Monatshefte für Chemie 122, 59–70 (1991)

Monatshefte für Chemie
Chemical Monthly

Synthesis of 2′,3′-Dideoxynucleosides from 5-Alkoxymethyluracils

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Summary. A modified synthesis of protected 2,3-dideoxyribose **5** starting from *L*-glutamic acid (**1**) is described. Reaction of **5** with silylated 5-hydroxymethyluracil **7a** and 5-alkoxymethyluracils **7b–e** in the presence of trimethylsilyl triflate afforded an anomeric mixture of 2′,3′-dideoxyuridine derivatives **8a–e** and **9a–e**. Deprotection with methanolic ammonia and separation by chromatography gave the corresponding nucleosides **10a–e** and **11a–e**. Treatment of **9b–e** with tri(1*H*-1,2,4-triazol-1-yl)phosphine oxide and subsequent reaction of **12b–e** with ammonia in dioxane afforded the cytosine derivatives **13b–e** which on treatment with methanolic ammonia gave the corresponding 2′,3′-dideoxycytidine derivatives **14b–e** and **15b–e**. In contrast with the parent compounds, these alkoxymethyl derivatives had no appreciable activity against human immunodeficiency virus (HIV-1).

Keywords. 2′,3′-Dideoxycytidines; 2′,3′-Dideoxyuridines; 5-Alkoxymethyluracils; Human immunodeficiency virus.

Synthese von 2′,3′-Dideoxynucleosiden aus 5-Alkoxymethyluracilen

Zusammenfassung. Ausgehend von *L*-Glutaminsäure (**1**) wird eine modifizierte Synthese von geschützter 2,3-Dideoxyribose (**5**) beschrieben. Reaktion von **5** mit silyliertem 5-Alkoxymethyluracilen **7b–e** in Gegenwart von Trimethylsilyltriflat ergab anomere Mischungen der 2′,3′-Dideoxyuridinderivate **8a–e** und **9a–e**. Abspaltung der Schutzgruppe mit methanolischen Ammoniak und chromatographische Trennung ergab die entsprechenden Nucleoside **10a–e** und **11a–e**. Behandlung von **9b–e** mit Tri(1*H*-1,2,4-triazol-1-yl)phosphinoxid und nachfolgende Reaktion von **12b–e** mit Ammoniak in Dioxan ergab die Cytosinderivate **13b–e**, welche nach Behandlung mit methanolischem Ammoniak die entsprechenden 2′,3′-Dideoxycytidinderivate **14b–e** und **15b–e** ergaben. Im Gegensatz zur Stammverbindung hatten diese Alkoxymethylderivate keine nennenswerte Wirksamkeit gegen den menschlichen Immunschwächevirus (HIV-1).

Introduction

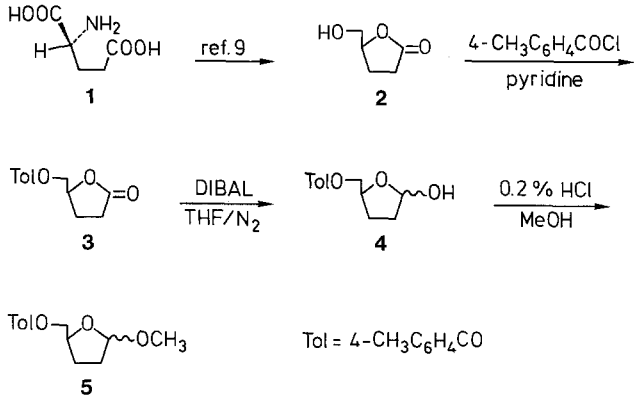
Aquired immunodeficiency syndrome (AIDS) has become the most important epidemic in modern times. It is caused by human immunodeficiency virus (HIV) which passes a number of steps in the replicative cycle which are adequate targets for

antiviral agents. The virus is cytopathic for helper/inducer T-cells [1–4]. There is a need for new compounds that may be effective in the therapy of that disease although some compounds have been identified as having an inhibitory effect. First of all they include 2′,3′-dideoxynucleosides [5] of which 2′,3′-dideoxycytidine (ddC), 3′-azido-3′-deoxythymidine (AZT) and 3′-deoxy-3′-fluorothymidine (FddThd) were most potent, but they also caused difficulties due to side effects [6]. In the case of AZT, the key toxicity which should be obviated is the suppression of bone marrow; in the case of ddC, the key toxicity is peripheral neuropathy.

The present work describes the synthesis of some new 2′,3′-dideoxynucleosides from 5-alkoxymethyluracils with the purpose to find new active compounds with less prominent side effects than those observed for AZT and ddC. Since analogues of ddC are rather difficult to prepare, very few examples with substituents in 5-position of the nucleobase have been tested for their activity against HIV. Substitution with 5-fluoro resulted in slightly reduced activity, compared to the lead compound ddC, whereas the corresponding 5-methyl of 5-bromo compounds were devoid of protective effects [7]. In this investigation we have therefore selected 5-alkoxymethyl substituents ($\sigma_m = 0.02$ and $\sigma_p = 0.03$) with no electron attracting or donating properties like hydrogen [8], but with lipophilicities [8] lower and higher than that of hydrogen.

Results and Discussion

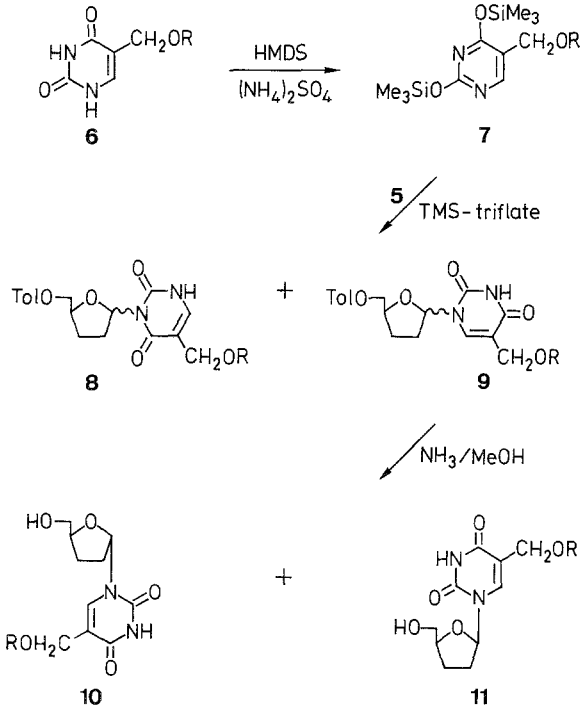
The lactone alcohol **2** was prepared following the method of Taniguchi et al. [9] in which nitrous acid deamination of *L*-glutamic acid (**1**) in aqueous solution gave a lactone acid which was converted to the corresponding lactone ester and subsequently reduced with sodium borohydride in ethanol at room temperature. Toluoylation of **2** was accomplished with 1 equivalent of toluoyl chloride at 0°C in pyridine yielding crystalline **3** in 42% yield from **2**. The toluoyl ester **3** was treated with diisobutylaluminum hydride (*DIBAL*) in *THF* at −75°C to give the lactol **4**. The hemiacetal **4** was unstable and therefore treated immediately with methanolic hydrogen chloride to give the corresponding methyl furanoside **5** in 70% yield from **3**. Furanosides of type **5** are important synthons for preparation of ddC analogues and this paper demonstrates that the synthesis of **5** can be accomplished in good yields using less sophisticated reagents.



Scheme 1

5-Pentyloxymethyluracil (**6 d**) was obtained by the method of Bubbar and Gupta [10] by heating 5-hydroxymethyluracil (**6 a**) in *n*-pentanol in the presence of conc. hydrogen chloride in 81% yield. Coupling of 5-hydroxymethyluracil (**6 a**) and its ether derivatives **6 b–e** after silylation with hexamethyldisilazane (*HMDS*) by the trimethylsilyl triflate method of Vorbrüggen [11] gave anomeric mixtures of N 3-coupled nucleosides **8 a–e** (20–34%) and N 1-coupled nucleosides **9 a–e** (37–54%). The ^{13}C NMR shift values of α/β-anomers of N-3 coupled nucleosides are typical of the sugar moiety of **8 a** (Me_2SO-d_6) δ 28.3 (C-3′), 30.1 and 30.2 (C-2′), 67.2 and 67.3 (C-5′), 68.1 and 68.2 (C-4′), 85.5 and 85.6 (C-1′). In all cases the β/α ratio of **9** was close to 2 : 3. Treatment of **9 a–e** with a 1 : 1 mixture of methanol and conc. ammonia at room temperature for 48–72 h resulted in complete deprotection of the hydroxy group. The anomeric mixtures were separated by chromatography on silica gel to give 16–39% of the α-anomers and 9–24% of the β-anomers.

4-(1,2,4-Triazol-1-yl)pyrimidin-2-ones **12 b–e** (α- and β-anomers) were prepared by treating **9 b–e** with putative tris(1H-1,2,4-triazol-1-yl)phosphine oxide [12] in the presence of 1,2,4-triazole and triethylamine in acetonitrile at room temperature. Reaction of the 4-triazolo derivatives **12 b–e** with aqueous ammonia in dioxane solution at room temperature yielded the cytosine derivatives **13 b–e**. Subsequent removal of the toluoyl group by treatment with methanolic ammonia at room

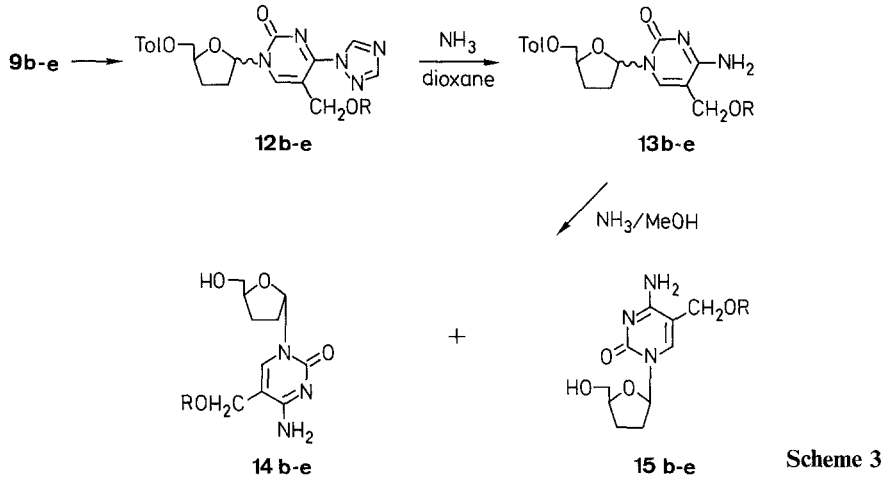


6, **7**, **8**, **9**, **10**, **11**

6-15	R
a	H
b	CH_3
c	$CH(CH_3)C_2H_5$
d	$CH_2CH_2CH_2CH_2CH_3$
e	$CH_2C_6H_5$

Scheme 2

temperature, followed by chromatographic purification, afforded the deprotected α-anomers **14b–e** (21–32%) and the β-anomers **15b–e** (14–29%).



Scheme 3

The β-anomer assignment of compound **11** was made by comparison of ^{13}C-NMR and ^{1}H-NMR spectra with those of 5-ethyl-2′,3′-dideoxyuridine [13]. The α- and β-isomer assignments of **14** and **15** were made by comparison with the ^{1}H-NMR of α- and β-anomers of 2′,3′-dideoxycytidine [14], for which the 4′-H proton of an α-anomer appears at a lower field than that of β-anomer and 5′-H protons of an α-anomer appear at a higher field than those of a β-anomer.

Biological Evaluation

5-Alkoxymethyl substituted 2,3-dideoxyuridines **11a–e**, cytidines **15b–e** and their α-anomers **10a–e** and **14c–e**, respectively, as well as their 5-O protected analogues **9a–e** and **13b, d, e** were devoid of any anti-HIV activity, strain HTLV-IIIB in MT-4 cells. Cytotoxicity against MT-cells was found for compound **9b** (TD_{50} = 200 μM) and when the growth medium was 0.1 × was saturated with **13d** and 0.16 saturated with **13e**.

Experimental Part

Melting points were determined in glass capillary tubes on a Büchi apparatus. Silica gel TLC was performed on 60 F-254 precoated plates (Merck) and column chromatography was performed on Merck silica gel (0.040–0.063 mm). Elemental analyses were carried out at NOVO Microanalytical Laboratory, Novo Allé, DK-2880 Bagsvaerd. Mass spectra were obtained on a Varian MAT 311 A mass spectrometer, the ^{1}H-NMR and ^{13}C-NMR were determined on a Bruker AC 250 FT-NMR spectrometer using tetramethylsilane as the internal standard; chemical shifts are recorded in parts per million.

(S)-γ-(4-Methylbenzoyloxymethyl)-γ-butyrolactone [**3**; $C_{13}H_{14}O_4$]

To a stirred solution of **2** (23.2 g, 0.20 mol) in dry pyridine (300 ml) at 0°C, *p*-toluoyl chloride (30.9 g, 0.20 mol) was added during 15 min. The reaction mixture was stirred at room temperature for 0.5 h, heated at 80°C for 3 h, and then evaporated in vacuo to dryness. The residue was shaken with water

(250 ml), $CHCl_3$ (500 ml) was added and the organic layer was separated, washed with 10% Na_2CO_3 aq., H_2O, 10% HCl aq., H_2O, dried, and evaporated under reduced pressure to give a syrup, ether (150 ml) was added to afford 19.72 g (42%) of pure **3** as a crystalline compound: M.p. 102–103°C; MS, *m/z* 235 (M^+); ^{1}H-NMR ($CDCl_3$) δ 2.05–2.70 (m, *p*-CH_3 and $-CH_2-CH_2-$), 4.42 (dd, J = 12.2 and 5.2 Hz, 5-H), 4.53 (dd, J = 12.2 and 3.0 Hz, 5-H), 4.87 (m, 4-H), 7.24 (d, J = 7.9 Hz, 2 *Ar*H), 7.91 (d, J = 7.9 Hz, 2 *Ar*H); ^{13}C-NMR ($CDCl_3$) δ 21.5 (*p*-CH_3), 23.8 (CH_2), 28.0 (CH_2), 65.4 (CH_2O-), 77.4 (CH), 126.5 (C-1′), 129.1 (C-3′), 129.6 (C-2′), 144.0 (C-4′), 166.0 (C=O), 176.3 (C=O).

Methyl 2,3-Dideoxy-5-O-(4-methylbenzoyl)-D-glycero-pentofuranoside [**5**; $C_{14}H_{18}O_4$]

To a solution of **3** (10 g, 42.7 mmol) in 100 ml of dry *THF* at −75°C under nitrogen with magnetic stirring for 2 h was added dropwise a 1 *M* solution of *DIBAL* in hexane (78 ml, 76.5 mmol). After stirring for additional 0.5 h the excess of reagent was destroyed by cautious addition of water, then 6 *M* hydrochloric acid was added to dissolve the gelatinous precipitate. The aqueous solution was extracted with ether (3 × 150 ml), the organic solution was dried (Na_2SO_4) and evaporated at room temperature to give **4** as a syrup which at once was dissolved in 0.2% HCl-*Me*OH (60 ml). The solution was left for 15 min at room temperature with stirring, 5% KOH-*Me*OH was added to neutralize the mixture and the solvent was evaporated in vacuo. Benzene (100 ml) was added to the residue and the insoluble material was filtered off. Evaporation of the filtrate under reduced pressure gave a syrup (9.8 g) which was chromatographed on silica gel with petroleum ether-ether (98 : 2). This afforded 7.47 g (70%) of **5** as a colourless oil: MS, *m/z* 250 (M^+); ^{1}H-NMR ($CDCl_3$) δ 1.97 (m, 2-H, and 3-H), 2.40 (s, *p*-CH_3), 3.31 (s, OCH_3), 3.36 (s, OCH_3), 4.26–4.46 (m, 4-H and 5-H), 5.06 (dd, J = 2.8 and 4.6 Hz, 1-H), 7.33 (d, J = 7.7 Hz, *Ar*H), 7.94 (d, J = 7.7 Hz, *Ar*H), 7.98 (d, J = 7.7 Hz, *Ar*H); ^{13}C-NMR ($CDCl_3$), δ 21.5 (*p*-CH_3), 25.7 (C-3), 31.8 and 32.7 (C-2), 54.2 and 54.5 (OCH_3), 66.2 and 67.5 (C-5), 75.6 and 77.7 (C-4), 105.1 and 105.4 (C-1), 127.2 and 127.3 (C-1′), 128.9 (C-3′), 129.5 and 129.6 (C-2′), 143.4 and 143.5 (C-4′), 166.4 (C=O).

5-Pentyloxymethyluracil [**6 d**; $C_{16}H_{16}N_2O_3$]

Conc. HCl (4 ml) and 5-hydroxymethyluracil (**6 a**) (8 g, 56.3 mmol) were added to *n*-pentanol (400 ml). The suspension was stirred at room temperature for 15 min and then kept on an oil bath for 3 h at 100°C. The reaction mixture became homogenous after 20 min. The reaction mixture was cooled at −20°C. The crystals were collected by filtration and recrystallized from ethanol to afford 9.7 g (81%): M.p. 220–221°C; MS *m/z* 212 (M^+); ^{1}H-NMR (Me_2SO-d_6) δ 0.86 (t, J = 6.5 Hz, CH_3), 1.26 (m, CH_2CH_2), 1.47 (m, CH_2), 3.36 (t, J = 6.5 Hz, OCH_2), 4.06 (s, CH_2O), 7.41 (s, 6-H), 9.87 (b, NH); ^{13}C-NMR (Me_2SO-d_6) δ 13.8 (CH_3), 21.9 (CH_2), 27.9 (CH_2), 28.8 (CH_2), 64.3 (CH_2O), 69.4 (OCH_2), 108.9 (C-5), 141.5 (C-6), 152 (C-4), 163.9 (C-2).

1-(2,3-Dideoxy-5-O-(4-methylbenzoyl)-D-glycero-pentofuranosyl)uracils, α- and β-Anomers **9 a–e**

To a stirred solution of compound **5** (3.75 g, 15 mmol) and the silylated uracil derivatives [15] **7 a–e** (17 mmol) in anhydrous dichloromethane (50 ml) was added dropwise trimethylsilyl triflate (3.1 ml, 17 mmol) in dichloromethane (10 ml) at 0°C. After the addition, the reaction solutions were stirred for 2–3 h at room temperature. The reaction solutions were diluted with CH_2Cl_2 (250 ml) and extracted with ice-cold saturated aq. $NaHCO_3$ solution. The aqueous solutions were extracted with dichloromethane (2 × 150 ml). The combined organic solutions were washed with cold H_2O (300 ml), dried (Na_2SO_4) and evaporated under reduced pressure to give a syrup which was chromatographed on silica gel with $CHCl_3$-*Me*OH (98 : 2) to give 20–37% of **8 a–e** and 37–54% of **9 a–e** [compound **9 e** with ether-petroleum ether (8 : 2)]. The anomers of compound **9 a, b, e** were separated by HPLC with isocratic 29–40% ethanol in water on a reverse phase column (RP-4, 15–20 μm, 300 A) to give pure α- und β-anomers.

1-(2,3-Dideoxy-5-O-(4-methylbenzoyl)-α-D-glycero-pentofuranosyl)-5-hydroxymethyluracil [**9 a** (α)]

0.97 g (18%): M.p. 118–120°C; MS, *m/z* 360 (M^+); ^{1}H-NMR ($CDCl_3$) δ 1.93–2.59 (m, *p*-CH_3, 2′-H and 3′-H), 4.29–4.48 (m, CH_2O, 5′-H), 4.74 (m, 4′-H), 6.13 (t, J = 4.9 Hz, 1′-H), 7.24 (d, J = 8.0 Hz, *Ar*H), 7.44 (s, 6-H), 7.93 (d, J = 8.1 Hz, *Ar*H); ^{13}C-NMR ($CDCl_3$) δ 20.4 (*p*-CH_3), 25.2 (C-3′), 31.2 (C-2′), 57.1 (5-CH_2), 64.8 (C-5′), 77.8 (C-4′), 86.7 (C-1′), 112.4 (C-5), 125.7 (C-1″), 128.0 (C-3″), 128.5 (C-2″), 135.8 (C-6), 142.8 (C-4″), 149.0 (C-2), 162.8 (C-4), 165.2 (C=O).

2′,3′-Dideoxy-5′-O-(4-methylbenzoyl)-5-hydroxymethyluridine [**9 a** (β)]

0.65 g (12%): M.p. 79–81°C; MS, *m/z* 360 (M^+); ^{1}H-NMR ($CDCl_3$) δ 1.99–2.40 (m, *p*-CH_3, 2′-H and 3′-H), 4.23 (s, CH_2O), 4.43 (br s, 4′-H), 4.55 (br s, 5′-H), 6.08 (br s, 1′-H), 7.46 (d, J = 7.5 Hz, *Ar*H), 7.90 (s, 6-H), 7.92 (d, J = 7.5 Hz, *Ar*H); ^{13}C-NMR ($CDCl_3$) δ 21.5 (*p*-CH_3), 25.9 (C-3′), 32.2 (C-2′), 58.2 (5-CH_2), 65.1 (C-5′), 78.7 (C-4′), 86.5 (C-1′), 113.7 (C-5), 126.6 (C-1″), 129.2 (C-3″), 129.5 (C-2″), 136.9 (C-6), 144.2 (C-4″), 150.3 (C-2), 163.9 (C-2), 166.3 (C=O).

1-(2,3-Dideoxy-5-O-(4-methylbenzoyl)-α-D-glycero-pentofuranosyl)-5-methoxymethyluracil [**9 b** (α)]

1.35 g (24%), M.p. 89–92°C; MS, *m/z* 374 (M^+); ^{1}H-NMR ($CDCl_3$) δ 1.99–2.59 (m, *p*-CH_3, 2′-H and 3′-H), 3.44 (s, OCH_3), 4.20 (d, J = 12.7 Hz, CH_2O), 4.27 (d, J = 12.9 Hz, CH_2O), 4.39 (m, 5′-H), 4.75 (br s, 4′-H), 6.16 (br s, 1′-H), 7.27 (d, J = 7.4 Hz, *Ar*H), 7.43 (s, 6-H), 7.95 (d, J = 7.7 Hz, *Ar*H), 9.23 (br s, N 3-H); ^{13}C-NMR (Me_2SO-d_6) δ 21.0 (*p*-CH_3), 26.1 (C-3′), 31.0 (C-2′), 57.2 (OCH_3), 65.9 (CH_2O), 66.1 (C-5′), 78.0 (C-4′), 86.4 (C-1′), 110.1 (C-5), 126.7 (C-1″), 129.1 (C-3″), 129.2 (C-2″), 139.0 (C-6), 143.7 (C-4″), 150.1 (C-2), 162.7 (C-4), 165.5 (C=O).

2′,3′-Dideoxy-5-O-(4-methylbenzoyl)-5-methoxymethyluridine [**9 b** (β)]

0.89 g (16%); M.p. 119–120°C; *m/z* 374 (M^+); ^{1}H-NMR ($CHCl_3$) δ 2.02–2.51 (m, *p*-CH_3, 2′-H, and 3′-H), 3.25 (s, OCH_3), 4.05 (s, CH_2O), 4.48–4.63 (m, 4′-H and 5′-H), 6.11 (br s, 1′-H), 7.26 (d, J = 7.7 Hz, *Ar*H), 7.64 (s, 6-H), 7.95 (d, J = 7.7 Hz, *Ar*H), 9.17 (s, N 3-H); ^{13}C-NMR (Me_2SO-d_6) δ 21.0 (*p*-CH_3), 25.6 (C-3′), 30.7 (C-2′), 57.1 (OCH_3), 65.5 (C-5′), 65.9 (CH_2O), 77.6 (C-4′), 85.3 (C-1′), 110.1 (C-5), 126.6 (C-1″), 129.1 (C-3″), 129.2 (C-2″), 138.2 (C-6), 143.7 (C-4″), 150.1 (C-2), 162.7 (C-4), 165.5 (C=O).

5-Benzyloxymethyl-1-(2,3-dideoxy-5-O-(4-methylbenzoyl)-α-D-glycero-pentofuranosyl)uracil [**9 e** (α)]

1.63 g (24%): M.p. 120–121°C; MS, *m/z* 344 (M^+-C_6H_5CHO); ^{1}H-NMR (Me_2SO-d_6) δ 1.86–2.51 (m, *p*-CH_3, 2′-H and 3′-H), 4.23–4.29 (m, CH_2O and 5′-H), 4.36 (dd, J = 11.8 and 3.4 Hz, 5′-H), 4.51 (s, OCH_2), 4.73 (m, 4′-H), 6.09 (t, J = 5.4 Hz, 1′-H), 7.33 (m, 7 *Ar*H), 7.68 (s, 6-H), 7.88 (d, J = 8.0 Hz, 2 *Ar*H), 11.42 (br, N 3-H); ^{13}C-NMR (Me_2SO-d_6) δ 21.1 (*p*-CH_3), 26.1 (C-3′), 31.0 (C-2′), 64.2 (CH_2O), 66.1 (C-5′), 71.4 (OCH_2), 78.4 (C-4′), 86.5 (C-1′), 110.3 (C-5′), 126.7 (C-1″), 127.3 (C-2‴), 128.1 (C-3‴), 129.2 (C-3″), 129.3 (C-2″), 138.4 (C-1‴), 139.1 (C-6), 143.7 (C-4″), 150.1 (C-2), 162.7 (C-4), 165.5 (C=O).

5-Benzyloxymethyl-2′,3′-dideoxy-5-O-(4-methylbenzoyl)uridine [**9 e** (β)]

1.09 g (16%); M.p. 119–120°C; MS, *m/z* 344 (M^+-C_6H_5CHO); ^{1}H-NMR (Me_2SO-d_6) δ 1.84–2.45 (m, *p*-CH_3, 2′-H and 3′-H), 4.03 (d, J = 11.7 Hz, CH_2O), 4.10 (d, J = 11.7 Hz, CH_2O), 4.26–4.54 (m, OCH_2, 4′-H, 5′-H), 6.03 (dd, J = 6.7 and 3.9 Hz, 1′-H), 7.28 (m, 7 *Ar*H), 7.65 (s, 6-H), 7.87 (d, J = 8.0 Hz, 2 *Ar*H), 11.43 (br, N 3-H); ^{13}C-NMR (Me_2SO-d_6) δ 21.1 (*p*-CH_3), 25.8 (C-3′), 30.9 (C-2′), 64.2 (CH_2O), 65.6 (C-5′), 71.3 (OCH_2), 77.8 (C-4′), 85.5 (C-1′), 110.5 (C-5), 126.7 (C-1″), 127.3 (C-2‴), 128.1 (C-3‴), 129.2 (C-2‴), 129.3 (C-3″), 138.3 (C-6), 138.4 (C-1‴), 143.8 (C-4″), 150.2 (C-2), 162.6 (C-4), 165.6 (C=O).

5-Alkoxy and 5-Hydroxymethyl-2′,3′-dideoxyuridines **10 a–e, 11 a–e**

A solution of **9 a–e** (1.6 mmol) in a 1 : 1 mixture (50 ml) of methanol and conc. ammonia was stirred at room temperature for 48–72 h. The reaction mixtures were concentrated under reduced pressure to obtain **10 a + 11 a**, $C_{10}H_{14}N_2O_5 \cdot \frac{1}{4}H_2O$; **10 b + 11 b**, $C_{11}H_{16}N_2O_5$; **10 c + 11 c**, $C_{14}H_{22}N_2O_5$; **10 d + 11 d**, $C_{15}H_{24}N_2O_5 \cdot \frac{1}{2}H_2O$; **10 e + 11 e**, $C_{17}H_{20}N_2O_5$. The anomeric mixtures were chromatographed on silica gel with $CHCl_3$ as eluent [compound **9 a** with $CHCl_3$-*Me*OH (98 : 2) to give pure α- and β-anomers.

1-(2,3-Dideoxy-α-D-glycero-pentofuranosyl)-5-hydroxymethyluracil (**10 a**)

101 mg (26%), M.p. 161–163°C; MS *m/z* 242 (M^+); ^{1}H-NMR (Me_2SO-d_6) δ 1.78–2.37 (m, 2′-H and 3′-H), 3.41 (m, 5′-H), 4.16 (s, 5-CH_2), 4.36 (m, 4′-H), 4.84 (br s, OH), 6.03 (t, J = 5.1 Hz, 1′-H), 7.45 (s, 6-H); ^{13}C-NMR (Me_2SO-d_6) δ 25.7 (C-3′), 31.3 (C-2′), 55.8 (5-CH_2), 63.4 (C-5′), 81.4 (C-4′), 86.0 (C-1′), 113.8 (C-5), 136.3 (C-6), 150.1 (C-2), 162.7 (C-4).

2′,3′-Dideoxy-5-hydroxymethyluridine (**11 a**)

93 mg (24%), M.p. 142–143°C; MS, *m/z* 242 (M^+); ^{1}H-NMR (Me_2SO-d_6) δ 1.81–2.28 (m, 2′-H and 3′-H), 3.61 (m, 5′-H), 4.02 (s, 4′-H), 4.14 (s, 5-CH_2), 4.95 (br, OH), 6.00 (s, 1′-H), 7.78 (s, 6-H); ^{13}C-NMR (Me_2SO-d_6) δ 25.3 (C-3′), 31.4 (C-2′), 56.0 (5-CH_2), 62.4 (C-5′), 81.2 (C-4′), 84.9 (C-1′), 113.6 (C-5), 136.8 (C-6), 150.2 (C-2), 162.7 (C-4).

1-(2,3-Dideoxy-α-D-glycero-pentofuranosyl)-5-methoxymethyluracil (**10 b**)

115 mg (28%); M.p. 110–111°C; MS, *m/z* 256 (M^+); ^{1}H-NMR ($CDCl_3$) δ 1.80–2.54 (m, 2′-H and 3′-H), 3.36 (s, OCH_3), 3.52 (dd, J = 12.0 and 5.3 Hz, 5′-H), 3.69 (dd, J = 11.93 and 3.2 Hz, 5′-H), 4.13 (d, J = 12.5 Hz, CH_2), 4.19 (d, J = 12.5 Hz, CH_2), 4.45 (m, 4′-H), 6.07 (dd, J = 5.7 and 4.2 Hz, 1′-H), 7.41 (s, 6-H); ^{13}C-NMR ($CDCl_3$) δ 25.4 (C-3′), 32.1 (C-2′), 58.2 (OCH_3), 64.1 (C-5′), 66.3 (5-CH_2), 81.7 (C-4′), 87.1 (C-1′), 111.0 (C-5), 137.4 (C-6), 150.3 (C-2), 163.0 (C-4).

2′,3′-Dideoxy-5-methoxymethyluridine (**11 b**)

37 mg (9%); M.p. 123–124°C; MS, *m/z* 256 (M^+); ^{1}H-NMR (Me_2SO-d_6) δ 1.81–2.36 (m, 2′-H and 3′-H), 3.22 (s, OCH_3), 3.54 (d, J = 11.2 Hz, 5′-H), 3.70 (d, J = 11.3 Hz, 5′-H), 4.03 (m, 5-CH_2 and 4′-H), 5.06 (br s, OH), 5.96 (dd, J = 6.6 and 3.3 Hz, 1′-H), 8.03 (s, 6-H), 11.31 (br s, N3-H); ^{13}C-NMR (Me_2SO-d_6) δ 24.7 (C-3′), 31.8 (C-2′), 57.1 (OCH_3), 61.9 (C-5′), 66.2 (5-CH_2), 81.5 (C-4′), 85.1 (C-1′), 109.3 (C-5), 139.3 (C-6), 150.1 (C-2), 162.7 (C-4).

1-(2,3-Dideoxy-α-D-glycero-pentofuranosyl)-5-(1-methylpropoxymethyl)uracil (**10 c**)

186 mg (39%); M.p. 86–88°C; MS *m/z* 298 (M^+); ^{1}H-NMR ($CDCl_3$) δ 0.91 and 0.92 (2 xt, J = 7.4 Hz, CH_3), 1.17 (d, J = 6.1 Hz, CH_3), 1.54 (m, CH_2), 1.85–2.59 (m, 2′-H and 3′-H), 3.46 (hex, J = 6.1 Hz, OCH), 3.57 (dd, J = 12.0 and 5.4 Hz, 5′-H), 3.75 (dd, J = 12.0 and 3.2 Hz, 5′-H), 4.27 (m, CH_2O), 4.46 (br s, 4′-H), 6.15 (dd, J = 5.9 and 4.1 Hz, 1′-H), 7.44 (s, 6-H); ^{13}C-NMR ($CDCl_3$) δ 9.6 (CH_3), 19.0 (CH_3), 25.7 (C-3′), 29.0 (CH_2), 32.3 (C-2′), 62.4 (CH_2O), 64.4 (C-5′), 77.2 (OCH), 81.8 (C-4′), 87.3 (C-1′), 112.4 (C-5), 136.5 (C-6), 150.3 (C-2), 162.7 (C-4).

2′,3′-Dideoxy-5-(1-methylpropoxymethyl)uridine (**11 c**)

67 mg (14%); hygroscopic (solid); MS, *m/z* 298 (M^+); ^{1}H-NMR ($CDCl_3$) δ 0.91 (t, J = 6.4 Hz, CH_3), 1.17 (d, J = 6.1 Hz, CH_3), 1.54 (m, CH_2), 1.93–2.48 (m, 2′-H and 3′-H), 3.48 (hex, J = 6.0 Hz, OCH),

3.71 (dd, $J = 12.2$ and 4.4 Hz, 5′-H) 3.94 (dd, $J = 12$ and 2.4 Hz, 5′-H), 4.18–4.35 (m, 5-CH_2 and 4′-H), 5.34 (br s, OH), 6.10 (dd, $J = 6.6$ and 3.6 Hz, 1′-H), 7.78 (s, 6-H); ^{13}C-NMR ($CDCl_3$) δ 9.5 (CH_3), 18.9 (CH_3), 25.1 (C-3′), 28.5 (CH_2), 32.1 (C-2′), 62.3 (CH_2O), 63.3 (C-5′), 77.1 (OCH), 81.6 (C-4′), 86.3 (C-1′), 111.9 (C-5), 137.7 (C-6), 150.4 (C-2), 163.0 (C-4).

1-(2,3-Dideoxy-α-D-glycero-pentofuranosyl)-5-pentyloxymethyluracil (**10 d**)

80 mg (16%): M.p. 86–89°C; MS, *m/z* 312 (M^+); ^{1}H-NMR ($CDCl_3$) δ 0.92 (t, $J = 6.6$ Hz, CH_3), 1.33 (m, CH_2CH_2), 1.63 (m, CH_2), 1.92–2.56 (m, 2′-H and 3′-H), 3.53–3.63 (m, OCH_2 and 5′-H), 3.77 (dd, $J = 11.9$ and 3.1 Hz, 5′-H), 4.24 (d, $J = 13.0$ Hz, CH_2O, 4.31 (d, $J = 13.0$ Hz, CH_2O), 4.51 (br s, 4′-H), 6.16 (t, $J = 4.9$ Hz, 1′-H), 7.44 (s, 6-H); ^{13}C-NMR ($CDCl_3$) δ 13.8 (CH_3), 22.3 (CH_2), 25.6 (C-3′), 28.1 (CH_2), 29.1 (CH_2), 29.5 (CH_2), 32.3 (C-2′), 64.3 (C-5′), 64.6 (CH_2O), 71.1 (OCH_2), 81.8 (C-4′), 87.2 (C-1′), 111.8 (C-5), 136.9 (C-6), 150.4 (C-2), 162.8 (C-4).

2′,3′-Dideoxy-5-pentyloxymethyluridine (**11 d**)

70 mg (14%): M.p. 83–85°C; MS, *m/z* 312 (M^+); ^{1}H-NMR ($CDCl_3$) δ 0.89 (t, $J = 6.7$ Hz, CH_3), 1.30 (m, CH_2CH_2), 1.60 (m, CH_2), 1.87–2.48 (m, 2′-H and 3′-H), 3.51 (t, $J = 6.7$ Hz, OCH_2), 3.71 (dd, $J = 12.0$ and 4.3 Hz, 5′-H), 3.93 (dd, $J = 12.0$ and 2.7 Hz, 5′-H), 4.16–4.29 (m, 5-CH_2 and 4′-H), 6.09 (dd, $J = 6.7$ and 3.6 Hz, 1′-H), 7.83 (s, 6-H); ^{13}C-NMR ($CDCl_3$) δ 13.7 (CH_3), 22.2 (CH_2), 24.9 (C-3′), 28.0 (CH_2), 29.0 (CH_2), 32.1 (C-2′), 63.2 (CH_2O), 64.6 (C-5′), 70.9 (OCH_2), 81.6 (C-4′), 86.3 (C-1′), 111.3 (C-5), 138.1 (C-6), 150.3 (C-2), 162.9 (C-4).

5-Benzyloxymethyl-1-(2,3-dideoxy-α-D-glycero-pentofuranosyl)uracil (**10 e**)

160 mg (30%): M.p. 72–74°C; MS, *m/z* 332 (M^+); ^{1}H-NMR ($CDCl_3$) δ 1.98–2.46 (m, 2′-H and 3′-H), 3.56 (br s, 5′-H), 3.69 (br s, 5′-H), 4.31 (s, CH_2O), 4.39 (br s, 4′-H), 4.59 (s, OCH_2), 6.10 (br s, 1′-H), 7.33 (br s, *Ar*H), 7.44 (s, 6-H); ^{13}C-NMR ($CDCl_3$) δ 25.4 (C-3′), 32.1 (C-2′), 64.0 (C-5′), 64.2 (CH_2O), 72.6 (OCH_2), 81.7 (C-4′), 87.2 (C-1′), 111.2 (C-5), 127.3 (C-4″), 127.5 (C-2″), 128.1 (C-3″), 137.3 (C-6), 137.6 (C-1″), 150.2 (C-2), 162.9 (C-4).

5-Benzyloxymethyl-2′,3′-dideoxyuridine (**11 e**)

128 mg (24%): M.p. 75–77°C; MS, *m/z* 332 (M^+); ^{1}H-NMR ($CDCl_3$) 1.87–2.39 (m, 2′-H and 3′-H), 3.62 (dd, $J = 12.0$ and 4.0 Hz, 5′-H), 3.85 (dd, $J = 12.0$ and 2.4 Hz, 5′-H), 4.09 (br s, 4′-H), 4.27 (s, CH_2O), 4.56 (s, OCH_2), 6.04 (dd, $J = 6.5$ and 3.3 Hz, 1′-H), 7.27 (m, *Ar*H), 7.89 (s, 6-H); ^{13}C-NMR ($CDCl_3$) δ 24.7 (C-3′), 32.0 (C-2′), 62.9 (C-5′), 64.2 (CH_2O), 72.4 (OCH_2), 81.5 (C-4′), 86.2 (C-1′), 110.7 (C-5), 127.3 (C-6″), 127.4 (C-2″), 128.0 (C-3″), 137.6 (C-1″), 138.5 (C-6), 150.2 (C-2), 163.0 (C-4).

1-(2,3-Dideoxy-5-O-(4-methylbenzoyl)-D-glycero-pentofuranosyl)-5-alkoxymethyl-4-(1,2,4-triazol-1-yl)pyrimidin-2-one **12 b–e**

Triethylamine (6.48 g, 46 mmol) was added dropwise to a stirred, cooled (ice-water bath) mixture of 1,2,4-triazole (3.4 g, 48 mmol), phosphoryl chloride (0.97 ml, 10 mmol) and acetonitrile (30 ml). Compounds **9 b–e** (5 mmol) in acetonitrile (20 mmol) were added and the reaction mixture was stirred at room temperature for 3–4 h. Triethylamine (4.5 ml, 32 mmol) and water (1.2 ml) were then added and the solvents were evaporated under reduced pressure. The residue was partitioned between $CHCl_3$ (250 ml) and saturated aqueous $NaHCO_3$. The organic layers were dried ($MgSO_4$) and evaporated to give **12 b–e** in 83–89%.

5-Alkoxymethyl-1-(2,3-dideoxy-5-O-(4-methylbenzoyl)-D-glycero-pentofuranosyl)cytosine **13b–e**

A solution of **12b–e** (4.6 mmol) and 20% aqueous ammonia (26 ml) in dioxane (80 ml) were stirred at room temperature. After 0.5–2 h the mixture was evaporated under reduced pressure. The anomers of compound **13b, d, e** were separated by HPLC with isocratic 29–41% ethanol in water on a reverse phase solumn (RP-4, 15–20 µm, 300 A).

1-(2,3-Dideoxy-5-O-(4-methylbenzoyl)-α-D-glycero-pentofuranosyl)-5-methoxymethylcytosine [**13b** (α)]

0.82 g (48%): M.p. 161–162°C; MS, *m/z* 373 (M^+); ^{1}H-NMR ($CDCl_3$) δ 1.90–2.67 (m, *p*-CH_3, 2′-H and 3′-H), 3.33 (s, OCH_3), 4.23 (s, CH_2O), 4.36 (dd, J = 11.8 and 5.4 Hz, 5′-H), 4.43 (dd, J = 11.8 and 4.0 Hz, 5′-H), 4.74 (m, 4′-H), 6.12 (dd, J = 6.0 and 3.4 Hz, 1′-H), 7.26 (d, J = 8.1 Hz, *Ar*H), 7.41 (s, 6-H), 7.95 (d, J = 8.1 Hz, *Ar*H); ^{13}C-NMR ($CDCl_3$) δ 21.5 (*p*-CH_3), 26.0 (C-3′), 32.7 (C-2′), 57.3 (OCH_3) 65.9 (CH_2O), 69.5 (C-5′), 78.7 (C-4′), 88.5 (C-1′), 101.7 (C-5), 126.8 (C-1″), 129.0 (C-3″), 129.5 (C-2″), 138.9 (C-6), 143.8 (C-4″), 155.5 (C-2), 165.4 (C-4), 166.3 (C=O).

2,3-Dideoxy-5-O-(4-methylbenzoyl)-5-methoxymethylcytidine [**13b** (β)]

0.38 g (22%): M.p. 70–71°C; MS, *m/z* 373 (M^+); ^{1}H-NMR ($CDCl_3$) δ 1.90–2.54 (m, *p*-CH_3, 2′-H and 3′-H), 3.16 (s, OCH_3), 3.96 (s, CH_2O), 4.48–4.66 (m, 4′-H and 5′-H), 6.05 (br s, 1′-H), 7.26 (d, J = 7.4 Hz, *Ar*H), 7.65 (s, 6-H), 7.93 (d, J = 7.4 Hz, *Ar*H); ^{13}C-NMR (Me_2SO-d_6) δ 21.1 (*p*-CH_3), 25.6 (C-3′), 31.6 (C-2′), 56.6 (OCH_3), 65.5 (CH_2O), 67.4 (C-5′), 77.6 (C-4′), 85.8 (C-1′) 102.0 (C-5), 126.7 (C-1″), 129.2 (C-3″), 129.3 (C-2″), 140.0 (C-6), 143.8 (C-4″), 154.7 (C-2), 164.4 (C-4), 165.5 (C=O).

1-(2′,3′-Dideoxy-5-O-(4-methylbenzoyl)-α-D-glycero-pentofuranosyl)-5-pentyloxymethylcytosine [**13d** (α)]

0.91 g (46%): M.p. 110–111°C; MS, *m/z* 429 (M^+); ^{1}H-NMR ($CDCl_3$) δ 0.89 (t, J = 6.5 Hz, CH_3), 1.30 (m, CH_2CH_2), 1.59 (m, CH_2), 1.90–2.67 (m, *p*-CH_3, 2′-H and 3′-H), 3.41 (t, J = 6.7 Hz, OCH_2), 4.26 (s, CH_2O), 4.35 (dd, J = 11.8 and 5.4 Hz, 5′-H), 4.43 (dd, J = 11.8 and 4.0 Hz, 5′-H), 4.73 (t, J = 5.1 Hz, 4′-H), 5.85 (br, NH_2), 6.12 (dd, J = 5.9 and 3.2 Hz, 1′-H), 7.26 (d, J = 8.0 Hz, *Ar*H), 7.39 (s, 6-H), 7.64 (br, NH_2), 7.95 (d, J = 8.1 Hz, 2 *Ar*H); ^{13}C-NMR ($CDCl_3$) δ 13.8 (CH_3), 21.5 (*p*-CH_3), 22.3 (CH_2), 26.0 (C-3′), 28.1 (CH_2), 29.0 (CH_2), 32.7 (C-2′), 65.9 (CH_2O), 67.9 (C-5′), 70.0 (OCH_2), 78.7 (C-4′), 88.5 (C-1′), 102.0 (C-5), 126.8 (C-1″), 129.0 (C-3″), 129.5 (C-2″), 138.6 (C-6), 143.8 (C-4″), 155.5 (C-2), 165.4 (C-4), 166.4 (C=O).

2′,3′-Dideoxy-5-O-(4-methylbenzoyl)-5-pentyloxymethylcytidine [**13d** (β)]

0.67 g (34%): M.p. 82–84°C; MS, *m/z* 429 (M^+), ^{1}H-NMR ($CDCl_3$) δ 0.88 (t, J = 6.6 Hz, CH_3), 1.28 (m, CH_2CH_2), 1.52 (m, CH_2), 1.84–2.68 (m, *p*-CH_3, 2′-H and 3′-H), 3.23 (t, J = 6.6 Hz, OCH_2), 3.98 (d, J = 12.4 Hz, CH_2O), 4.04 (d, J = 12.3 Hz, CH_2O), 4.48–4.66 (m, 4′-H and 5′-H), 6.06 (dd, J = 6.4 and 3.4 Hz, 1′-H), 7.26 (d, J = 8.0 Hz, *Ar*H), 7.64 (s, 6-H), 7.93 (d, J = 8.0 Hz, *Ar*H); ^{13}C-NMR ($CDCl_3$) δ 13.8 (CH_3), 21.5 (*p*-CH_3), 22.3 (CH_2), 25.6 (C-3′), 28.1 (CH_2), 29.0 (CH_2), 33.0 (C-2′), 65.2 (CH_2O), 67.7 (C-5′), 69.9 (OCH_2), 78.8 (C-4′), 87.4 (C-1′), 102.1 (C-5), 126.8 (C-1″), 129.2 (C-3″), 129.5 (C-2″), 138.9 (C-6), 144.0 (C-4″), 155.5 (C-2), 165.2 (C-4), 166.2 (C=O).

5-Benzyloxymethyl-1-(2,3-dideoxy-5-O-(4-methylbenzoyl)-α-D-glycero-pentofuranosyl)cytosine [**13e** (α)]

0.91 g (44%): M.p. 162–163°C; MS, *m/z* 449 (M^+); ^{1}H-NMR (Me_2SO-d_6) δ 1.93–2.51 (m, *p*-CH_3, 2′-H and 3′-H), 4.28 (m, CH_2O, 5′-H), 4.48 (s, OCH_2), 4.76 (br s, 4′-H), 6.06 (br s, 1′-H), 6.70 (br s,

NH_2), 7.33–7.45 (m, NH_2 and 7 *Ar*H), 7.88 (d, $J = 8.0$ Hz, 2 *Ar*H); ^{13}C-NMR (Me_2SO-d_6) δ 21.1 (*p*-CH_3), 25.9 (C-3′), 31.6 (C-2′), 65.8 (CH_2O), 66.2 (C-5′), 70.8 (OCH_2), 77.8 (C-4′), 87.0 (C-1′), 102.0 (C-5), 126.7 (C-1″), 127.3 (C-2‴), 127.5 (C-4‴), 128.1 (C-3‴), 129.1 (C-3″), 129.3 (C-2″), 138.2 (C-6), 140.7 (C-1‴), 143.7 (C-4″), 154.8 (C-2), 164.6 (C-4), 165.5 (C=O).

5-Benzyloxymethyl-1-(2′,3′-dideoxy-5-O-(4-methylbenzoyl)cytidine [**13e** (β)]

0.50 g (24%): M.p. 138–139°C; MS, *m/z* 449 (M^+); ^{1}H-NMR ($CDCl_3$) δ 1.85–2.62 (m, *p*-CH_3, 2′-H and 3′-H), 4.07 (d, $J = 12.5$ Hz, CH_2O), 4.13 (d, $J = 12.5$ Hz, CH_2O), 4.32 (s, OCH_2), 4.49–4.66 (m, 4′-H and 5′-H), 6.07 (dd, $J = 6.3$ and 3.3 Hz, 1′-H), 7.22–7.36 (m, 7 *Ar*H), 7.67 (s, 6-H), 7.91 (d, $J = 8.1$ Hz, 2 *Ar*H); ^{13}C-NMR (Me_2SO-d_6) δ 21.1 (*p*-CH_3), 25.9 (C-3′), 31.6 (C-2′), 65.8 (C-5′), 65.8 (CH_2O), 70.8 (OCH_2), 77.7 (C-4′), 85.9 (C-1′), 102.0 (C-5), 127.4 (C-2‴), 128.1 (C-3‴), 129.2 (C-3″), 129.3 (C-2″), 138.1 (C-6), 140.1 (C-1‴), 143.7 (C-4″), 154.7 (C-2), 164.4 (C-4), 165.5 (C=O).

5-Alkoxymethyl-1-(2,3-dideoxy-D-glycero-pentofuranosyl)cytosines **14b–e** *and* **15b–e**

A solution of **13b–e** in half saturated solution of methanolic ammonia (120 ml) was stirred at room temperature for 24–48 h. The solvent was evaporated to give **14b+15b**, $C_{11}H_{17}N_3O_4$; **14c+15c**, $C_{14}H_{23}N_3O_4$; **14d+15d**, $C_{15}H_{25}N_3O_4$; **14e+15e**, $C_{17}H_{21}N_3O_4$. The anomeric mixture was chromatographed on silica gel with 5–10% methanol in ether to give pure α-anomer (**14**) and β-anomer (**15**).

1-(2,3-Dideoxy-α-D-glycero-pentofuranosyl)-5-methoxymethylcytosine (**14b**)

376 mg (32%): M.p. 135–138°C; MS, *m/z* 255 (M^+); ^{1}H-NMR ($CDCl_3$) δ 1.89–2.63 (m, 2′-H and 3′-H), 3.32 (s, OCH_3), 3.59 (dd, $J = 11.8$ and 5.8 Hz, 5′-H), 3.72 (dd, $J = 11.9$ and 3.0 Hz, 5′-H), 4.22 (s, CH_2O), 4.47 (br s, 4′-H), 6.09 (d, $J = 3.8$ Hz, 1′-H), 7.42 (s, 6-H); ^{13}C-NMR ($CDCl_3$) δ 25.4 (C-3′), 32.9 (C-2′), 57.3 (OCH_3), 64.5 (C-5′), 69.3 (CH_2O), 81.8 (C-4′), 88.0 (C-1′), 101.9 (C-5), 139.0 (C-6), 155.8 (C-2), 165.2 (C-4).

2′,3′-Dideoxy-5-methoxymethylcytidine (**15b**)

340 mg (29%): M.p. 170–171°C; MS *m/z* 255 (M^+); ^{1}H-NMR (Me_2SO-d_6) δ 1.70–2.30 (m, 2′-H and 3′-H), 3.21 (s, OCH_3), 3.55 (d, $J = 11.9$ Hz, 5′-H), 3.72 (d, $J = 11.9$ Hz, 5′-H), 4.02–4.16 (m, 4′-H and CH_2O), 5.06 (s, OH), 5.91 (t, $J = 3.6$ Hz, 1′-H), 6.58 (br s, NH_2), 7.27 (br s, NH_2), 8.01 (s, 6-H); ^{13}C-NMR (Me_2SO-d_6), δ 24.4 (C-3′), 32.4 (C-2′), 56.6 (OCH_3), 61.8 (C-5′), 67.7 (CH_2O), 81.5 (C-4′), 85.6 (C-1′), 101.2 (C-5), 141.0 (C-6), 154.8 (C-2), 164.4 (C-4).

1-(2,3-Dideoxy-α-D-glycero-pentofuranosyl)-5-(1-methylpropoxymethyl)cytosine (**14c**)

287 mg (21%): M.p. 119–121°C; MS, *m/z* 297 (M^+); ^{1}H-NMR (Me_2SO-d_6) δ 0.83 (t, $J = 7.4$ Hz, CH_3), 1.09 (d, $J = 6.0$ Hz, CH_3), 1.44 (m, CH_2), 1.76–2.32 (m, 2′-H and 3′-H), 3.36–3.68 (m, OCH, 5′-H), 4.17 (d, $J = 12.2$ Hz, CH_2O), 4.28 (d, $J = 12.2$ Hz, CH_2O), 4.40 (br s, 4′-H), 4.80 (br s, OH), 5.98 (br s, 1′-H), 6.40 (br s, NH_2), 7.30 (br s, NH_2), 7.55 (s, 6-H); ^{13}C-NMR (Me_2SO-d_6) δ 9.4 (CH_3), 18.8 (CH_3), 25.4 (C-3′), 28.5 (CH_2), 31.9 (C-2′), 63.4 (C-5′), 63.4 (CH_2O), 74.6 (OCH), 81.2 (C-4′), 86.7 (C-1′), 102.5 (C-5), 139.5 (C-6), 154.8 (C-2), 164.5 (C-4).

2′,3′-Dideoxy-5-(1-methylpropoxymethyl)cytidine (**15c**)

191 mg (14%): M.p. 150–152°C; MS, *m/z* 297 (M^+); ^{1}H-NMR (Me_2SO-d_6) δ 0.82 and 0.83 (2 × t, $J = 7.3$ Hz, CH_3), 1.08 (d, $J = 6.0$ Hz, CH_3), 1.36 (m, CH_2), 1.73–2.37 (m, 2′-H and 3′-H), 3.39 (m, OCH), 3.55 (dd, $J = 11.7$ and 3.8 Hz, 5′-H), 3.70 (d, $J = 11.7$ Hz, 5′-H), 4.02–4.26 (m, CH_2O and

4′-H), 5.05 (br s, OH), 5.92 (d, $J = 5.9$ Hz, 1′-H), 6.41 (br s, NH_2), 7.31 (br s, NH_2) 7.97 and 7.99 (2 × s, 6-H); ^{13}C-NMR (Me_2SO-d_6) δ 9.4 (CH_3), 18.7 (CH_3), 24.5 (C-3′), 28.5 (CH_2), 32.4 (C-2′), 62.0 (C-5′), 63.5 (CH_2O), 74.4 (OCH), 81.5 (C-4′), 85.6 (C-1′), 101.9 (C-5), 140.2 (C-6), 154.8 (C-2), 164.5 (C-4).

1-(2,3-Dideoxy-α-D-glycero-pentofuranosyl)-5-pentyloxymethylcytosine (**14 d**)

444 mg (31%): M.p. 90–92°C; MS, *m/z* 311 (M^+); ^{1}H-NMR (Me_2SO-d_6) δ 0.86 (t, $J = 6.6$ Hz, CH_3), 1.28 (m, CH_2CH_2), 1.50 (m, CH_2), 1.74–2.34 (m, 2′-H and 3′-H), 3.34–3.68 (m, OCH_2 and 5′-H), 4.20 (s, CH_2O), 4.40 (m, 4′-H), 4.82 (br s, OH), 5.98 (dd, $J = 6.0$ and 3.6 Hz, 1′-H), 6.53 (br s, NH_2), 7.33 (br s, NH_2), 7.55 (s, 6-H); ^{13}C-NMR (Me_2SO-d_6) δ 13.8 (CH_3), 21.8 (CH_2), 25.4 (C-3′), 27.8 (CH_2), 28.7 (CH_2), 31.9 (C-2′), 63.4 (C-5′), 65.8 (CH_2O), 68.8 (OCH_2), 81.2 (C-4′), 86.7 (C-1′), 102.0 (C-5), 140.0 (C-6), 154.8 (C-2), 164.3 (C-4).

2′,3′-Dideoxy-5-pentyloxymethylcytidine (**15 d**)

329 mg (23%): M.p. 128–129°C; MS, *m/z* 311 (M^+); ^{1}H-NMR (Me_2SO-d_6) δ 0.86 (t, $J = 6.6$ Hz, CH_3), 1.19 (m, CH_2), 1.49 (m, CH_2), 1.69–2.32 (m, 2′-H and 3′-H), 3.35 (t, $J = 6.5$ Hz, OCH_2), 3.55 (dd, $J = 11.9$ and 3.5 Hz, 5-H), 3.71 (dd, $J = 11.9$ and 2.9 Hz, 5′-H), 4.03 (m, 4′-H), 4.15 (s, CH_2O), 5.08 (br s, OH), 5.92 (dd, $J = 6.5$ and 2.5 Hz, 1′-H), 6.52 (br s, NH_2), 7.31 (br s, NH_2), 7.99 (s, 6-H); ^{13}C-NMR (Me_2SO-d_6) δ 13.8 (CH_3), 21.8 (CH_2), 24.5 (C-3′), 27.8 (CH_2), 32.4 (C-2′), 61.9 (C-5′), 66.0 (CH_2O), 68.8 (OCH_2), 81.5 (C-4′), 85.6 (C-1′), 101.5 (C-5), 140.6 (C-6), 154.8 (C-2), 164.4 (C-4).

1-(2,3-Dideoxy-α-D-glycero-pentofuranosyl)-5-benzyloxymethylcytosine (**14 e**)

381 mg (25%): M.p. 181–183°C; MS, *m/z* 331 (M^+); ^{1}H-NMR (Me_2SO-d_6) δ 1.76–2.35 (m, 2′-H and 3′-H), 3.45 (m, 5′-H), 4.33 (s, CH_2O), 4.41 (t, $J = 5.0$ Hz, 4′-H), 4.49 (s, OCH_2), 4.85 (t, $J = 5.6$ Hz, OH), 5.99 (dd, $J = 5.9$ and 3.5 Hz, 1′-H), 6.69 (br, NH_2), 7.34 (m, *Ar*H), 7.59 (s, 6-H); ^{13}C-NMR (Me_2SO-d_6) δ 25.5 (C-3′), 31.9 (C-2′), 63.4 (C-5′), 65.7 (CH_2O), 70.7 (OCH_2), 81.3 (C-4′), 86.7 (C-1′), 101.8 (C-5), 127.3 (C-4″), 127.5 (C-2″), 128.1 (C-3″), 138.2 (C-1″), 140.2 (C-6), 154.8 (C-2), 164.5 (C-4).

5-Benzyloxymethyl-2′,3′-dideoxycytidine (**15 e**)

274 mg (18%): M.p. 156–158°C; MS, *m/z* 331 (M^+); ^{1}H-NMR (Me_2SO-d_6) δ 1.73–2.30 (m, 2′-H and 3′-H), 3.55 (m, 5′-H), 3.71 (m, 5′-H), 4.02 (m, 4′-H), 4.27 (s, CH_2O), 4.46 (s, OCH_2), 5.07 (t, $J = 5.3$ Hz, OH), 5.92 (t, $J = 3.6$ Hz, 1′-H), 6.65 (br s, NH_2), 7.33 (m, *Ar*H), 8.02 (s, 6-H); ^{13}C-NMR (Me_2SO-d_6) δ 24.5 (C-3′), 32.4 (C-2′), 61.9 (C-5′), 66.0 (CH_2O), 70.7 (OCH_2), 81.5 (C-4′), 85.7 (C-1′), 101.3 (C-5), 127.3 (C-4″), 127.5 (C-2″), 128.1 (C-3′), 138.2 (C-1″), 141.0 (C-6), 154.8 (C-2), 164.4 (C-4).

Acknowledgement

Danish Natural Science Research Council, Assurandør-Societetet, and Egyptian Ministry of Higher Education are gratefully acknowledged for their support.

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Received May 17, 1990. Accepted June 25, 1990