31}H_{28}N_2O_{10}S$ (516.5) calculated: 59.99% C, 4.55% H, 4.51% N, 5.17% S; found: 59.76% C, 4.59% H, 4.42% N, 5.40% S. ^{1}H NMR spectrum: 2.24 s, 3 H (CH_3); 2.60 m, 1 H, *J*(2a′,2b′) = 14.0 (H-2a′); 2.82 m, 1 H (H-2b′); 4.38 d, 1 H, *J*(5a′,5b′) = 10.4 (H-5a′); 4.67 s, 2 H (CH_2O); 4.50 d, 1 H (H-5b′); 5.16 d, 1 H, *J*(5,6) = 7.9 (H-5); 5.88 dd, 1 H, *J*(3′,2a′) = 4.9, *J*(3′,2b′) = 7.3 (H-3′); 6.26 t, 1 H, *J*(1′,2a′) = *J*(1′,2b′) = 6.7 (H-1′); 7.25– 7.97 m, 15 H (H-6, H-arom.); 11.41 s, 1 H (H-3).

1-{4-*C*-[(Benzoyloxy)methyl]-2-deoxy-3,5-di-*O*-methanesulfonyl-α-L-*threo*-pentofuranosyl}uracil (**10**)

Methanesulfonyl chloride (4.7 ml, 60 mmol) was added at 0 °C to a stirred solution of benzoyl derivative **5** (3.62 g, 10 mmol) in pyridine (30 ml). The mixture was allowed to stand at 0 °C for 0.5 h

and at room temperature for 3 h. Water (0.5 ml) was added at 0 °C and after 15 min the solvent was evaporated. The residue was partitioned between water (30 ml) and ethyl acetate (100 ml) and the organic layer was washed successively with water (30 ml), 5% hydrochloric acid to an acid reaction of the washings, water (30 ml) and 5% sodium hydrogen carbonate solution (30 ml). After drying and evaporation, the residue was chromatographed on a column of silica gel (150 g) in ethyl acetate to give 4.32 g (83%) of dimesyl derivative **10** as a solid foam. For $C_{19}H_{22}N_2O_{11}S_2$ (518.5) calculated: 44.01% C, 4.28% H, 5.40% N, 12.37% S; found: 44.24% C, 4.41% H, 5.15% N, 12.27% S. ^{1}H NMR spectrum: 2.64–2.92 m, 2 H (2 × H-2′); 3.27 s, 3 H (CH_3SO_2); 3.36 s, 3 H (CH_3SO_2); 4.48 d, 1 H, *J*(a,b) = 11.0 (CHaH-O); 4.49 d, 1 H, *J*(c,d) = 11.0 (CHcH-O); 4.53 d, 1 H (CHbH-O); 4.54 d, 1 H (CHdH-O); 5.57 dd, 1 H, *J*(5,3) = 2.1, *J*(5,6) = 7.9 (H-5); 5.64 dd, 1 H, *J*(3′,2a′) = 4.9, *J*(3′,2b′) = 7.0 (H-3′); 6.27 t, 1 H, *J*(1′,2a′) = *J*(1′,2b′) = 6.7 (H-1′); 7.51–7.75 m and 8.00–8.04 m, 4 H and 2 H (H-6, H-arom.); 11.44 d, 1 H (H-3).

1-{5-*O*-Benzoyl-4-*C*-[(benzoyloxy)methyl]-3-chloro-3-deoxy-α-L-*threo*-pentofuranosyl}uracil (**11**) and 3-{5-*O*-Benzoyl-4-*C*-[(benzoyloxy)methyl]-3-chloro-3-deoxy-α-L-*threo*-pentofuranosyl}uracil (**13**)

Anhydronucleoside **3** (897 mg, 2 mmol) was dissolved in 1 M HCl in dimethylformamide (4 ml). The solution was heated at 100 °C for 40 min, cooled, mixed with ethyl acetate (20 ml) and washed with 10% sodium hydrogen carbonate solution. After drying and evaporation, the residue was subjected to column chromatography on silica gel (180 g) in ethyl acetate–toluene (3 : 2). The first fraction gave 433 mg (45%) of chloro derivative **11** as a solid foam. For $C_{24}H_{21}ClN_2O_7$ (484.9) calculated: 59.45% C, 4.37% H, 7.31% Cl, 5.78% N; found: 59.73% C, 4.50% H, 7.06% Cl, 5.53% N. IR spectrum (*c* = 2%, $CHCl_3$): 3 390, 3 169 (NH); 1 725 (C=O, benzoate + uracil); 1 694 (C=O, 1-substituted uracil); 1 635 (C=C). ^{1}H NMR spectrum: 2.74–3.05 m, 2 H (2 × H-2′); 4.57 d, 1 H, *J*(a,b) = 11.9 (CHaH-O); 4.62 d, 1 H, *J*(5a′,5b′) = 11.9 (H-5a′); 4.66 d, 1 H (H-5b′); 4.76 d, 1 H (CHbH-O); 5.19 t, 1 H, *J*(3′,2a′) = 7.9, *J*(3′, 2b′) = 7.6 (H-3′); 5.51 d, 1 H, *J*(5,6) = 8.2 (H-5); 6.33 dd, 1 H, *J*(1′,2a′) = 7.3, *J*(1′,2b′) = 4.9 (H-1′); 7.50–7.76 m and 7.98–8.03 m, 7 H and 4 H (H-6, H-arom.); 11.40 s, 1 H (H-3).

Evaporation of the second fraction afforded 314 mg (33%) of chloro derivative **13**, also as a solid foam. For $C_{24}H_{21}ClN_2O_7$ (484.9) calculated: 59.45% C, 4.37% H, 7.31% Cl, 5.78% N; found: 59.69% C, 4.51% H, 7.11% Cl, 5.72% N. IR spectrum (*c* = 2%, $CHCl_3$): 3 425, 3 236, 3 190, 3 109 (NH); 1 724 (C=O, benzoate + uracil); 1 660 (C=O, 3-substituted uracil). ^{1}H NMR spectrum: 2.75 ddd, 1 H, *J*(2a′,1′) = 9.0, *J*(2a′,2b′) = 13.4, *J*(2a′,3′) = 8.5 (H-2a′); 3.14 ddd, 1 H, *J*(2b′,1′) = 3.6, *J*(2b′,3′) = 8.5 (H-2b′); 4.54 d, 1 H, *J*(5a′,5b′) = 11.4 (H- 5a′); 4.60 d, 1 H (H-5b′); 4.60 d, 1 H, *J*(a,b) = 11.9 (CHaH-O); 4.78 d, 1 H (CHbH-O); 5.20 t, 1 H (H-3′); 5.59 d, 1 H, *J*(5,6) = 7.5 (H-5); 6.78 dd, 1 H (H-1′); 7.45–7.74 m and 7.98–8.06 m 7 H and 4 H (H-6, H-arom.); 11.22 s, 1 H (H-3).

1-(3-Chloro-3-deoxy-4-*C*-hydroxymethyl-α-L-*threo*-pentofuranosyl)uracil (**12**)

A solution of chloro derivative **11** (388 mg, 0.8 mmol) in 0.1 M methanolic sodium methoxide (4 ml) was allowed to stand overnight at room temperature. The mixture was neutralized with Dowex 50 (H^+ form) and the solvent was evaporated. Crystallization from propan-2-ol afforded 171 mg (77%) of free chloro derivative **12**, m.p. 170–172 °C. For $C_{10}H_{13}ClN_2O_5$ (276.7) calculated: 43.41% C, 4.74% H, 12.81% Cl, 10.13% N; found: 43.67% C, 4.80% H, 12.82% Cl, 9.98% N. UV spectrum (water): λ_{max} 262 nm (ε 10 480); (0.1 M NaOH): λ_{max} 262 nm (ε 7 560). ^{1}H NMR spectrum: 2.66 t, 2 H (2 × H-2′); 3.43–3.69 m, 4 H (2 × H-5′, CH_2O); 4.17 t, 1 H, *J*(3′,2a′) = *J*(3′, 2b′) = 7.3 (H-3′); 4.19 t, 1 H, *J*(OH,CH_2) = 5.5 (CH_2OH); 5.27 t, 1 H, *J*(OH,5′) = 5.3 (5′-OH); 5.63 d, 1 H, *J*(5,6) = 7.9 (H-5); 6.23 t, 1 H, *J*(1′,2a′) = 5.8, *J*(1′,2b′) = 6.1 (H-1′); 7.89 d, 1 H (H-6); 11.31 s, 1 H (H-3).

3-(3-Chloro-3-deoxy-4-*C*-hydroxymethyl-α-L-*threo*-pentofuranosyl)uracil (**14**)

Chloro derivative **13** (388 mg, 0.8 mmol) was converted into compound **14** (160 mg; 72%), m.p. 134–136 °C, exactly as described for the chloro derivative **12**. For $C_{10}H_{13}ClN_2O_5$ (276.7) calculated: 43.41% C, 4.74% H, 12.81% Cl, 10.13% N; found: 43.59% C, 4.82% H, 12.75% Cl, 9.94% N. UV spectrum (water): λ_{max} 264 nm (ε 7 550); (0.1 M NaOH): λ_{max} 294 nm (ε 10 550). ^{1}H NMR spectrum: 2.58 ddd, 1 H, *J*(2a′,1′) = 8.9, *J*(2a′,2b′) = 12.6, *J*(2a′,3′) = 8.6 (H-2a′); 2.88 ddd, 1 H, *J*(2b′,1′) = 3.9, *J*(2b′,3′) = 8.6 (H-2b′); 3.47 d, 2 H, *J*(5′,OH) = 4.3 (2 × H-5′); 3.54–3.78 m, 2 H (CH_2O); 4.63 t, 1 H (OH); 4.76–4.83 m, 2 H (H-3′, OH); 5.56 d, 1 H, *J*(5,6) = 7.8 (H-5); 6.68 dd, 1 H (H-1′); 7.43 d, 1 H (H-6); 11.12 bs, 1 H (H-1); exchange with D_2O: 3.47 s, 2 H (2 × H-5′); 3.59 d, 1 H, *J*(a,b) = 11.6 (CHaH-O); 3.73 d, 1 H (CHbH-O); 4.79 t, 1 H (H-3′).

1-{3-Acetylsulfanyl-5-*O*-benzoyl-4-*C*-[(benzoyloxy)methyl]-2,3-dideoxy-α-L-*threo*-pentofuranosyl}-uracil (**15**)

A solution of anhydro derivative **3** (224 mg, 0.5 mmol) in a mixture of thioacetic acid (1.5 ml) and HMPTA (1.5 ml) was heated at 110 °C for 1 h in a closed vessel (Wheaton Screw-top V-Vial, 5 ml). The reaction mixture was cooled and added dropwise into a solution of sodium hydrogen carbonate (2 g) in water (30 ml). The product was taken up in ethyl acetate (20 ml), the extract was washed with water (2 × 10 ml), dried and the solvent evaporated. Column chromatography on silica gel (25 g) in ethyl acetate–toluene (3 : 2) afforded 130 mg (50%) of mercapto derivative **15** as a solid foam. For $C_{26}H_{24}N_2O_8S$ (524.5) calculated: 59.53% C, 4.61% H, 5.34% N, 6.11% S; found: 59.75% C, 4.77% H, 5.10% N, 5.95% S. IR spectrum (*c* = 2%, $CHCl_3$): 3 390, 3 168 (NH); 1 725 (C=O, benzoyl + uracil); 1 693 (C=O, 1-substituted uracil + acetyl); 1 634 (C=C); 1 357 (CH_3, acetyl). ^{1}H NMR spectrum: 2.31 s, 3 H ($SCOCH_3$); 2.62–2.81 m, 2 H (2 × H-2′); 4.47–4.74 m, 5 H (H-3′, 2 × H-5′, CH_2-O); 5.7 dd, 1 H, *J*(5,3) = 2.1, *J*(5,6) = 7.9 (H-5); 6.18 dd, 1 H, *J*(1′,2a′) = 3.1, *J*(1′,2b′) = 8.2 (H-1′); 7.50–7.72 m and 7.94–8.01 m, 6 H and 4 H (H-arom.); 7.76 d, 1 H (H-6); 11.38 d, 1 H (H-3).

1-(2,3-Dideoxy-4-*C*-hydroxymethyl-3-sulfanyl-α-L-*threo*-pentofuranosyl)uracil (**16**)

A solution of benzoyl derivative **15** (263 mg, 0.5 mmol) in 0.15 M methanolic sodium methoxide (6 ml) was allowed to stand at room temperature under argon overnight and then neutralized by addition of Dowex 50 (H^+ form). The ion exchanger was filtered off, washed with methanol and the combined filtrates were concentrated. Column chromatography on silica gel in ethyl acetate–acetone–ethanol–water (19 : 3 : 2 : 1) and subsequent crystallization from propan-2-ol afforded 72 mg (52%) of the free thiol **16**, m.p. 182–184 °C. For $C_{10}H_{14}N_2O_5S$ (274.3) calculated: 43.79% C, 5.14% H, 10.21% N, 11.69% S; found: 43.52% C, 5.20% H, 10.05% N, 11.95% S. UV spectrum (water): λ_{max} 264 nm (ε 10 200); (0.1 M NaOH): λ_{max} 263 nm (ε 8 270). ^{1}H NMR spectrum: 2.31–2.58 m, 2 H (2 × H-2′); 2.65 d, 1 H, *J*(SH,3′) = 9.8 (3′-SH); 3.31–3.70 m, 5 H (H-3′, 2 × H-5′, CH_2O); 4.92 t, 1 H, *J*(OH,CH_2) = 4.9 (CH_2OH); 5.19 t, 1 H, *J*(OH,5′) = 5.3 (5′-OH); 5.58 dd, 1 H, *J*(5,3) = 2.1, *J*(5,6) = 7.9 (H-5); 6.11 dd, 1 H, *J*(1′,2a′) = 2.4, *J*(1′,2b′) = 7.3 (H- 1′); 7.98 d, 1 H (H-6); 11.26 d, 1 H (H-3).

1,1′-[Disulfandiylbis(2,3-dideoxy-4-hydroxymethyl-α-L-*threo*-pentofuranose-3,1-diyl]di(pyrimidine-2,4(1*H*,3*H*)-dione) (**17**)

To a solution of thiol **16** (82 mg, 0.3 mmol) in methanol (1 ml) was added dropwise 0.3 M methanolic solution of iodine (1 ml). The solution was set aside at 4 °C for 2 h and the crystalline product was collected and washed with methanol. Yield 59 mg (72%) of disulfide **17**, m.p. 180.5–183 °C. For $C_{20}H_{26}N_4O_{10}S_2$ (546.6) calculated: 43.95% C, 4.80% H, 10.25% N, 11.73% S; found: 43.69% C, 4.70% H, 9.96% N, 11.42% S. ^{1}H NMR spectrum: 2.43–2.74 m, 2 H (2 × H-2′); 3.41–3.85 m, 5 H

(CH_2O, 2 × H-5′, H-3′); 4.99 t, 1 H, J(CH_2,OH) = 5.2 (CH_2OH); 5.23 t, 1 H, J(5′,OH) = 5.4 (5′-OH); 5.62 dd, 1 H, J(5,3) = 1.8, J(5,6) = 8.2 (H-5); 6.16 dd, 1 H, J(1′,2a′) = 2.5, J(1′, 2b′) = 7.0 (H-1′); 7.93 d, 1 H (H-6); 11.28 d, 1 H (H-3).

1-(3,5-Di-*O*-benzoyl-4-*C*-chloromethyl-2-deoxy-β-D-*erythro*-pentofuranosyl)uracil (**18**)

Dibenzoyl derivative **7** (466 mg, 1 mmol) was added to a stirred solution of thionyl chloride (0.3 ml) in HMPTA (2 ml). After heating at 80 °C for 2 h, the mixture was added dropwise into a solution of sodium hydrogen carbonate (3.6 g) in water (20 ml) . The product was taken up in ethyl acetate (40 ml), the organic layer was washed with water (3 × 20 ml), dried and the solvent was evaporated. Column chromatography on silica gel (50 g) in ethyl acetate–toluene (3 : 2) gave a fraction of R_F 0.51 which on crystallization from propan-2-ol afforded 170 mg (35%) of chloro derivative **18**, m.p. 199–201 °C. For $C_{24}H_{21}ClN_2O_7$ (484.9) calculated: 59.45% C, 4.38% H, 7.31% Cl, 5.78% N; found: 59.33% C, 4.31% H, 7.28% Cl, 5.78% N. ^{1}H NMR spectrum: 2.65 m, 1 H (H-2a′); 2.85 pent, 1 H, J(2a′,2b′) = 14.0 (H-2b′); 4.14 d, 1 H, J(5a′,5b′) = 12.1 (H-5a′); 4.21 d, 1 H (H-5b′); 4.62 s, 2 H (CH_2O); 5.60 dd, 1 H, J(5,3) = 2.0, J(5,6) = 8.1 (H-5); 5.91 dd, 1 H, J(3′,2a′) = 4.9, J(3′,2b′) = 7.3 (H-3′); 6.38 t, 1 H, J(1′,2a′) = 6.7, J(1′,2b′) = 7.0 (H- 1′); 7.41–7.77 m, 7.93–7.97 m and 8.06–8.11 m, 7 H, 2 H and 2 H (H-6, H-arom.); 11.42 s, 1 H (H-3).

1-(4-*C*-Chloromethyl-2-deoxy-β-D-*erythro*-pentofuranosyl) uracil (**19**)

A solution of benzoyl derivative **18** (145 mg, 0.3 mmol) in 0.3 M methanolic sodium methoxide (1.5 ml) was set aside at room temperature for 1 h and then neutralized with Dowex 50 (H^+ form). The ion exchanger was filtered off and washed with methanol, the combined filtrates were evaporated and the residue was crystallized from propan-2-ol to give 69 mg (83%) of chloro derivative **19**, m.p. 147–149 °C. For $C_{10}H_{13}ClN_2O_5$ (276.7) calculated: 43.41% C, 4.74% H, 12.81% Cl, 10.13% N; found: 43.25% C, 4.70% H, 12.69% Cl, 10.07% N. ^{1}H NMR spectrum: 2.13–2.38 m, 2 H (2 × H-2′); 3.57 d, 2 H, J(CH_2,OH) = 5.2 (CH_2O); 3.73 d, 1 H, J(5a′,5b′) = 11.4 (H-5a′); 3.77 d, 1 H (H-5b′); 4.39 sext, 1 H, J(3′,2a′) = 3.4, J(3′,2b′) = 5.2, J(3′,OH) = 5.2 (H-3′); 5.23 t, 1 H (CH_2OH); 5.48 d, 1 H (3′-OH); 5.64 d, 1 H, J(5,6) = 7.9 (H-5); 6.24 dd, 1 H, J(1′,2a′) = 6.4, J(1′,2b′) = 7.6 (H-1′); 7.99 d, 1 H (H-6); 11.32 s, 1 H (H-3).

1-{3,5-Di-*O*-benzoyl-2-deoxy-4-*C*-[(acetylsulfanyl)methyl]-β-D-*erythro*-pentofuranosyl}uracil (**20**)

A solution of tosylate **9** (931 mg, 1.5 mmol) and sodium thioacetate (615 mg, 7.5 mmol) in HMPTA (6 ml) was heated at 110°C for 1 h. The reaction mixture was cooled, diluted with ethyl acetate, washed with water (3 × 20 ml), dried and the solvent was evaporated. Column chromatography on silica gel 80 g) in ethyl acetate–toluene (3 : 2) and subsequent crystallization from propan-2-ol gave 702 mg (89%) of sulfanyl derivative **20**, m.p. 141–143 °C. For $C_{26}H_{24}N_2O_8S$ (524.5) calculated: 59.53% C, 4.61% H, 5.34% N, 6.11% S; found: 59.67% C, 4.55% H, 5.14% N, 6.15% S. ^{1}H NMR spectrum: 2.32 s, 3 H (CH_3CO); 2.58–2.91 m, 2 H (2 × H-2′); 3.53 d, 1 H, J(5a′,5b′) = 14.0 (H-5a′); 3.57 d, 1 H (H-5b′); 4.49 s, 2 H (CH_2O); 5.56 dd, 1 H, J(5,3) = 2.1, J(5,6) = 8.2 (H-5); 5.87 dd, 1 H, J(3′,2a′) = 5.2, J(3′,2b′) = 7.0 (H-3′); 6,29 t, 1 H, J(1′,2a′) = 6.4, J(1′,2b′) = 6.7 (H-1′); 7.42–7.78 m and 7.94–8.09 m, 7 H and 4 H (H-6, H-arom.); 11.40 s, 1 H (H-3).

1-(2-Deoxy-4-*C*-sulfanylmethyl-β-D-*erythro*-pentofuranosyl) uracil (**21**)

A solution of benzoate **20** (525 mg, 1 mmol) in 0.5 M methanolic sodium methoxide (6 ml) was set aside under argon at room temperature overnight and then neutralized with Dowex 50 (H^+ form). The

ion exchanger was filtered off and washed with methanol and the combined filtrates were concentrated. The residue was chromatographed on a column of silica gel in ethyl acetate–acetone–ethanol–water (19 : 3 : 2 : 1) to give 193 mg (70%) of thiol **21** as a solid foam. For $C_{10}H_{14}N_2O_5S$ (274.3) calculated: 43.79% C, 5.14% H, 10.21% N, 11.69% S; found: 43.49% C, 5.26% H, 9.98% N, 11.91% S. ^{1}H NMR spectrum: 2.09–2.26 m, 3 H (2 × H-2′, HS); 2.57–2.79 m, 2 H (2 × H- 5′); 3.61 d, 2 H, J(CH$_2$,OH) = 5.2 (CH$_2$O); 4.31 m, 1 H, J(3′, 2a′) = 5.2, J(3′,2b′) = 4.3, J(3′,OH) = 4.9 (H-3′); 5.12 t, 1 H (CH$_2$OH); 5.36 d, 1 H (3′-OH); 5.63 d, 1 H, J(5,6) = 7.9 (H- 5); 6.19 t, 1 H, J(1′,2a′) = 7.0, J(1′,2b′) = 6.7 (H-1′); 7.87 d, 1 H (H-6); 11.29 s, 1 H (H-3).

1,1′-[Disulfandiylbis(2,5-dideoxy-4-hydroxymethyl-α-L-*threo*-pentofuranose-5,1-diyl]di(pyrimidine-2,4(1*H*,3*H*)-dione) (**22**)

A solution of thiol **21** (55 mg, 0.2 mmol) in 0.1 M methanolic sodium methoxide (0.8 ml) was stirred at room temperature for 3 days under sodium hydroxide protecting tube. After neutralization with Dowex 50 (H^+ form), the ion exchanger was filtered off and washed with methanol. The combined filtrates afforded 52 mg (95%) of disulfide **22** as a solid foam. For $C_{20}H_{26}N_4O_{10}S_2$ (546.6) calculated: 43.95% C, 4.80% H, 10.25% N, 11.73% S; found: 43.58% C, 5.01% H, 9.97% N, 11.98% S. ^{1}H NMR spectrum: 2.20 m, 2 H (2 × H-2′); 2.99 d, 1 H, J(5a′,5b′) = 13.8 (H-5a′); 3.20 d, 1 H (H-5b′); 3.57 d, 2 H, J(CH$_2$,OH) = 4.3 (CH$_2$O); 4.32 m, 1 H, J(3′,2a′) = J(3′,2b′) = 4.3, J(3′,OH) = 4.9 (H-3′); 5.12 t, 1 H (CH$_2$OH); 5.39 d, 1 H (3′-OH); 5.63 d, 1 H, J(5,6) = 8.2 (H-5); 6.19 t, 1 H, J(1′,2a′) = J(1′,2b′) = 6.7 (H-1′); 7.86 d, 1 H (H-6); 11.15 bs, 1 H (H-3).

3,2′-Anhydro-1-{4-*C*-[(benzoyloxy)methyl]-5-*O*-methanesulfonyl-α-L-*erythro*-pentofuranosyl}uracil (**23**)

To a solution of dimesylate **10** (3.63 g, 7 mmol) in acetonitrile (40 ml), 1,8-diazabicyclo[5.4.0]undec-7-ene (2 ml, 13 mmol) was added. The solution was heated at 50 °C for 20 h, cooled, and the deposited crystals were collected and washed with acetonitrile and ether. Yield 1.56 g (53%) of anhydro derivative **23**, m.p. 225–227 °C. The mother liquors were concentrated and the residue was partitioned between water (15 ml) and ethyl acetate (150 ml). The organic layer was washed with water (2 × 15 ml), dried over magnesium sulfate and concentrated to 20 ml to give another portion (490 mg; 16%) of the product **23**. For $C_{18}H_{18}N_2O_8S$ (422.4) calculated: 51.18% C, 4.30% H, 6.63% N, 7.59% S; found: 51.08% C, 4.23% H, 6.69% N, 7.53% S. ^{1}H NMR spectrum: 2.69 d, 1 H, J(2a′,2b′) = 13.6 (H-2a′); 2.84 m, 1 H (H-2b′); 3.26 s, 3 H (SO$_2$CH$_3$); 4.33 d, 1 H, J(a,b) = 11.9 (CHaH-O); 4.40 s, 2 H (2 × H-5′); 4.47 d, 1 H (CHbH-O); 5.48 bs, 1 H (H-3′); 5.80 d, J(5,6) = 7.3 (H-5); 6.05 d, 1 H, J(1′,2b′) = 3.7 (H- 1′); 7.67 d, 1 H (H-6); 7.47–7.55 m, 7.63–7.72 m and 7.95–8.00 m, 2 H, 1 H and 2 H (H-arom.).

1-{3-Acetylsulfanyl-5-*O*-methanesulfonyl-4-*C*-[(benzoyloxy)methyl]-2,3-dideoxy-α-L-*threo*-pentofuranosyl}uracil (**24**)

A solution of anhydro derivative **23** (1.06 g, 2.5 mmol) in a mixture of dioxane (5 ml) and thioacetic acid (5 ml) was heated at 120 °C for 1.5 h in a pressure vessel. After cooling, the reaction mixture was added dropwise into a solution of sodium hydrogen carbonate (10 g) in water (150 ml) and the product was taken up in ethyl acetate (150 ml). The organic phase was washed with water (50 ml), dried over magnesium sulfate, and the solvent was evaporated. Column chromatography on silica gel (130 g) in ethyl acetate–toluene (5 : 1) gave 536 mg (43%) of mercapto derivative **24** as a solid foam. For $C_{20}H_{22}N_2O_9S_2$ (422.4) calculated: 48.18% C, 4.45% H, 5.62% N, 12.86% S; found: 47.89% C, 4.23% H, 5.42% N, 12.58% S. IR spectrum (chloroform): 3 390 (NH), 3 064 (CH arom.), 1 726 (C=O benzoate), 1 712 (C=O uracil), 1 695 (C=O 1-substituted uracil + acetate), 1 633 (C=C),

1 369 (SO_2 asym.), 1 178 (SO_2 sym.), 624 (C-S). ^{1}H NMR spectrum: 2.34 s, 3 H (CH_3CO); 2.57–2.73 m, 2 H (2 × H-2′); 3.31 s, 3 H (CH_3SO_2); 4.35–4.69 m, 5 H (H-3′, 2 × H-5′, CH_2O); 5.46 dd, 1 H, *J*(1′,2a′) = 3.1, *J*(1′, 2b′) = 7.9 (H-1′); 7.50–7.60 m, 7.65–7.76 m and 7.96–8.01 m, 2 H, 2 H and 2 H (H-6, H-arom.); 11.37 s, 1 H (H-3).

1-(3,5-Anhydro-2,3-dideoxy-4-*C*-hydroxymethyl-3-sulfanyl-α-L-*threo*-pentofuranosyl)uracil (**25**)

A solution of acetylsulfanyl derivative **24** (499 mg, 1 mmol) in 0.3 M methanolic sodium methoxide (7 ml) was set aside at room temperature overnight. The deposited solid was filtered off, washed with methanol and the combined filtrates were neutralized with Dowex 50 (H^+ form). The ion exchanger was removed by filtration, washed with methanol and the combined filtrates were evaporated. Column chromatography of the residue on silica gel (15 g) in ethyl acetate and subsequent crystallization from methanol gave 165 mg (64%) of anhydro derivative **25**, m.p. 214–216.5 °C. The mother liquors gave another 30 mg (12%) of the product. For $C_{10}H_{12}N_2O_4S$ (256.3) calculated: 46.86% C, 4.72% H, 10.93% N, 12.51% S; found: 46.75% C, 4.72% H, 11.04% N, 12.69% S. UV spectrum (water): λ_{max} 262 nm (ε 10 480); (0.1 M NaOH): λ_{max} 261 nm (ε 7 660). ^{1}H NMR spectrum: 2.09 ddd, 1 H, *J*(2a′,1′) = 8.5, *J*(2a′,2b′) = 14.0, *J*(2a′,3′) = 6.4 (H-2a); 2.37 dd, 1 H, *J*(2b′,1′) = 5.5 (H-2b′); 2.99 d, 1 H, *J*(5a′,5b′) = 10.4 (H-5a′); 3.33 d, 1 H (H-5b′); 3.52 m, 2 H (CH_2O); 4.14 d, 1 H (H-3′); 5.20 t, 1 H, *J*(OH,CH_2) = 5.8 (CH_2OH); 5.68 d, 1 H, *J*(5,6) = 8.2 (H-5); 6.81 dd, 1 H (H-1′); 7.76 d, 1 H (H-6); 11.41 s, 1 H (H-3).

1-(3,5-Anhydro-2-deoxy-4-*C*-hydroxymethyl-α-L-*threo*-pentofuranosyl)uracil (**26**)

A) A solution of tosylate **8** (517 mg, 1 mmol) in 0.3 M methanolic sodium methoxide (4 ml) was allowed to stand at room temperature overnight. Dowex 50 (H^+ form) was added to the neutral reaction, the ion exchanger was removed by filtration, washed with methanol and the combined filtrates were evaporated. The residue was subjected to column chromatography on silica gel (40 g) in ethyl acetate–acetone–ethanol–water (19 : 3 : 2 : 1). The fraction of R_F 0.64, upon crystallization from propan-2-ol, afforded 140 mg (34%) of 1-(2-deoxy-4-*C*-hydroxymethyl-5-*O*-*p*-toluenesulfonyl-α-L-*threo*-pentofuranosyl)uracil (**27**), m.p. 191–192.5 °C. For $C_{17}H_{20}N_2O_8$ S (412.4) calculated: 49.51% C, 4.81% H, 6.79% N, 7.77% S; found: 49.27% C, 4.88% H, 6.73% N, 7.41% S. ^{1}H NMR spectrum: 2.01–2.27 m, 2 H (2 × H-2′); 2.40 s, 3 H (CH_3); 3.42 d, 2 H, *J*(CH_2,OH) = 5.0 (CH_2O); 4.10 s, 2 H (2 × H-5′); 4.30–4.37 m, 1 H (H-3′); 5.27 t, 1 H (CH_2OH); 5.45 d, 1 H, *J*(OH,3′) = 4.9 (3′-OH); 5.62 dd, 1 H, *J*(5,3) = 2.1, *J*(5,6) = 8.2 (H-5); 6.05 dd, 1 H, *J*(1′,2a′) = 6.3, *J*(1′,2b′) = 7.5 (H-1′); 7.44 d, 2 H, *J*(*o*,*m*) = 8.2 (2 × *o*-H tosyl); 7.67 d, 1 H (H-6); 7.77 d, 2 H (2 × *m*-H tosyl); 11.33 d, 1 H (H-3).

The second fraction (R_F 0.39), upon crystallization from propan-2-ol, afforded 97 mg (40%) of anhydro derivative **26**, m.p. 191–192.5 °C. For $C_{10}H_{12}N_2O_5$ (240.2) calculated: 50.00% C, 5.04% H, 11.66% N; found: 49.78% C, 4.94% H, 11.49% N. ^{1}H NMR spectrum: 1.88 ddd, 1 H, *J*(2a′,1′) = 9.2, *J*(2a′,2b′) = 14.3, *J*(2a′,3′) = 4.3 (H-2a′); 2.37 dd, 1 H, *J*(2b′,1′) = 5.5 (H-2b′); 3.58–3.74 m, 2 H (CH_2O); 4.31 d, 1 H, *J*(5a′,5b) = 7.6 (H-5a′); 4.64 d, 1 H (H-5b′); 5.13 t, 1 H, *J*(OH,CH_2) = 5.6 (CH_2OH); 5.22 d, 1 H (H-3′); 5.69 d, 1 H, *J*(5,6) = 7.9 (H-5); 6.59 dd, 1 H (H-1); 7.72 d, 1 H (H-6); 11.42 s, 1 H (H-3) .

B) A solution of tosyl derivative **8** (129 mg, 0.25 mmol) in 0.3 M methanolic sodium methoxide (3 ml) was set aside at room temperature overnight. The mixture was neutralized with Dowex 50 (H^+ form), the ion exchanger was filtered off and washed with methanol. The filtrates were combined and the solvent was evaporated. Crystallization from propan-2-ol afforded 50 mg (83%) of compound **26**.

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