Synthesis of Some 2',3'-Didehydro-2',3'-dideoxynucleosides Derived from Modified Pyrimidine Bases

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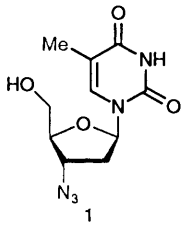
3',5'-Bis-*O*-(4-tolylsulfonyl)-thymidine and -2'-deoxyuridine (**13a** and **13b**) reacted with sodium ethoxide in boiling ethanol to give the corresponding ethoxy-oxetanes **12a** and **12b** in 67 and 66% overall yield for the two-step processes starting from thymidine **4a** and 2'-deoxyuridine **4b**, respectively. Treatment of the ethoxy-oxetanes **12a** and **12b** with hydrogen sulfide and N^1,N^1,N^3,N^3-tetramethylguanidine in dry pyridine solution gave the 2-thiothymine- and 2-thiouracil-derived oxetanes **19a** and **19b** in 62 and 68.5% yield, respectively. When the latter compounds were treated with potassium *tert*-butoxide in dimethyl sulfoxide, the corresponding 2',3'-didehydro-2',3'-dideoxynucleosides (d4 nucleosides) **10a** and **10b** were obtained in 66 and 60% yield, respectively. The 2-thiothymine-derived oxetane **19a** was converted *via* the 5-methyl-2-thiocytosine-derived oxetane **21a** into the 5-methyl-2-thiocytosine-derived d4 nucleoside **11a** in 59.5% overall yield; the 2-thiouracil-derived oxetane **19b** was similarly converted into the 2-thiocytosine- and 4-*N*-methyl-2-thiocytosine-derived d4 nucleosides **11b** and **23** in 51 and 50% overall yield, respectively. Finally, the ethoxy-oxetane **12b** was converted into the corresponding amino- and methylamino-oxetanes **25a** and **25b** in 74 and 83% yield, respectively. The latter compound, **25b**, was successfully converted into the 2-*N*-methylisocytosine-derived d4 nucleoside **26b** in 62% yield.

Work on the synthesis of nucleoside analogues has recently received a considerable stimulus from the discovery that 3'-azido-3'-deoxythymidine (AZT, 1) and a number of related 2',3'-dideoxynucleoside derivatives possess high anti-HIV activity.[1,2] The 2',3'-didehydro-2',3'-dideoxynucleosides (d4 nucleosides) constitute one such group of nucleoside analogues that has been examined in this context, and indeed 2',3'-didehydro-3'-deoxythymidine (d4T) **2** and 2',3'-didehydro-2',3'-dideoxycytidine (d4C) **3** have both been found[1] to be powerful anti-HIV agents.



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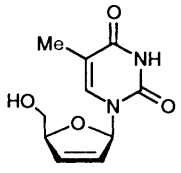

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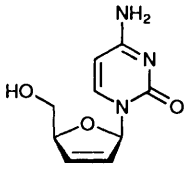

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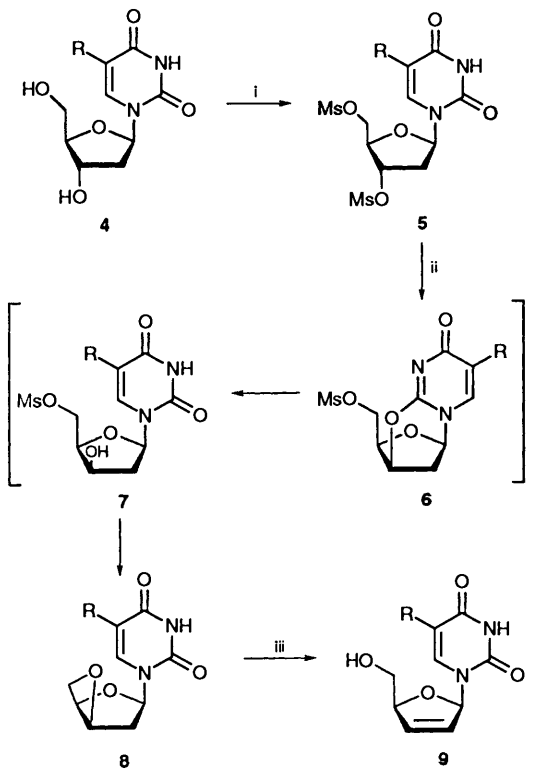
Methods have been developed for the transformation of both 2'-deoxyribonucleosides[3-10] and ribonucleosides[11-15] into the corresponding d4 nucleosides. In general, these transformations involve the modification only of the sugar moiety of the nucleoside with the aglycone remaining unchanged. One of the simplest and most efficient procedures for the conversion of 2'-deoxynucleosides into d4 nucleosides is that originally reported by Horwitz *et al.*;[3a] this procedure (Scheme 1) involves first converting the 2'-deoxynucleoside **4** into its 3',5'-bis-*O*-(methylsulfonyl) derivative **5** and then heating the latter product with aq. sodium hydroxide, under reflux, to give[16] the corresponding oxetane derivative **8**, usually in satisfactory yield. It is assumed that when the 3',5'-bis-*O*-(methylsulfonyl) derivative **5** obtained in step i is heated in alkaline solution, it first cyclizes[16] to give the 2,3'-anhydronucleoside **6** which then readily undergoes alkaline hydrolysis to give the monomethylsulfonyl derivative **7**. The latter derivative **7** is the putative precursor of the corresponding oxetane **8**. Following Horwitz's procedure,[16] we recently converted thymidine **4a** and 2'-deoxyuridine **4b** into the corresponding oxetanes in 65 and 68% overall isolated yield,[10] respectively. Horwitz *et al.* showed[3a] that the latter oxetanes **8a** and **8b** may readily be transformed into the corresponding d4 nucleosides **9a** and **9b** by treatment with potassium *tert*-butoxide in dimethyl sulfoxide (DMSO) at room temperature. We have since reported[10] that these transformations can also be effected by sodium hydride in *N*,*N*-dimethylacetamide (DMA) at 100 °C.

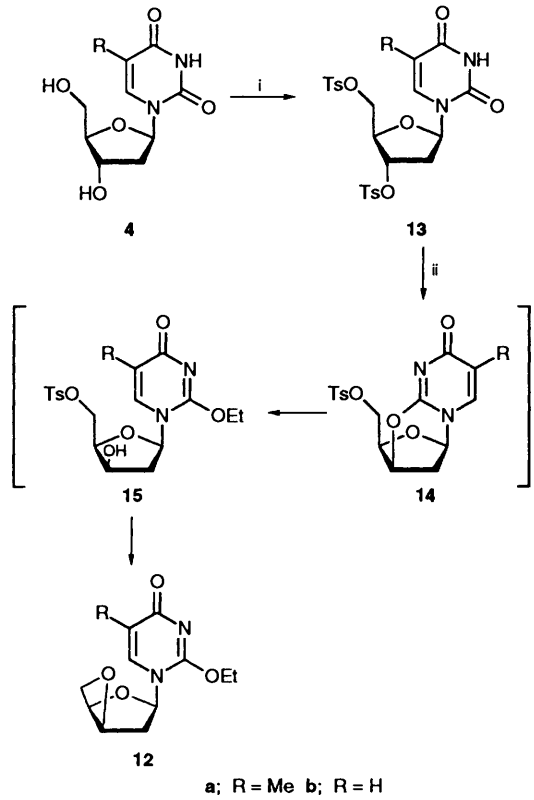
Results and Discussion

In a continuing search for other nucleoside analogues with potential anti-HIV activity, we have undertaken the synthesis of d4 nucleosides derived from 2-mercapto- and 2-aminopyrimidines. Our principal synthetic targets were the previously unreported d4 nucleosides **10a**, **10b**, **11a** and **11b** derived from 2-thiothymine, 2-thiouracil, 5-methyl-2-thiocytosine and 2-thiocytosine, respectively. Common 2'-deoxynucleosides (*i.e.*, thymidine **4a** and 2'-deoxyuridine **4b**) were again used as starting materials, but a novel synthetic strategy that involved the simultaneous modification both of the sugar moiety and the aglycone was adopted. Thus when crude 3',5'-bis-*O*-(methylsulfonyl)thymidine **5a**, obtained by the action of methanesulfonyl chloride on thymidine **4a** and not further purified, was heated with ~2 mol equiv. of sodium ethoxide in ethanol solution, under reflux, the ethoxy-oxetane **12a** was obtained and was isolated as a crystalline solid in 61% overall yield. The overall yield for this two-step process was increased to 67% when thymidine **4a** was first treated with toluene-4-sulfonic anhydride[17] in pyridine solution and the crude 3',5'-bis-*O*-(4-tolylsulfonyl) derivative **13a** (Scheme 2) was then heated, under reflux, with sodium ethoxide in ethanol solution. The suggested pathway for the conversion of the bis-*O*-(4-tolylsulfonyl) derivative **13a**, *via* the putative intermediates **14a** and **15a**, into the ethoxy-oxetane **12a** is indicated in Scheme 2. This pathway is very similar to that suggested above (Scheme 1) for the conversion of the bis-*O*-(methylsulfonyl) derivatives **5** into the corresponding simple oxetanes **8** except that the putative intermediate 2,3'-anhydronucleoside **14a** undergoes ethanolysis rather than hydrolysis at C-2. In the same way (Scheme 2), 2'-deoxyuridine **4b** was converted, *via* its 3',5'-bis-



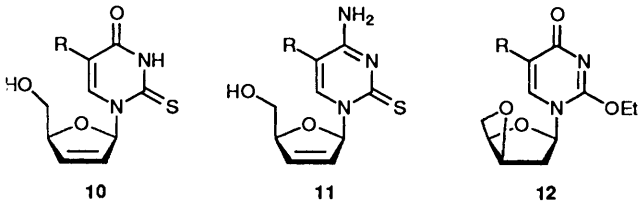
a; R = Me b; R = H (9a ≡ 2)

Scheme 1 *Reagents and conditions:* i, $MeSO_2Cl$, C_5H_5N; ii, aq. NaOH, reflux; iii, KOBu^t, DMSO, room temp. **or** NaH, DMA, 100 °C

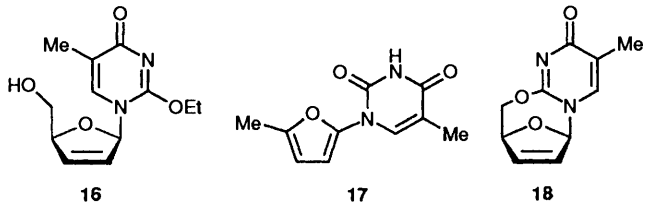


a; R = Me b; R = H

Scheme 2 *Reagents and conditions:* i, Ts_2O, C_5H_5N, 0 °C to room temp.; ii, NaOEt, EtOH, reflux, 10 min

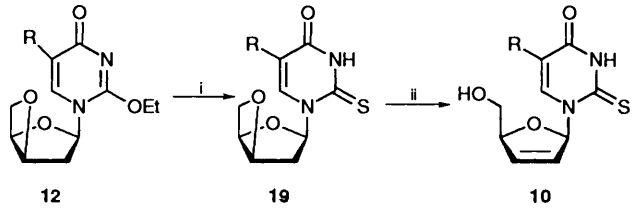


a; R = Me b; R = H



O-(4-tolylsulfonyl) derivative **13b** and the putative intermediates **14b** and **15b**, into the corresponding ethoxy-oxetane **12b** in 66% isolated yield. When the more accessible toluene-4-sulfonyl chloride was used instead of toluene-4-sulfonic anhydride in the first step of the conversion of 2′-deoxyuridine **4b** into the ethoxy-oxetane **12b**, the overall yield for the two-step process fell to 51%, and two uncharacterized by-products (Experimental section) were obtained. It is believed that nucleophilic attack by chloride ions at C-5′ of the 3′,5′-bis-*O*-(4-tolylsulfonyl) derivative **13b** may have occurred, and that this may have contributed to the lowering of the yield of the ethoxy-oxetane. However, this has not been fully investigated.

Attempts to convert the ethoxy-oxetane **12a** into the corresponding d4 nucleoside derivative **16** were unsuccessful. Hence, when compound **12a** was treated with potassium *tert*-butoxide in DMSO solution at room temperature, none of the desired d4 compound **16** was obtained. The only products isolated were 2-methyl-5-(thymin-1-yl)furan [3c] **17** and d4T [3a] **2** in 32.5 and 3.5% yield, respectively. A possible explanation for the formation of the furan derivative **17** involves the desired d4 nucleoside derivative **16** as an intermediate. It is not unlikely that potassium *tert*-butoxide would react with compound **16** in DMSO solution to give the 2,5′-anhydronucleoside **18**, and then react further with compound **18** by promoting an elimination reaction followed by a prototropic rearrangement, thereby leading to the furan derivative **17**. The outcome of this experiment led us to conclude that it would be necessary to modify the aglycones of the ethoxy-oxetanes **12a** and **12b** in the desired manner before carrying out the ring-opening reaction with potassium *tert*-butoxide. The latter approach proved to be successful. Thus when hydrogen sulfide was bubbled into a solution of the ethoxy-oxetane **12a** and an excess of N^1,N^1,N^3,N^3-tetramethylguanidine (TMG) in dry pyridine at 0 °C (Scheme 3) and the reactants were then stirred at room



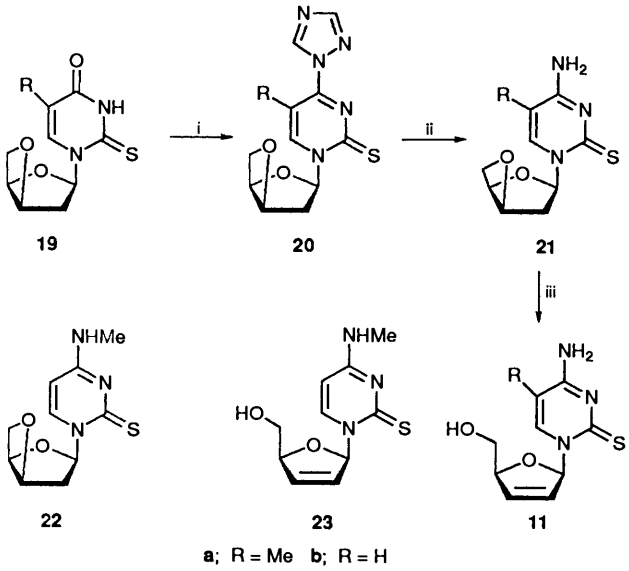
a; R = Me b; R = H

Scheme 3 *Reagents and conditions:* i, H_2S, TMG, C_5H_5N, 0 °C to room temp.; ii, KOBu^t, DMSO, room temp.

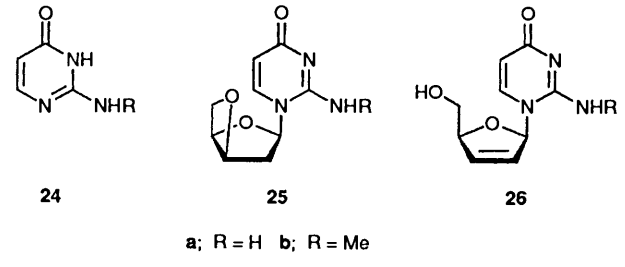
temperature, the 2-thiothymine-derived oxetane **19a** was obtained in 62% isolated yield. When compound **19a** was allowed to react with 2 mol equiv. of potassium *tert*-butoxide in DMSO at room temperature, 2′,3′-didehydro-3′-deoxy-2-thiothymidine **10a** was obtained in 66% isolated yield. In the same way, the ethoxy-oxetane **12b** was converted (Scheme 3) *via* the

2-thiouracil-derived oxetane **19b** into 2',3'-didehydro-2',3'-dideoxy-2-thiouridine **10b** and isolated in 41% overall yield for the two steps.

The d4 nucleosides derived from 5-methyl-2-thiocytosine and 2-thiocytosine (**11a** and **11b**, respectively) were prepared (Scheme 4) from the oxetanes **19a** and **19b**. The latter compounds, **19a** and **19b**, were first converted by the usual procedure[18] into the 4-(1,2,4-triazolo) derivatives **20a** and **20b**, respectively, in very high yield (Experimental section). Treatment of these triazolo-oxetanes **20a** and **20b** with ammonia in methanol solution at room temperature overnight gave[18] the amino-oxetanes **21a** and **21b**, respectively, in almost quantitative yield. While the 5-methyl-2-thiocytosine-derived oxetane derivative **21a** rather surprisingly failed to react with potassium *tert*-butoxide in DMSO at room temperature, it reacted readily with sodium hydride[10] in DMSO at 100 °C (Scheme 4) to give the corresponding d4 nucleoside **11a** which was isolated in 62% yield. However, the 2-thiocytosine-derived oxetane **21b** reacted in the usual way with potassium *tert*-butoxide in DMSO at room temperature to give the d4 nucleoside **11b** which was isolated in 60% yield. The overall yields for the three-step conversions of oxetanes **19a** and **19b** into d4 nucleosides **11a** and **11b** were 59.5 and 51%, respectively. Finally, the triazolo-oxetane **20b** was allowed to react[18] with methylamine in ethanol solution at room temperature to give the methylamino-oxetane **22** in 88% isolated yield. Treatment of this compound with potassium *tert*-butoxide in DMSO at room temperature gave 2',3'-didehydro-2',3'-dideoxy-4-*N*-methyl-2-thiocytidine **23** in 60% isolated yield.



Scheme 4 *Reagents and conditions:* i, 1,2,4-triazole, $POCl_3$, Et_3N, MeCN, 0 °C to room temp.; ii, NH_3, MeOH, room temp.; iii, NaH, DMSO, 100 °C **or** KOBu^t, DMSO, room temp.



The final two d4 nucleoside target molecules included in this study were derived from isocytosine **24a** and 2-*N*-methylisocytosine **24b**. When the ethoxy-oxetane **12b** was allowed to react with conc. aq. ammonia at room temperature, the corresponding amino-oxetane **25a** was obtained[19] in 74% isolated yield. In the same way, the methylamino-oxetane **25b** was isolated in 83% yield from the products of the reaction between the ethoxy-oxetane **12b** and alcoholic methylamine. When the amino-oxetane **25a** was treated with potassium *tert*-butoxide in DMSO in the usual way, what is believed to be a ~1:1 mixture of the desired isocytosine derivative **26a** and isocytosine **24a** itself was obtained in ~68% combined yield (Experimental section). Both products are extremely polar and attempts so far to obtain the pure d4 nucleoside derivative **26a** free from its aglycone **24a** have been unsuccessful. However, the d4 nucleoside **26b** derived from 2-*N*-methylisocytosine **24b** was readily isolated as a pure crystalline solid in 62% yield from the products of the reaction between potassium *tert*-butoxide and the methylamino-oxetane derivative **25b** in DMSO solution. All of the d4 nucleoside derivatives described in this report are in the process of being screened for antiviral activity.

Experimental

M.p.s were measured with a Büchi melting point apparatus and are uncorrected. ^1H NMR spectra, unless otherwise stated, were measured at 360 MHz with a Bruker AM 360 spectrometer; ^{13}C NMR spectra were measured at 90.6 MHz with the same spectrometer. Tetramethylsilane was used as an internal standard, and *J* values are given in Hz. UV spectra were measured with a Perkin-Elmer Lambda-3 spectrophotometer. Merck silica gel 60 F_{254} TLC plates were developed in solvent systems A [chloroform–methanol (9:1 v/v)], B [chloroform–methanol (19:1 v/v)] and C [propan-2-ol–aq. ammonia (*d* 0.88)–water (7:1:2 v/v)]. Merck silica gel H was used for short-column chromatography. Acetonitrile, triethylamine and pyridine were dried by heating, under reflux, over calcium hydride and were then distilled; DMSO, 1-methylimidazole and TMG were dried by distillation over calcium hydride under reduced pressure. Potassium *tert*-butoxide (purchased from the Aldrich Chemical Co.) was resublimed before use.

1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)-2-O-*ethylthymine* **12a**.—(*a*) Methanesulfonyl chloride (3.75 cm^3, 48.5 mmol) was added dropwise to a cooled (ice–water-bath), stirred solution of thymidine **4a** (5.335 g, 22.0 mmol) in dry pyridine (75 cm^3). After the reactants had been stirred at 0 °C for 1 h and then kept at 5 °C for 18 h, the products obtained were poured onto ice (500 g). The resultant mixture was filtered and the solid residue was washed with ice-cold water (3 × 150 cm^3) and then dried *in vacuo* over P_2O_5 at 60 °C (8.7 g).

Sodium ethoxide, freshly prepared by dissolution of sodium metal (1.01 g, 0.044 g-atom) in ethanol (29 cm^3), was added to a solution of the latter material (7.95 g) in ethanol (80 cm^3) and the reactants were heated, under reflux, for 10 min. The cooled products were neutralized with solid CO_2 and were then concentrated under reduced pressure. The residue was extracted with boiling acetone (4 × 100 cm^3). The combined extracts were evaporated under reduced pressure and the residue was fractionated by chromatography on silica gel. Elution of the column with chloroform–ethanol (19:1 v/v) and concentration of the appropriate fractions gave a solid (3.10 g, 61%). After crystallization from ethyl acetate, the *title compound* **12a** (Found: C, 57.2; H, 6.5; N, 11.1. $C_{12}H_{16}N_2O_4$ requires C, 57.1; H, 6.4; N, 11.1%) had m.p. 152 °C; R_f 0.32 (system **B**); $\delta_H[(CD_3)_2SO]$ 1.34 (3 H, t, *J* 7.1), 1.82 (3 H, d, *J* 1.0), 2.48 (1 H,

m), 2.67 (1 H, dd, *J* 1.6 and 16.2), 4.00 (1 H, dd, *J* 1.8 and 8.3), 4.39 (2 H, quart, *J* 7.1), 4.70 (1 H, dd, *J* 4.2 and 8.3), 4.97 (1 H, m), 5.51 (1 H, t, *J* 4.7), 6.48 (1 H, dd, *J* 1.8 and 8.1) and 8.10 (1 H, m); δ_C[$(CD_3)_2SO$] 13.50, 13.94, 37.10, 64.25, 75.20, 80.33, 86.69, 89.91, 115.86, 134.65, 155.43 and 170.39.

(*b*) Toluene-4-sulfonic anhydride[17] (5.87 g, 18.0 mmol) was added to a cooled (ice–water-bath), stirred solution of thymidine **4a** (1.452 g, 6.0 mmol) in dry pyridine (24 cm^3), and the reactants were allowed to warm up to room temperature. After a further period of 10 min, the products were poured into an ice–water mixture (100 g). The resulting mixture was extracted with chloroform (3 × 50 cm^3). The combined organic layers were washed successively with saturated aq. sodium hydrogen carbonate (2 × 75 cm^3) and water (2 × 100 cm^3), and were then dried ($MgSO_4$), and evaporated under reduced pressure. Toluene (2 × 100 cm^3) was added to the residue obtained and was then removed by evaporation under reduced pressure. The residue was purified by chromatography on silica gel (yield 2.76 g).

The latter material (2.20 g) was allowed to react with sodium ethoxide, freshly prepared from sodium metal (0.202 g, 0.0088 g-atom) following the procedure described in (*a*) above. After work-up and chromatography, 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-2-*O*-ethylthymine **12a** (0.811 g, 67%) was obtained as a solid. The latter material was identical (TLC, m.p., ^1H NMR) with the material described in (*a*) above.

1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)-2-O-*ethyluracil* **12b**.—(*a*) Toluene-4-sulfonyl chloride (22.5 g, 0.118 mol) was added to a stirred solution of 2′-deoxyuridine **4b** (7.69 g, 33.7 mmol) and 1-methylimidazole (13.46 cm^3, 0.169 mol) in pyridine (140 cm^3)–acetonitrile (140 cm^3) at 0 °C (ice–water-bath). The reactants were stirred at room temperature for 16 h and were then concentrated (to ~ 100 cm^3) under reduced pressure. Ice-cold water (200 cm^3) was then added and the resulting mixture was extracted with chloroform (3 × 150 cm^3). The combined extracts were washed successively with saturated aq. sodium hydrogen carbonate (2 × 200 cm^3) and brine (2 × 200 cm^3), and were then dried ($MgSO_4$). Toluene (3 × 200 cm^3) was added to the residue obtained and was then removed by evaporation under reduced pressure. After work-up and chromatography, a colourless solid [14.91 g, R_f 0.35 (system B)] was obtained; it was clear from its ^1H NMR spectrum {δ_H[$(CD_3)_2SO$] *inter alia*: 6.01 (0.75 H, t, *J* 6.9) and 6.13 (0.25 H, t, *J* 7.2)} that this material was a ~ 3 : 1 mixture of two compounds.

The latter material was heated under reflux, with sodium ethoxide, freshly prepared from sodium metal (1.40 g, 0.061 g-atom), in ethanol (167 cm^3) solution for 10 min. After work-up and chromatography following the procedure described above in preparation (*a*) of the corresponding thymine derivative **12a**, the *title compound* **12b** (4.14 g, 51% based on 2′-deoxyuridine **4b**) was obtained (Found, in material crystallized from ethyl acetate: C, 55.5; H, 6.0; N, 11.7. $C_{11}H_{14}N_2O_4$ requires C, 55.5; H, 5.9; N, 11.8%), m.p. 112 °C; R_f 0.48 (system A); δ_H[$(CD_3)_2SO$] 1.34 (3 H, t, *J* 7.1), 2.46 (1 H, m), 2.66 (1 H, d, *J* 16.2), 3.99 (1 H, dd, *J* 1.4 and 8.2), 4.39 (2 H, quart, *J* 7.1), 4.69 (1 H, dd, *J* 4.1 and 8.3), 4.97 (1 H, m), 5.50 (1 H, t, *J* 4.6), 5.89 (1 H, d, *J* 7.7), 6.47 (1 H, d, *J* 7.1) and 8.19 (1 H, d, *J* 7.7); δ_C[$(CD_3)_2SO$] 13.90, 37.11, 64.24, 75.11, 80.49, 86.63, 90.11, 107.90, 138.90, 155.64 and 169.64. Two other compounds, with R_f-values 0.39 and 0.43 (system A), were also isolated from the products.

(*b*) Toluene-4-sulfonic anhydride[17] (13.69 g, 41.9 mmol) was added to a cooled (ice–water-bath) solution of 2′-deoxyuridine **4b** (3.192 g, 13.9 mmol) in dry pyridine (42 cm^3), and the reactants were allowed to warm up to room temperature. After a further period of 10 min, the products were poured into an ice–water mixture (200 g), and then worked up and chromatographed as in the above reaction between toluene-4-sulfonic anhydride and thymidine. The product (6.37 g) obtained was found by ^1H and ^{13}C NMR spectroscopy {δ_C[$(CD_3)_2SO$] 21.13, 21.17, 35.52, 68.63, 79.35, 80.24, 85.26, 102.06, 125.50, 127.64, 127.66, 128.05, 130.14, 130.37, 131.79, 132.23, 141.20, 145.24, 145.57, 150.14 and 162.98} to contain only one nucleoside component, assumed to be 2′-deoxy-3′,5′-bis-*O*-(4-tolylsulfonyl)uridine **13b**; R_f 0.35 (system B).

The latter material (5.48 g) was heated, under reflux, with sodium ethoxide, freshly prepared from sodium metal (0.517 g, 0.022 g-atom), in ethanol (60 cm^3) solution for 10 min. After work-up and chromatography following the procedure described above in preparation (*a*) of the corresponding thymidine derivative **12a**, 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-2-*O*-ethyluracil **12b** (1.89 g, 66% based on 2′-deoxyuridine **4b**) was obtained as a solid. The latter material was identical (TLC, m.p., ^1H NMR) with the material described in (*a*) above.

Action of Potassium tert-Butoxide in DMSO Solution on 1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)-2-O-*ethylthymine* **12a**.—Resublimed potassium *tert*-butoxide (0.247 g, 2.2 mmol) was added to a stirred solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-2-*O*-ethylthymine (0.252 g, 1.0 mmol) in dry DMSO (4 cm^3) under nitrogen at room temperature. After 1 h, the reaction was quenched with solid carbon dioxide and the products were evaporated under reduced pressure (oil-pump) below 40 °C. The residue was extracted with acetone (2 × 25 cm^3) at room temperature. The combined extracts were concentrated under reduced pressure, and the residue obtained was fractionated by chromatography on silica gel. Elution of the column with chloroform–ethanol (98 : 2 to 95 : 5 v/v) and concentration of the appropriate fractions gave (a) 2-methyl-5-(thymin-1-yl)furan **17** (0.067 g, 32.5%), m.p. 165 °C (lit.,[3c] 165–166.5 °C), R_f 0.48 (system B), identical (TLC, ^1H and ^{13}C NMR) with authentic material; and (b) 2′,3′-didehydro-3′-deoxythymidine **2** (0.008 g, 3.5%), R_f 0.26 (system B), identical (TLC, ^1H NMR) with authentic material.[3a]

1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)-2-*thiothymine* **19a**.—A slow continuous stream of hydrogen sulfide gas was introduced into a stirred solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-2-*O*-ethylthymine **12a** (2.36 g, 9.35 mmol) and TMG (11.70 cm^3, 93 mmol) in dry pyridine (50 cm^3) at 0 °C (ice–water-bath) for 1 h. The reactants were then stirred at room temperature for a further period of 10 h, after which nitrogen gas was bubbled through the solution. The products were then evaporated under reduced pressure to ~ one-half volume, and were poured into ice-cold hydrochloric acid (~ 1.0 mol dm^{-3}; 200 cm^3). The resulting mixture was extracted with chloroform (2 × 150 cm^3) and the extract was washed with water (2 × 100 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was fractionated by chromatography on silica gel: elution of the column with chloroform–ethanol (98 : 2 v/v) and concentration of the appropriate fractions gave the *title compound* **19a** (1.40 g, 62%). Crystallization from absolute ethanol gave fine needles (Found: C, 50.1; H, 5.0; N, 11.55. $C_{10}H_{12}N_2O_4S$ requires C, 50.0; H, 5.0; N, 11.7%), m.p. 152 °C; R_f 0.44 (system A); δ_H[$(CD_3)_2SO$] 1.87 (3 H, d, *J* 1.2), 2.44 (1 H, dd, *J* 2.8 and 16.0), 2.63 (1 H, m), 4.18 (1 H, m), 4.71 (1 H, dd, *J* 3.8 and 8.3), 4.96 (1 H, m), 5.48 (1 H, m), 7.20 (1 H, dd, *J* 2.8 and 8.1), 8.15 (1 H, m) and 12.68 (1 H, br s); δ_C[$(CD_3)_2SO$] 12.99, 39.07, 74.82, 81.65, 86.98, 94.45, 116.19, 137.63, 161.10 and 175.99.

1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)-2-*thiouracil* **19b**.—A solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-

pentofuranosyl)-2-*O*-ethyluracil **12b** (2.21 g, 9.3 mmol) and TMG (11.64 cm^3, 93 mmol) in dry pyridine (46 cm^3) was treated with hydrogen sulfide at 0 °C for 1 h and then at room temperature for 6 h according to the procedure described above in the preparation of the corresponding 2-thiothymine derivative **19a**. The products were worked up and chromatographed in the same way to give the *title compound* **19b** (1.438 g, 68.5%). Crystallization from absolute ethanol gave needles (Found: C, 47.65; H, 4.5; N, 12.2. $C_9H_{10}N_2O_3S$ requires C, 47.8; H, 4.5; N, 12.4%), m.p. 185 °C; R_f 0.44 (system A); $\delta_H[(CD_3)_2SO]$ 2.43 (1 H, dd, *J* 2.5 and 6.1), 2.62 (1 H, m), 4.14 (1 H, m), 4.69 (1 H, dd, *J* 3.7 and 8.3), 4.96 (1 H, m), 5.47 (1 H, m), 6.09 (1 H, dd, *J* 2.2 and 8.1), 7.19 (1 H, dd, *J* 2.6 and 8.1), 8.27 (1 H, d, *J* 8.2) and 12.69 (1 H, br s); $\delta_C[(CD_3)_2SO]$ 38.86, 74.24, 81.43, 86.47, 94.16, 107.24, 141.32, 159.53 and 176.84.

2′,3′-*Didehydro*-3′-*deoxy*-2-*thiothymidine* **10a**.—Resublimed potassium *tert*-butoxide (0.224 g, 2.0 mmol) was added to a stirred solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-2-thiothymine **19a** (0.24 g, 1.0 mmol) in dry DMSO (6 cm^3) under nitrogen at room temperature. After 2 h, the reaction was quenched with ethanol–acetic acid (98:2 v/v) and the products were evaporated under reduced pressure (oil-pump) below 40 °C. The residue was extracted with acetone (2 × 20 cm^3) at room temperature. The combined extracts were concentrated under reduced pressure, and the residue obtained was fractionated by chromatography on silica gel. Elution of the column with chloroform–ethanol (96:4 v/v) and concentration of the appropriate fractions gave a solid (0.159 g, 66%). After crystallization from absolute ethanol, the *title compound* **10a** (Found: C, 49.9; H, 5.0; N, 11.6. $C_{10}H_{12}N_2O_3S$ requires C, 50.0; H, 5.0; N, 11.7%) was obtained, m.p. 189 °C; R_f 0.29 (system **B**); $\delta_H[(CD_3)_2SO]$ 1.78 (3 H, d, *J* 1.2), 3.69 (2 H, dd, *J* 2.9 and 4.9), 4.87 (1 H, m), 5.17 (1 H, t, *J* 5.1), 5.97 (1 H, m), 6.43 (1 H, m), 7.68 (1 H, m), 8.03 (1 H, m) and 12.61 (1 H, br s); $\delta_C[(CD_3)_2SO]$ 12.31, 61.63, 87.90, 94.94, 114.73, 125.80, 135.22, 137.55, 160.59 and 175.05.

2′,3′-*Didehydro*-2′,3′-*dideoxy*-2-*thiouridine* **10b**.—Resublimed potassium *tert*-butoxide (0.224 g, 2.0 mmol) was added to a solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-2-thiouracil **19b** (0.226 g, 1.0 mmol) in dry DMSO (6 cm^3) under nitrogen at room temperature. After 2 h, the reaction was quenched, and the products were worked-up and fractionated as in the above preparation of 2′,3′-didehydro-3′-deoxy-2-thiothymidine **10a**, to give a solid (0.135 g, 60%). After crystallization from methanol–benzene, the *title compound* **10b** (Found: C, 47.6; H, 4.4; N, 12.25. $C_9H_{10}N_2O_3S$ requires C, 47.8; H, 4.5; N, 12.4%) was obtained, m.p. 220–225 °C (decomp.); R_f 0.29 (system B); $\delta_H[(CD_3)_2SO]$ 3.67 (2 H, s), 4.87 (1 H, m), 5.11 (1 H, br), 5.97 (2 H, m), 6.43 (1 H, m), 7.66 (1 H, m), 8.07 (1 H, d, *J* 8.1) and 12.64 (1 H, br); $\delta_C[(CD_3)_2SO]$ 61.94, 88.30, 94.54, 106.66, 125.92, 135.71, 141.91, 160.09 and 176.61.

1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)-5-*methyl*-4-(1,2,4-*triazol*-1-*yl*)*pyrimidine*-2(1H)-*thione* **20a**.—Phosphoryl trichloride (0.54 cm^3, 5.8 mmol) was added to a stirred solution of 1,2,4-triazole (1.863 g, 27 mmol) in acetonitrile (18 cm^3) and the products were cooled to 0 °C (ice–water-bath). Triethylamine (3.78 cm^3, 27 mmol) was added slowly to the resulting suspension. After a further period of 10 min, a solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-2-thiothymine **19a** (0.72 g, 3.0 mmol) in acetonitrile (8 cm^3) was added slowly to the resulting stirred slurry. The reactants were then stirred for 6 h at room temperature. Additional triethylamine (3.78 cm^3, 27 mmol) and water (0.3 cm^3) were added and, after 10 min, the products were concentrated under reduced pressure. The residue was extracted with chloroform (2 × 100 cm^3) at room temperature, and the combined extracts were washed with saturated aq. sodium hydrogen carbonate (2 × 200 cm^3). The dried ($MgSO_4$) organic layer was evaporated under reduced pressure to give the *title compound* **20a** (0.87 g, 99%) as a yellow solid. Crystallization from absolute ethanol gave yellow needles (Found: C, 49.65; H, 4.4; N, 23.8. $C_{12}H_{13}N_5O_2S$ requires C, 49.5; H, 4.5; N, 24.0%), m.p. 189 °C; R_f 0.39 (system B); $\delta_H[(CD_3)_2SO]$ 2.51 (3 H, s), 2.60 (1 H, dd, *J* 2.3 and 16.1), 2.83 (1 H, m), 4.42 (1 H, d, *J* 8.7), 4.76 (1 H, dd, *J* 3.5 and 8.7), 5.19 (1 H, m), 5.49 (1 H, m), 6.97 (1 H, dd, *J* 2.3 and 7.4), 8.32 (1 H, s), 8.85 (1 H, s) and 9.31 (1 H, s); $\delta_C[(CD_3)_2SO]$ 16.69, 40.52, 73.75, 83.73, 85.74, 97.26, 110.82, 145.06, 148.14, 152.52, 153.60 and 177.45.

1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)-4-(1,2,4-*triazol*-1-*yl*)pyrimidine-2(1H)-*thione* **20b**.—A solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-2-thiouracil **19b** (1.438 g, 6.36 mmol) in acetonitrile (20 cm^3) was added to the products obtained from the reaction between 1,2,4-triazole (3.955 g, 57.3 mmol), phosphoryl trichloride (1.15 cm^3, 12.3 mmol) and triethylamine (8.0 cm^3, 57.4 mmol) in acetonitrile (38 cm^3) at 0 °C. After the reaction had been allowed to proceed for 6 h at room temperature, triethylamine (8.0 cm^3, 57.4 mmol) and water (1.0 cm^3) were added and the products were worked up as in the above preparation of the 2-thiothymine derivative **20a**, to give the *title compound* **20b** (1.585 g, 90%) as a yellow solid. Crystallization from absolute ethanol gave yellow crystals (Found: C, 47.55; H, 3.8; N, 24.8. $C_{11}H_{11}N_5O_2S$ requires C, 47.6; H, 4.0; N, 25.25%); R_f 0.40 (system B); $\delta_H(CDCl_3)$ 2.70 (1 H, dd, *J* 2.5 and 16.4), 2.89 (1 H, m), 4.35 (1 H, dd, *J* 0.9 and 8.3), 4.87 (1 H, dd, *J* 3.4 and 8.8), 5.21 (1 H, m), 5.55 (1 H, dd, *J* 3.9 and 4.7), 7.09 (1 H, dd, *J* 2.4 and 7.5), 7.40 (1 H, d, *J* 7.4), 8.16 (1 H, s), 8.80 (1 H, d, *J* 7.3) and 9.35 (1 H, s); $\delta_C(CDCl_3)$ 41.10, 74.27, 84.08, 86.28, 97.70, 99.25, 143.50, 146.44, 153.49, 154.36 and 180.70.

1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)-5-*methyl*-2-*thiocytosine* **21a**.—Methanolic ammonia (~8 mol dm^{-3}; 6 cm^3) was added to a stirred solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-5-methyl-4-(1,2,4-triazol-1-yl)pyrimidin-2(1*H*)-thione **20a** (0.545 g, 1.87 mmol) in methanol (6 cm^3) at room temperature. After 16 h, the products were concentrated under reduced pressure, and the residue was fractionated by chromatography on silica gel: elution of the column with chloroform–ethanol (19:1 v/v) and concentration of the appropriate fractions gave the *title compound* **21a** (0.438 g, 97%). Crystallization from absolute ethanol gave colourless crystals (Found: C, 50.2; H, 5.4; N, 17.4. $C_{10}H_{13}N_3O_2S$ requires C, 50.2; H, 5.5; N, 17.6%), m.p. 211–212 °C; R_f 0.35 (system A); $\delta_H[(CD_3)_2SO]$ 1.95 (3 H, d, *J* 0.9), 2.31 (1 H, dd, *J* 3.1 and 15.8), 2.65 (1 H, m), 4.23 (1 H, m), 4.69 (1 H, dd, *J* 3.7 and 8.2), 4.97 (1 H, m), 5.44 (1 H, m), 7.28 (1 H, br s), 7.31 (1 H, dd, *J* 3.1 and 7.9), 7.94 (1 H, br s) and 8.11 (1 H, m); $\delta_C[(CD_3)_2SO]$ 13.54, 39.93, 74.02, 81.12, 86.27, 94.76, 106.42, 138.92, 160.24 and 178.65.

1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)-2-*thiocytosine* **21b**.—Methanolic ammonia (~8 mol dm^{-3}; 12 cm^3) was added to a stirred solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-4-(1,2,4-triazol-1-yl)pyrimidin-2(1*H*)-thione **20b** (0.70 g, 2.52 mmol) in methanol (12 cm^3) at room temperature. After 16 h, the products were concentrated under reduced pressure and the residue was fractionated by chromatography on silica gel: elution of the column with chloroform–ethanol (19:1 v/v) and concentration of the appropriate fractions gave the *title compound* **21b** (0.545 g,

95%). Crystallization from absolute ethanol gave plates (Found: C, 48.3; H, 4.8; N, 18.6. $C_9H_{11}N_3O_2S$ requires C, 48.0; H, 4.9; N, 18.65%), m.p. 193 °C; R_f 0.30 (system A); $\delta_H[(CD_3)_2SO]$ 2.30 (1 H, dd, *J* 2.9 and 15.9), 2.65 (1 H, m), 4.23 (1 H, d, *J* 8.3), 4.68 (1 H, dd, *J* 3.7 and 8.3), 4.98 (1 H, m), 5.44 (1 H, m), 6.18 (1 H, d, *J* 7.5), 7.29 (1 H, dd, *J* 2.9 and 7.9), 7.65 (1 H, br s), 7.77 (1 H, br s) and 8.27 (1 H, d, *J* 7.5); $\delta_C[(CD_3)_2SO]$ 40.09, 73.90, 81.43, 86.23, 94.91, 98.36, 141.47, 160.17 and 180.11.

1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)-4-N-*methyl*-2-*thiocytosine* **22**.—Alcoholic methylamine (~8 mol dm^{-3}; 20 cm^3) was added to a stirred solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-4-(1,2,4-triazol-1-yl)pyrimidin-2(1*H*)-thione **20b** (0.70 g, 2.52 mmol) in absolute ethanol (10 cm^3) at room temperature. After 6 h, the products were concentrated under reduced pressure and the residue was fractionated by chromatography on silica gel: elution of the column with chloroform–ethanol (19:1 v/v) and concentration of the appropriate fractions gave the *title compound* **22** (0.535 g, 88%). Crystallization from ethanol–ethyl acetate gave needles (Found: C, 50.2; H, 5.5; N, 17.5. $C_{10}H_{13}N_3O_2S$ requires C, 50.2; H, 5.5; N, 17.6%), m.p. 148 °C; R_f 0.40 (system A); $\delta_H[(CD_3)_2SO]$ 2.31 (1 H, m), 2.65 (1 H, m), 2.81 (2.5 H, d, *J* 5.1), 2.87 (0.5 H, d, *J* 4.8), 4.22 (1 H, d, *J* 8.1), 4.69 (1 H, m), 4.97 (1 H, m), 5.44 (1 H, m), 6.19 (0.88 H, d, *J* 7.6), 6.31 (0.12 H, d, *J* 7.8), 7.30 (1 H, m), 8.13 (0.85 H, m), 8.19 (1 H, d, *J* 7.6) and 8.40 (0.15 H, d, *J* 7.7) [at 80 °C, various signals coalesced; thus in $(CD_3)_2SO$–D_2O, a signal at δ 2.89 (3 H, s) was observed]; $\delta_C[(CD_3)_2SO]$ (main signals) 27.17, 40.13, 73.96, 81.44, 86.31, 95.05, 99.21, 140.05, 158.24 and 180.53.

2′,3′-*Didehydro*-2′,3′-*dideoxy*-5-*methyl*-2-*thiocytidine* **11a**.—Sodium hydride (60% dispersion in oil; 0.88 g, 2.2 mmol) was added to a solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-5-methyl-2-thiocytosine **21a** (0.239 g, 1.0 mmol) in dry DMSO (6 cm^3) under nitrogen at room temperature. The stirred reaction mixture was heated at 100 °C for 30 min. The products were then cooled, neutralized with ethanol–acetic acid (98:2 v/v) and evaporated under reduced pressure (oil-pump) below 40 °C. The residual material was extracted with acetone (2 × 20 cm^3) and purified as above in the preparation of 2′,3′-didehydro-3′-deoxy-2-thiothymidine **10a**, to give a solid (0.148 g, 62%). Crystallization from 96% ethanol gave the *title compound* **11a** (Found: C, 50.3; H, 5.6; N, 17.35. $C_{10}H_{13}N_3O_2S$ requires C, 50.2; H, 5.5; N, 17.6%), m.p. 225 °C (decomp.); R_f 0.19 (system A); $\delta_H[(CD_3)_2SO]$ 1.87 (3 H, d, *J* 0.8), 3.70 (2 H, dd, *J* 3.0 and 4.9), 4.86 (1 H, m), 5.12 (1 H, t, *J* 5.1), 5.95 (1 H, m), 6.34 (1 H, m), 7.22 (1 H, br s), 7.88 (1 H, br s), 7.92 (1 H, m) and 8.06 (1 H, m); $\delta_C[(CD_3)_2SO]$ 13.37, 61.90, 87.73, 94.97, 105.90, 126.86, 133.90, 139.83, 160.45 and 178.40.

2′,3′-*Didehydro*-2′,3′-*dideoxy*-2-*thiocytidine* **11b**.—Resublimed potassium *tert*-butoxide (0.228 g, 2.0 mmol) was added to a stirred solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-2-thiocytosine **21b** (0.216 g, 0.96 mmol) in dry DMSO (4 cm^3) under nitrogen at room temperature. After 2 h, the reaction was quenched, and the products were worked up and fractionated as in the above preparation of 2′,3′-didehydro-3′-deoxy-2-thiothymidine **10a**, to give a solid (0.13 g, 60%). Crystallization from methanol—ethyl acetate (1:1 v/v) gave the *title compound* **11b** (Found: C, 47.45; H, 4.6; N, 18.1. $C_9H_{11}N_3O_2S$ requires C, 48.0; H, 4.9; N, 18.65%), m.p. 128 °C (decomp.); R_f 0.17 (system A); $\delta_H[(CD_3)_2SO]$ 3.65 (2 H, m), 4.85 (1 H, m), 5.14 (1 H, br), 5.98 (1 H, m), 6.06 (1 H, d, *J* 7.5), 6.36 (1 H, m), 7.66 (1 H, br), 7.82 (1 H, br), 7.89 (1 H, m) and 8.08 (1 H, d, *J* 7.5); $\delta_C[(CD_3)_2SO]$ 61.90, 87.70, 94.99, 97.83, 126.65, 134.12, 142.00, 160.19 and 180.00.

2′,3′-*Didehydro*-2′,3′-*dideoxy*-4-N-*methyl*-2-*thiocytidine* **23**.—Resublimed potassium *tert*-butoxide (0.178 g, 1.6 mmol) was added to a stirred solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-4-*N*-methyl-2-thiocytosine **22** (0.19 g, 0.79 mmol) in dry DMSO (3.5 cm^3) under nitrogen at room temperature. After 2 h, the reaction was quenched and the products were worked up and fractionated as in the above preparation of 2′,3′-didehydro-3′-deoxy-2-thiothymidine **10a** and crystallized from ethanol–ethyl acetate to give the *title compound* **23** as a solid (0.12 g, 63%) (Found: C, 50.2; H, 5.5; N, 17.5. $C_{10}H_{13}N_3O_2S$ requires C, 50.2; H, 5.5; N, 17.6%), m.p. 153 °C; R_f 0.28 (system A); $\delta_H[(CD_3)_2SO$–$D_2O]$ 2.81 (0.4 H, s), 2.88 (2.6 H, s), 3.68 (2 H, m), 4.87 (1 H, m), 5.97 (1 H, m), 6.09 (0.87 H, d, *J* 7.7), 6.22 (0.13 H, d, *J* 7.7), 6.37 (1 H, m), 7.86 (1 H, m), 8.02 (0.87 H, d, *J* 7.6) and 8.25 (0.13 H, d, *J* 7.7); $\delta_C[(CD_3)_2SO]$ 26.96, 27.01, 62.00, 87.70, 95.02, 95.14, 98.62, 98.69, 126.70, 134.03, 140.41, 158.24, 158.32 and 180.40.

1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)*isocytosine* **25a**.—A solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-2-*O*-ethyluracil **12b** (1.0 g, 4.2 mmol) in conc. aq. ammonia (*d* 0.88; 20 cm^3) was stirred in a sealed flask at room temperature for 24 h. The products were then concentrated to dryness under reduced pressure and any remaining water was removed by azeotropic evaporation, first with absolute ethanol and then with toluene. The solid residue obtained was washed with ethyl acetate (4 × 15 cm^3) at room temperature and the washings were discarded; it was then dried *in vacuo* in a desiccator over P_2O_5 at room temperature to give the title compound **25a** (0.65 g, 74%). Crystallization from ethanol–ethyl acetate gave colourless crystals (Found: C, 51.45; H, 5.3; N, 19.8. $C_9H_{11}N_3O_3$ requires C, 51.7; H, 5.3; N, 20.1%), m.p. 179 °C (decomp.); R_f 0.10 (system A); $\delta_H[(CD_3)_2SO]$ 2.41 (1 H, m), 2.73 (1 H, d, *J* 16.3), 3.98 (1 H, dd, *J* 1.8 and 8.1), 4.69 (1 H, dd, *J* 4.3 and 8.2), 5.00 (1 H, m), 5.51 (1 H, m), 5.63 (1 H, d, *J* 7.8), 6.26 (1 H, d, *J* 7.3), 7.07 (2 H, br) and 7.94 (1 H, d, *J* 7.8); $\delta_C[(CD_3)_2SO]$ 36.59, 75.28, 80.07, 86.67, 90.36, 106.74, 137.80, 155.39 and 169.76.

1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)-2-N-*methylisocytosine* **25b**.—A solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-2-*O*-ethyluracil **12b** (0.62 g, 2.6 mmol) in alcoholic methylamine (~8 mol dm^{-3}; 8 cm^3) was stirred in a sealed flask at room temperature. After 48 h, the products were evaporated under reduced pressure. The residue was washed with ethyl acetate (3 × 15 cm^3) and the washings were discarded; it was then dried *in vacuo* in a desiccator over P_2O_5 at room temperature to give the *title compound* **25b** (0.485 g, 83%). Crystallization from absolute ethanol gave colourless crystals (Found: C, 53.9; H, 5.75; N, 18.8. $C_{10}H_{13}N_3O_3$ requires C, 53.8; H, 5.9; N, 18.8%), m.p. 180 °C; R_f 0.15 (system A); $\delta_H[(CD_3)_2SO]$ 2.39 (1 H, m), 2.78 (1 H, m), 2.80 (3 H, d, *J* 4.3), 3.96 (1 H, m), 4.69 (1 H, dd, *J* 4.4 and 8.2), 5.02 (1 H, m), 5.52 (1 H, t, *J* 4.7), 5.59 (1 H, d, *J* 7.8), 6.23 (1 H, m), 7.15 (1 H, m) and 7.96 (1 H, d, *J* 7.9); $\delta_C[(CD_3)_2SO]$ 28.35, 36.30, 75.49, 79.99, 86.73, 89.77, 105.57, 138.15, 154.00 and 169.42.

Action of Potassium tert-*Butoxide on* 1-(3,5-*Anhydro*-2-*deoxy*-β-D-threo-*pentofuranosyl*)*isocytosine* **25a**.—Resublimed potassium *tert*-butoxide (0.224 g, 2.0 mmol) was added to a stirred solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)isocytosine **25a** (0.209 g, 1.0 mmol) in dry DMSO (4.0 cm^3) under nitrogen at room temperature. After 2 h, the reaction was quenched with solid carbon dioxide and the

products were concentrated under reduced pressure (oil-pump) below 40 °C. The residue was extracted with acetone (3 × 50 cm^3) at room temperature. The combined extracts were filtered, and the filtrate was concentrated under reduced pressure. The residue was triturated with ethyl acetate–methanol (95:5 v/v) (2 × 10 cm^3) to give a solid (0.108 g); R_f 0.51 and 0.59 (system C); the slower moving product, crude compound **26a**, had $\delta_H[(CD_3)_2SO]$ 3.60 (0.95 H, m), 4.81 (0.48 H, m), 5.09 (0.48 H, m), 5.51 (0.52 H, d, *J* 6.6), 5.59 (0.48 H, d, *J* 7.7), 6.01 (0.48 H, m), 6.44 (0.48 H, m), 6.58 (0.48 H, m), 6.81 (~0.85 H, br), 7.30 (~0.6 H, br) and 7.54 (1 H, m). Isocytosine **24a** had R_f 0.59 (system C) and $\delta_H[(CD_3)_2SO]$ 5.51 (1 H, d, *J* 6.6), 6.77 (2 H, br), 7.52 (1 H, d, *J* 6.6) and 11.11 (1 H, br).

2′,3′-Didehydro-2′,3′-dideoxy-2-N-methylisocytidine **26b**.— Resublimed potassium *tert*-butoxide (0.224 g, 2.0 mmol) was added to a stirred solution of 1-(3,5-anhydro-2-deoxy-β-D-*threo*-pentofuranosyl)-2-*N*-methylisocytosine **25b** (0.223 g, 1.0 mmol) in dry DMSO (4.5 cm^3) under nitrogen at room temperature. After 2 h, the reaction was quenched with ethanol–acetic acid (98:2 v/v), and the products were evaporated under reduced pressure (oil-pump) below 40 °C. The residue was extracted with hot acetone (4 × 20 cm^3). The combined extracts were concentrated under reduced pressure, and the residue was recrystallized from ethyl acetate–methanol to give the *title compound* **26b** (0.14 g, 62%) (Found: C, 53.5; H, 6.0; N, 18.6. $C_{10}H_{13}N_3O_3$ requires C, 53.8; H, 5.9; N, 18.8%), m.p. 128 °C; R_f 0.10 (system A); $\delta_H[(CD_3)_2SO]$ 2.74 (3 H, s), 3.59 (2 H, m), 4.81 (1 H, m), 5.19 (1 H, br), 5.52 (1 H, d, *J* 7.7), 6.00 (1 H, m), 6.43 (1 H, m), 6.53 (1 H, m), 7.33 (1 H, br) and 7.49 (1 H, d, *J* 7.7); $\delta_C[(CD_3)_2SO]$ 28.01, 62.08, 87.54, 92.22, 105.33, 125.52, 134.90, 138.92, 153.38 and 169.59.

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