USE OF 5-DEOXY-*ribo*-HEXOFURANOSE DERIVATIVES FOR THE PREPARATION OF 5'-NUCLEOTIDE PHOSPHONATES AND HOMORIBONUCLEOSIDES*

Sergei N. MIKHAILOV, Nelly Sh. PADYUKOVA, Marat Ya. KARPEISKII, Lidiya I. KOLOBUSHKINA and Leon N. BEIGELMAN

Institute of Molecular Biology, the USSR Academy of Sciences, 117984 Moscow, U.S.S.R.

Received January 11, 1988
Accepted October 4, 1988

A convenient and general method is proposed for the synthesis of 5'-nucleotide phosphonate analogs starting from 5-deoxy-1,2-O-isopropylidene-α-D-*xylo*-hexofuranose which can easily be produced in preparative quantities from D-glucose. Phosphonate *IIIe* was synthesized by means of the Arbuzov reaction between 3-O-benzoyl-6-bromo-5,6-dideoxy-1,2-O-isopropylidene-α-D-*ribo*-hexofuranose and triethyl phosphite. The consecutive acetolysis, condensation with uracil and N^6-benzoyladenine bis-trimethylsilyl derivatives and deblocking possessed phosphonate analogs of 5'-nucleotides in good yields. The intermediate 5-deoxy-1,2-O-isopropylidene-α-D-*ribo*-hexofuranose derivatives were used for the preparation of homonucleosides.

Unique properties of phosphonate analogs of the natural phosphoric acid esters make them exceptionally suitable for the use in a continuously increasing variety of applications. The substitution of the P—O—C fragment in substrates with P—CH_2—C creates an interesting class of compounds which effectively inhibit enzymes whose substrates are phosphoric acid esters and their derivatives[1].

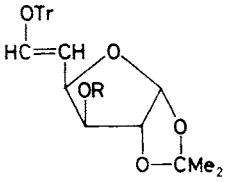
Two approaches have been elaborated for the preparation of phosphonate nucleotide analogs: the first one involving the Wittig reaction[2-9] and the next one utilizing the Arbuzov condensation[10]. For the preparation of 5'-nucleotide analogs the Wittig reaction with 5'-aldehyde derivatives of nucleosides was used[2-6]. Montgomery and Hewson[9] tried to synthesize these compounds starting from D-ribose. This route was not elaborated in details[9,11].

In the present work, we propose a general method for the preparation of 5'-deoxy-5'-dihydroxyphosphonylmethylnucleosides. The method is based on the synthesis of the phosphonate-containing carbohydrate component by means of the Arbuzov reaction, followed with glycosylation (for preliminary communication see ref.[12]).

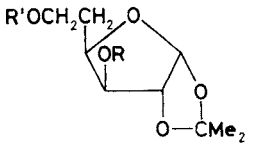
The synthesis can be accomplished starting from D-*xylo*-hexofuranose or D-*ribo*-hexofuranose derivatives. These compounds may also be used for the synthesis

* Part of this communication was presented at the 7th Symposium of Nucleic Acid Components at Bechyně Castle (Czechoslovakia), August 30—September 5, 1987.

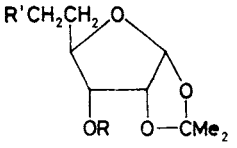
of 5-deoxy-β-D-*ribo*-hexofuranosylnucleosides (homonucleosides). The key step in the preparation of these analogs starting from nucleosides is the reaction of 5'--deoxy-5'-iodo or 5'-O-tosyl derivatives with cyanide, followed by reduction and deamination to give the required one carbon chain extension[6,13,14]. The overall



I a, R = H
I b, R = Bz

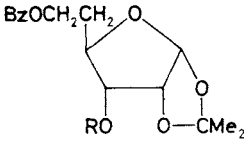


II a, R = R' = H
II b, R = H ; R' = Tr
II c, R = Bz ; R' = H
II d, R = H ; R' = Bz
II e, R = Bz ; R' = Tr

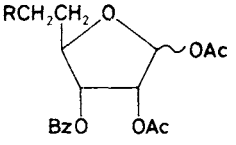


III a, R = H ; R' = OTr
III b, R = Bz ; R' = OTr
III c, R = Bz ; R' = OH
III d, R = Bz ; R' = Br
III e, R = Bz ; R' = $P(OEt)_2$ (=O)

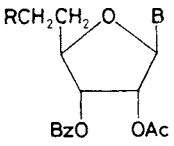
In formulae *I*–*III*: Tr = trityl



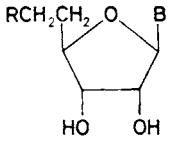
IV a, R = H
IV b, R = Bz



V a, R = $P(OEt)_2$ (=O)
V b, R = OBz



VI a, R = $P(OEt)_2$ (=O) ; B = Ura
VI b, R = $P(OEt)_2$ (=O) ; B = Ade^{Bz}
VI c, R = $P(OH)_2$ (=O) ; B = Ura
VI d, R = $P(OH)_2$ (=O) ; B = Ade^{Bz}
VI e, R = OBz ; B = Ura
VI f, R = OBz ; B = Ade^{Bz}



VII a, R = $P(OH)_2$ (=O) ; B = Ura
VII b, R = $P(OH)_2$ (=O) ; B = Ade
VII c, R = OH ; B = Ura
VII d, R = OH ; B = Ade

yields of these reaction sequences are moderate. Several schemes have been developed for the preparation of homonucleosides starting from glucose[15], ribose[16] and allose[17], the latter appearing to be the most efficient and comparable with the present one. Analysis of the data reported in literature implies that the method of 5-deoxy-D-*xylo*-hexofuranose synthesis developed by Whistler et al.[18] is the most effective one. The starting compound *Ia* can be prepared[18] in 100 g quantities from D-glucose. Its further reduction[18] yielded *IIa*.

For the preparation of 5-deoxy-D-*ribo*-hexofuranose derivatives 6-O-blocked compounds are necessary. The tritylation of *IIa* generated *IIb* in a high yield (another possibility was a multistep conversion). Benzoylation of *Ia* with a mixture of benzoyl cyanide and triethylamine[19] in dioxane resulted in *Ib* and further acidic hydrolysis, followed by borohydride reduction, yielded *IIc*. This step must be performed very carefully avoiding alkaline conditions, where 3 → 6-O-benzoyl migration occurs with the formation of *IId* which was also prepared by selective benzoylation of *IIa*. We have investigated this process and ascertained that migration took place not only in alkaline media, but also in the presence of strong organic bases such as 1,8-diazabicyclo[5.4.0]undec-7-ene. In D-glucose series 3→6-O-benzoyl migration is known[20]. Further tritylation of *IIc* gave *IIe*, and after debenzoylation, *IIb* was obtained in overall good yield. The configuration at C-3 was reversed employing a standard procedure[21] using dimethyl sulfoxide and acetic anhydride for 1 h at 70°C, followed by reduction with sodium borohydride. The yield of 5-deoxy-1,2-O-isopropylidene-6-O-trityl-α-D-*ribo*-hexofuranose (*IIIa*) was 78%. 5-Deoxy-1,2-O-isopropylidene-3-O-methylthiomethyl-6-O-trityl-α-D-*xylo*-hexofuranose was a by-product in this reaction.

The reversion of the configuration at C-3 (transition *II* → *III*) was accompanied by changes in the coupling values: $J(2, 3) = 0$ Hz for *xylo* derivatives and $J(2, 3) = 4{\cdot}7 - 5{\cdot}1$ Hz for their C-3 epimers. Benzoylation with the mixture of benzoyl cyanide and triethylamine in dioxane, followed by detritylation with a 1M tin tetrachloride solution in 1,2-dichloroethane[22] produced acetonide *IIIc* in high yield. Bromination of *IIIc* with a mixture of carbon tetrabromide and triphenylphosphine in N,N-dimethylformamide[23] gave bromide *IIId* (yield 78%). Phosphonate *IIIe* was synthesized by means of the Arbuzov reaction by boiling bromide *IIId* with triethylphosphite; the ^{1}H NMR spectrum of *IIIe* exhibited proton signals from the protecting groups and P—CH_2CH_2 in the region of $2{\cdot}1 - 1{\cdot}7$ ppm. Acetonide *IId* was converted to *IVa*, further benzoylation gave the known[17] dibenzoate *IVb*, the starting compound for the preparation of homonucleosides. Acetolysis of *IIIe* and *IVb* generated a mixture of α- and β-anomers *Va* and *Vb*, respectively, in a high yield.

The use of 2,4-bis(trimethylsilyl)uracil and trimethylsilyl trifluoromethanesulfonate[24] as a catalyst in the reaction of glycosylation resulted in the nucleotide *VIa* (30%) and N^1-ethyluracil (36%). A similar side reaction was already reported[8]. In

order to avoid this undesirable alkylation, bis-trimethylsilyl derivatives of uracil and N^6-benzoyladenine were glycosylated in the presence of tin tetrachloride[24]. The yield of the protected nucleotides *VIa* and *VIb* reached 83% and 80%, respectively. The signals of ethyl groups were diastereotopic in the ^{1}H NMR spectra of *IIIe*, *Va*, *VIa* and *VIb*. The ethyl protecting groups were selectively removed by treatment with bromotrimethylsilane in 1,2-dichloroethane[10,25]. The ^{1}H NMR spectra of phosphonates *VIc* and *VId* lacked proton signals from the ethyl groups, but showed proton signals from benzoyl and acetyl groups. Elimination of these groups with ammonia solution in methanol led to phosphonates *VIIa* and *VIIb* in high yields. Their UV spectra were identical with those of UMP and AMP, which confirmed the position of glycosylation.

Analogously, starting from *Vb* protected compounds, *VIe*, *VIf* and homonucleosides *VIIc* and *VIId* were prepared in overall high yield. The positive Cotton effect in the CD spectra is typical of β-pyrimidine nucleosides[26], and the negative one is characteristic of β-purine nucleosides[27]. The same situation was found for phosphonates *VIIa* and *VIIb* and homonucleosides *VIIc* and *VIId*, which confirmed the anomeric configuration. Moreover, chemical shifts and coupling constants in ^{1}H NMR spectrum of *VIIc* are essentially the same as they have been found for *VIIc* prepared starting from natural nucleoside by a multi-step procedure[14].

All the steps in this synthesis have a high yield which allows to perform 2–3 steps in succession without isolating the products. This scheme is suitable for the synthesis of phosphonate analogs of 5'-nucleotides and homonucleosides in preparative quantities and, being universal, has certain advantages in comparison with traditional procedures of the synthesis.

EXPERIMENTAL

^{1}H NMR spectra were measured on a Varian XL-100 spectrometer (100 MHz) in deuterochloroform with tetramethylsilane as internal standard. Spectra in deuterium oxide were measured with tert-butanol as internal standard (1·27 ppm) and recalculated to tetramethylsilane. ^{31}P NMR spectra were measured on the same spectrometer in deuterium oxide with 85% phosphoric acid as external lock. Chemical shifts are given in ppm (δ-scale), coupling constants and bands widths in Hz. All parameters were obtained by first-order analysis. UV spectra were monitored with a Specord UV–VIS spectrophotometer (G.D.R.) in water. CD spectra were determined on Jobin–Yvon Dichrograph III apparatus. Specific rotation was registered with an automatic Perkin–Elmer 141 polarimeter. Preparative chromatography was performed on silica gel L 40/100 (Kavalier, Czechoslovakia). Thin-layer chromatography (TLC) was performed on Silufol UV_{254} plates (Kavalier, Czechoslovakia) using the systems: S_1, chloroform; S_2, chloroform–ethanol (98 : 2); S_3, chloroform–ethanol (95 : 5); S_4, 2-propanol–concentrated aqueous ammonia–water (7 : 1 : 2).

(5*E*)-3-O-Benzoyl-5-deoxy-1,2,-O-isopropylidene-6-O-trityl-α-D-*xylo*-hexofuran-5-enose (*Ib*)

To a solution of *Ia* (ref.[18], 8·0 g, 18 mmol) in dioxane (100 ml), benzoylcyanide (2·6 g, 20 mmol) and triethylamine (2·8 ml, 20 mmol) were added. The solution was allowed to stand for 1 h at

room temperature, then methanol (3 ml) was added to it and, after 10 min, the mixture was evaporated to dryness. The residue was chromatographed on silica gel (50 g) in system S_1. Compound *Ib* was isolated as a syrup. Yield 9·5 g (96%). TLC: R_F 0·81 (S_1). ^{1}H NMR spectrum ($CDCl_3$): 8·05—7·95 m, 2 H (benzoyl); 7·64—7·24 m, 18 H (benzoyl, trityl): 6·34 d, 1 H (J(6, 5) = = 12·0, H-6); 5·86 d, 1 H (J(1, 2) = 3·8, H-1); 5·22 dd, 1 H (J(5, 6) = 12·0; J(5, 4) = 9·0, H-5); 5·16 d, 1 H (J(2, 1) = 3·8, H-2); 4·58 m, 2 H, (H-3, H-4); 1·47 s, 3 H (Me), 1·27 s, 3 H (Me). For $C_{35}H_{32}O_6$ (548·6) calculated: 76·62% C, 5·88% H; found: 76·21% C, 5·63% H.

5-Deoxy-1,2-O-isopropylidene-6-O-trityl-α-D-*xylo*-hexofuranose (*IIb*)

A) Chlorotriphenylmethane (9·9 g, 36 mmol) was added to a solution of compound *IIa* (ref.[18], 6·12 g, 30 mmol) in dry pyridine (150 ml), and the mixture was allowed to stand for 24 h at 20°C. The standard treatment and chromatography on silica gel (100 g) in the system S_1 yielded 11·9 g (89%) of derivative *IIb*. TLC: R_F 0·20 (S_1). $[\alpha]_D^{20}$ +3·9° (*c* 1, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$): 7·37—7·14 m, 15 H (trityl); 5·79 d, 1 H (J(1, 2) = 3·8, H-1); 4·46 d, 1 H (J(2, 1) = 3·8, H-2); 4·17 dt, 1 H (J(4, 3) = 2·5; J(4, 5) = J(4, 5') = 7·0, H-4), 4·00 dd, 1 H (J(3, 4) = 2·5; J(3, OH) = 4·0, H-3); 3·35 dt, 1 H (J(6, 6') = −10; J(6, 5) = J(6, 5') = 6·0, H-6); 3·11 dt, 1 H (J(6', 6) = −10; J(6', 5) = 6·0, H-6'); 2·63 d, 1 H (J(OH, 3) = 4·0, OH); 1·93 m, 2 H (5·5'-H); 1·44 s, 3 H (Me); 1·27 s, 3 H (Me). For $C_{28}H_{30}O_5$ (446·5) calculated: 75·31% C, 6·77% H; found: 74·82% C, 6·45% H.

B) Compound *IIe* (5·5 g, 10 mmol) was debenzoylated with 0·2M sodium methylate (60 ml) at room temperature for 30 min. The desired derivative *IIb* was obtained as a syrup 4·33 g (97%) after column chromatography on silica gel (50 g) in the system S_1.

3-O-Benzoyl-5-deoxy-1,2-O-isopropylidene-α-D-*xylo*-hexofuranose (*IIc*)

A solution of *Ib* (3·3 g, 6 mmol) in dioxane (10 ml), acetic acid (10 ml) and water (1 ml) was heated under reflux for 45 min. The solution was cooled, evaporated to dryness and coevaporated with ethanol (5 × 20 ml). The residue was dissolved in ethanol (15 ml) and sodium borohydride (120 mg) was added to the solution. The mixture was kept at room temperature for 15 min, neutralized with acetic acid and evaporated to dryness. The residue was dissolved in a mixture of chloroform (50 ml) and water (20 ml). Compound *IIc* was obtained from the organic layer as a syrup after column chromatography on silica gel (30 g) in the system S_1. Yield 1·2 g (65%). TLC: R_F 0·15 (S_1). ^{1}H NMR spectrum ($CDCl_3$): 8·05—7·85 m, 2 H (benzoyl), 7·59—7·27 m, 3 H (benzoyl); 5·91 d, 1 H (J(1, 2) = 3·8, H-1); 5·36 d, 1 H (J(3, 4) = 3·0, H-3); 4·60 d, 1 H (J(2, 1) = 3·8, H-2); 4·48 m, (1 H, 4-H), 3·75 t, 2 H (J(6, 5) = 6·0, H-6, 6'); 2·35 bs, 1 H (OH-6); 1·91 m, 2 H (H-5, 5'); 1·52 s, 3 H (Me); 1·30 s, 3 H (Me). For $C_{16}H_{20}O_6$ (308·3) calculated: 62·33% C, 6·54% H; found: 62·01% C, 6·40% H.

6-O-Benzoyl-5-deoxy-1,2-O-isopropylidene-α-D-*xylo*-hexofuranose (*IId*)

A) A solution of *IIc* (0·45 g, 1·46 mmol) in 5 mM NaOH in ethanol (10 ml) was kept at room temperature for 24 h, then neutralized with acetic acid and evaporated to dryness. The residue was dissolved in a mixture of chloroform (20 ml) and water (10 ml). From the organic layer *IId* was isolated after column cromatography on silica gel (30 g) in the system S_1. Yield 0·25 g (56%). M.p. 118—119°C, TLC: R_F 0·10 (S_1). ^{1}H NMR spectrum ($CDCl_3$); 8·03—7·93 m, 2 H (benzoyl), 7·60—7·28 m, 3 H (benzoyl); 5·89 d, 1 H (J(1, 2) = 3·8, H-1); 4·51 d, 1 H (J(2, 1) = 3·8, H-2); 4·49 dt, 1 H (J(6, 6') = −11·0; J(6, 5) = J(6, 5') = 6·5, H-6); 4·40 dt, 1 H (J(6', 6) = −11·0; J(6', 5) = J(6', 5') = 6·0, H-6'); 4·29 dt, 1 H (J(4, 3) = 3·0; J(4, 5) = J(4, 5') = 7·0, H-4);

4·13 dd, 1 H ($J(3, 4)$ = 3·0; $J(3, OH)$ = 7·0, H-3); 2·18 m, 3 H (OH-3, H-5, 5'); 1·46 s, 3 H (Me), 1·28 s, 3 H (Me). For $C_{16}H_{20}O_6$ (308·3) calculated: 62·33% C, 6·54% H; found: 62·43% C, 6·71% H.

B) A solution of *IIc* (1·1 g, 3·6 mmol), methanol (0·1 ml) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0·1 ml) in dioxane (15 ml) was kept for 1 month at room temperature and then evaporated to dryness. After column chromatography on silica gel (50 g) in the system S_1, 821 mg (74%) of *IId* was obtained.

C) To a solution of *IIa* (2·04 g, 10 mmol) in dry pyridine (15 ml) a solution of benzoyl chloride (1·3 ml, 11 mmol) in 1,2-dichloroethane was added dropwise, with cooling (−20°C) and stirring. The mixture was stirred 30 min at −20°C and 16 h at 0°C. Then water (2 ml) was added, the mixture was stirred another 20 min at room temperature, evaporated to dryness, coevaporated with toluene (3 × 10 ml) and the residue was dissolved in a mixture of chloroform (30 ml) and water (20 ml). From the organic layer *IId* was isolated after column chromatography on silica gel (100 g) in the system S_1. Yield 2·0 g (65%).

3-O-Benzoyl-5-deoxy-1,2-O-isopropylidene-6-O-trityl-α-D-*xylo*-hexofuranose (*IIe*)

Tritylation of *IIc* (4·6 g, 14·9 mmol) using chlorotriphenylmethane (5 g, 18·0 mmol) in 70 ml of dry pyridine in the same manner as described for *IIb*, afforded 7·8 g (95%) *IIe* as a syrup. TLC: R_F 0·80 (S_1). ^{1}H NMR spectrum ($CDCl_3$): 8·04—7·84 m, 2 H (benzoyl); 7·53—7·19 m, 18 H (benzoyl, trityl); 5·92 d, 1 H ($J(1, 2)$ = 3·8, H-1); 5·32 d, 1 H ($J(3, 4)$ = 3·0, H-3); 4·68 dt, 1 H ($J(4, 3)$ = 3·0; $J(4, 5)$ = $J(4, 5')$ = 6·5, H-4); 4·63 d, 1 H ($J(2, 1)$ = 3·8, H-2); 3·25 m, 2 H (H-6, 6'); 2·01 m, 2 H (H-5, 5'); 1·58 s, 3 H (Me); 1·34 s, 3 H (Me). For $C_{35}H_{34}O_6$ (550·7) calculated: 76·35% C, 6·22% H; found: 76·08% C, 6·12% H.

5-Deoxy-1,2-O-isopropylidene-6-O-trityl-α-D-*ribo*-hexofuranose (*IIIa*)

A solution of *IIb* (6·4 g, 14·3 mmol) in dry dimethyl sulfoxide (30 ml) and acetic anhydride (7·5 ml) was heated for 1·5 h at 70°C and evaporated under reduced pressure to dryness. The residue was dissolved in ethanol (25 ml), and sodium borohydride (240 mg, 6·3 mmol) was added, with cooling (0°C) and stirring. The mixture was stirred for 1 h at room temperature, evaporated and chloroform and water were added to the residue. 5-Deoxy-1,2-O-isopropylidene-3-O-methylthiomethyl-6-O-trityl-α-D-*xylo*-hexofuranose (1·2 g, 17%) was isolated from the organic layer by column chromatography on silica gel (100 g) in the system S_1. TLC: R_F 0·30 (S_1). ^{1}H NMR spectrum ($CDCl_3$): 7·50—7·20 m, 15 H (trityl); 5·88 d, 1 H ($J(1, 2)$ = 3·8, H-1); 4·70—4·44 m, 3 H (H-2, OCH_2—S—Me); 4·00 d, 1 H ($J(3, 4)$ = 3·0, H-3); 3·35—3·10 m, 3 H (H-4, H-6, 6'); 2·06 s, 3 H (CH_2—S—*Me*); 2·13—1·80 m, 2 H (H-5, 5'); 1·56 s, 3 H (Me); 1·36 s, 3 H (Me). Further, compound *IIIa* (5·0 g, 78%) was obtained by chromatography using solvent system S_1. TLC: R_F 0·15 (S_1). $[\alpha]_D^{20}$ +18·5° (*c* 1, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$): 7·43—7·15 m, 15 H (trityl); 5·68 d, 1 H ($J(1, 2)$ = 3·8, H-1); 4·50 dd, 1 H ($J(2, 1)$ = 3·8; $J(2, 3)$ = 5·1, H-2); 3·87 ddd, 1 H ($J(4, 3)$ = 8·5; $J(4, 5)$ = 5·0; $J(4, 5')$ = 6·5, H-4); 3·62 ddd, 1 H ($J(3, 2)$ = 5·1; $J(3, 4)$ = 8·5; $J(3, OH)$ = 9·0, H-3); 3·25 m, 2 H (H-6, 6'); 2·67 d, 1 H ($J(OH, 3)$ = 9·0, OH-3); 2·15—1·75 m, 2 H (H-5, 5'); 1·53 s, 3 H (Me); 1·33 s, 3 H (Me). For $C_{28}H_{30}O_5$ (446·5) calculated: 75·31% C, 6·77% H; found: 75·04% C, 6·53% H.

3-O-Benzoyl-5-deoxy-1,2-O-isopropylidene-6-O-trityl-α-D-*ribo*-hexofuranose (*IIIb*)

Triethylamine (1·4 ml, 9·9 mmol) and benzoylcyanide (1·3 g, 9·9 mmol) were added to a solution of *IIIa* (4·1 g, 9·2 mmol) in dioxane (60 ml). The solution was allowed to stand for 1 h at 20°C,

then methanol (2 ml) was added to the solution and, after 10 min, the mixture was evaporated to dryness in vacuo. The residue was chromatographed on a column with silica gel (50 g) in the system S_1. Compound *IIIb* (4·3 g, 85%) was isolated as a syrup. TLC: R_F 0·80 (S_1). $[\alpha]_D^{20}$ +52·2° (*c* 1, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$): 8·01–7·90 m, 2 H (benzoyl); 7·50–7·10 m, 18 H (benzoyl, trityl); 5·76 d, 1 H ($J(1, 2)$ = 3·8, H-1); 4·87 dd, 1 H ($J(2, 1)$ = 3·8; $J(2, 3)$ = 4·7, H-2); 4·62 dd, 1 H ($J(3, 2)$ = 4·7; $J(3, 4)$ = 9·0, H-3); 4·44 ddd, 1 H ($J(4, 3)$ = 9·0; $J(4, 5)$ = 5·0; $J(4, 5')$ = 6·0, H-4); 3·25 t, 2 H ($J(6, 5)$ = 6·5, H-6, 6'); 1·95 m, 2 H (H-5, 5'), 1·48 s, 3 H (Me); 1·25 s, 3 H (Me). For $C_{35}H_{34}O_6$ (550·7) calculated: 76·35% C, 6·22% H; found: 76·23% C, 5·92% H.

3-O-Benzoyl-5-deoxy-1,2-O-isopropylidene-α-D-*ribo*-hexofuranose (*IIIc*)

A 1M solution of tin tetrachloride (10 ml) in 1,2-dichloroethane was added to a solution of compound *IIIb* (4·9 g, 8·9 mmol) in 1,2-dichloroethane (40 ml). After 5 min at 20°C, chloroform (100 ml) and saturated aqueous sodium hydrogen carbonate solution (20 ml) were added to the reaction mixture. Product *IIIc* (2·4 g, 89%) was isolated as a syrup from the organic layer by column chromatography on silica gel (30 g) in the system S_1. TLC: R_F 0·13 (S_1). $[\alpha]_D^{20}$ +96·2° (*c* 1, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$): 8·03–7·92 m, 2 H (benzoyl); 7·50–7·23 m, 3 H (benzoyl); 5·81 d, 1 H ($J(1, 2)$ = 3·8, H-1); 4·88 dd, 1 H ($J(2, 1)$ = 3·8; $J(2, 3)$ = 4·7, H-2); 4·68 dd, 1 H ($J(3, 2)$ = 4·7; $J(3, 4)$ = 9·0, H-3); 4·43 ddd, 1 H ($J(4, 3)$ = 9·0; $J(4, 5)$ = 4·0; $J(4, 5')$ = 8·0, H-4); 3·77 t, 2 H ($J(6, 5)$ = 6·5, H-6, 6'); 1·93 m, 2 H (H-5, 5'); 1·53 s, 3 H (Me); 1·30 s, 3 H (Me). For $C_{16}H_{20}O_6$ (308·3) calculated: 62·33% C, 6·54% H; found: 61·95% C, 6·20% H.

3-O-Benzoyl-6-bromo-5,6-dideoxy-1,2-O-isopropylidene-α-D-*ribo*-hexofuranose (*IIId*)

Triphenylphosphine (2·56 g, 9·7 mmol) and carbon tetrabromide (4·8 g, 14·5 mmol) were added to a solution of compound *IIIc* (3·0 g, 9·7 mmol) in dry N,N-dimethylformamide (80 ml). The mixture was allowed to stand for 16 h at 20°C, then methanol (8 ml) was added to it, the solution was evaporated to dryness in vacuo and the residue was chromatographed on silica gel (100 g) in the system S_1. Product *IIId* (2·8 g, 78%) was isolated as a syrup. TLC: R_F 0·59 (S_1). ^{1}H NMR spectrum ($CDCl_3$): 8·11–8·00 m, 2 H (benzoyl); 7·51–7·20 m, 3 H (benzoyl); 5·86 d, 1 H ($J(1, 2)$ = 3·8, H-1); 4·94 dd, 1 H ($J(2, 1)$ = 3·8; $J(2, 3)$ = 4·7, H-2); 4·72 dd, 1 H ($J(3, 2)$ = = 4·7; $J(3, 4)$ = 9·0, H-3); 4·45 ddd, 1 H ($J(4, 3)$ = 9·0; $J(4, 5)$ = 4·5; $J(4, 5')$ = 7·0, H-4); 3·56 t, 2 H ($J(6, 5)$ = 6·7, H-6, 6'); 2·24 m, 2 H (H-5, 5'); 1·61 s, 3 H (Me); 1·37 s, 3 H (Me). For $C_{16}H_{19}BrO_5$ (371·2) calculated: 51·77% C, 5·16% H; found: 51·38% C, 5·02% H.

3-O-Benzoyl-5,6-deoxy-6-diethylphosphono-1,2-O-isopropylidene-α-D-*ribo*-hexofuranose (*IIIe*)

A solution of compound *IIId* (2·1 g, 5·7 mmol) in triethyl phosphite (17 ml) was refluxed with exclusion of moisture for 4 h, evaporated in vacuo to dryness, and the residue was subjected to chromatography on a column with silica gel (50 g). The column was washed with the system S_1 and eluted with the system S_2. Product *IIIe* was obtained as a syrup in a quantitative yield. TLC: R_F 0·15 (S_1). ^{1}H NMR spectrum ($CDCl_3$): 8·04–7·84 m, 2 H (benzoyl); 7·51–7·32 m, 3 H (benzoyl); 5·80 d, 1 H ($J(1, 2)$ = 3·8, H-1); 4·90 dd, 1 H ($J(2, 1)$ = 3·8; $J(2, 3)$ = 4·7, H-2); 4·60 dd, 1 H ($J(3, 2)$ = 4·7; $J(3, 4)$ = 9·0, H-3); 4·06 m, 5 H (2 × $POCH_2CH_3$, H-4); 2·10 to 1·70 m, 4 H (PCH_2CH_2); 1·50 s, 3 H (Me); 1·30 s, 3 H (Me); 1·26 m, 6 H (2 × $POCH_2CH_3$).

6-O-Benzoyl-5-deoxy-1,2-O-isopropylidene-α-D-*ribo*-hexofuranose (*IVa*)

Preparation of *IVa* was carried out starting from *IId* (1·65 g, 5·36 mmol), similarly as the preparation of *IIIa* from *IIb*, using 11 ml dry dimethyl sulfoxide, 2·8 ml acetic anhydride and 90 mg (2·37 mmol) $NaBH_4$. 6-O-Benzoyl-5-deoxy-1,2-O-isopropylidene-3-O-methylthiomethyl-α-D-*xylo*-hexofuranose was eluted with the system S_1. Yield 0·36 g (18%). TLC: R_F 0·28 (S_1). ^{1}H NMR spectrum ($CDCl_3$): 8·05–7·97 m, 2 H, (benzoyl); 7·60–7·42 m, 3 H (benzoyl); 5·91 d, 1 H (J(1, 2) = 3·9, H-1); 4·75 d, 1 H (J(H, H), = −11·7, C*H*HSMe); 4·61 d, 1 H (J(H, H) = −11·7, CH*H*SMe); 4·58 d, 1 H (J(2, 1) = 3·9, H-2); 4·55–4·40 m, 3 H (H-4, H-6, 6′); 4·16 d, 1 H (J(3, 4) = 3·2, H-3); 2·22–2·10 m, 2 H (H-5, 5′); 2·15 s, 3 H (CH_2SMe); 1·47 s, 3 H (Me); 1·31 s, 3 H (Me). Further, compound *IVa* was eluted from the column with the solvent system S_1. Yield 1·24 g (75%). M.p. 80–82°C. TLC: R_F 0·15 (S_1). ^{1}H NMR spectrum ($CDCl_3$): 8·02 to 7·92 m, 2 H (benzoyl); 7·50–7·22 m, 3 H (benzoyl); 5·75 d, 1 H (J(1, 2) = 3·8, H-1); 4·56 to 4·37 m, 3 H (H-2, H-6, 6′); 3·98–3·52 m, 2 H (H-3, H-4); 2·38 d, 1 H (J(OH, 3) = 11·0, OH-3); 2·33–1·86 m, 2 H (H-5, 5′); 1·59 s, 3 H (Me); 1·40 s, 3 H (Me). For $C_{16}H_{20}O_6$ (308·3) calculated: 62·33% C, 6·54% H; found: 62·50% C, 6·74% H.

3,6-Di-O-benzoyl-5-deoxy-1,2-O-isopropylidene-α-D-*ribo*-hexofuranose (*IVb*)

A) To the solution of *IIIc* (3·0 g, 9·74 mmol) in dioxane (40 ml), benzoylcyanide (1·39 g, 10·6 mmol) and triethylamine (1·4 ml) were added. The solution was allowed to stand for 1 h at 20°C, then methanol (2 ml) was added, and the mixture was evaporated to dryness. The residue was chromatographed on silica gel (70 g) in the system S_1. Yield of *IVb* 3·45 g (86%). M.p. 88–89°C (reported[17] m.p. 85–87°C). TLC: R_F 0·65 (S_1). ^{1}H NMR spectrum ($CDCl_3$): 8·01 to 7·90 m, 4 H (benzoyl); 7·51–7·24 m, 6 H (benzoyl); 5·87 d, 1 H (J(1, 2) = 3·8, H-1); 4·94 dd, 1 H (J(2, 1) = 3·8; J(2, 3) = 4·7, H-2); 4·76 dd, 1 H (J(3, 2) = 4·7; J(3, 4) = 8·8, H-3); 4·50 t, 2 H (J(6, 5) = 6·5, H-6, 6′); 4·24 m, 1 H (H-4); 2·19–2·08 m, 2 H (H-5, 5′); 1·56 s, 3 H (Me); 1·34 s, 3 H (Me).

B) *IVb* was prepared by benzoylation of *IVa* (2·5 g, 8·1 mmol) as described in procedure *A*, using benzoylcyanide (1·16 g, 8·85 mmol) and triethylamine (1·25 ml) in dioxane (40 ml). Yield of *IVb* 2·95 g (88%).

1,2-Di-O-acetyl-3-O-benzoyl-5,6-dideoxy-6-diethylphosphono-D-*ribo*-hexofuranose (*Va*)

Concentrated sulfuric acid (0·46 ml) was added to a solution of compound *IIIe* (1·38 g, 3·2 mmol) in acetic acid (12·3 ml) and acetic anhydride (4·6 ml). The reaction mixture was allowed to stand for 18 h at 20°C and then chloroform (100 ml) was added. The organic layer was washed successively with 10% aqueous sodium hydrogen carbonate (3 × 20 ml) and water (20 ml) and dried over sodium sulfate. The filtrates were concentrated in vacuo and the residue was subjected to chromatography on silica gel (50 g) in the system S_2. Product *Va* (1·2 g, 79%) was isolated as a syrup. ^{1}H NMR spectrum ($CDCl_3$): 8·02–7·86 m, 2 H (benzoyl); 7·53–7·10 m, 3 H (benzoyl); 6·37 d, 1/3H (J(1, 2) = 3·9, αH-1); 6·13 d, 2/3 H (J(1, 2) = 0·5, βH-1); 5·44–5·24 m, 2 H (H-2, H-3); 4·42–4·26 m, 1 H (H-4); 4·24–3·90 m, 4 H (2 × $POCH_2CH_3$); 2·12–1·72 m, 4 H (PCH_2CH_2); 2·11 s, 1 H (αAc), 2·10 s, 2 H (βAc); 2·03 s, 2 H (βAc); 1·95 s, 1 H (αAc); 1·29 t, 6 H (J(H, H) = 7·0, 2 × CH_2CH_3); (α/β ratio 1 : 2).

1,2-Di-O-acetyl-3,6-di-O-benzoyl-5-deoxy-D-*ribo*-hexofuranose (*Vb*)

Preparation of *Vb* was carried out starting from *IVb* (1·5 g, 3·6 mmol), similarly as the preparation of *Va* from *IIIe*. Compound *Vb* was obtained by means of chromatography on a column of silica

gel (50 g) in the solvent system S_1. Yield 1·33 g (80%). ^{1}H NMR spectrum ($CDCl_3$) was identical with that reported previously[17].

1-(2-O-Acetyl-3-O-benzoyl-5,6-dideoxy-6-diethylphosphono-β-D-*ribo*-hexofuranosyl)uracil (*VIa*)

A mixture of uracil (0·48 g, 4·3 mmol), 1,1,1,3,3,3-hexamethyldisilazane (5 ml) and dry pyridine (5 ml) was refluxed with exclusion of moisture to complete dissolution, evaporated in vacuo to dryness and then coevaporated with toluene (2 × 10 ml). Compound *Va* (1·35 g, 2·9 mmol) in dry acetonitrile (50 ml) and a 1M tin tetrachloride solution tin in 1,2-dichloroethane (3·2 ml, 3·2 mmol) were added to the residue. The solution was allowed to stand for 16 h at 20°C and then chloroform (100 ml) and 10% aqueous sodium hydrogen carbonate solution (20 ml) was added to it. The nucleotide *VIa* (1·25 g, 83%) was isolated as a foam from the organic layer by chromatography on silica gel (50 g) in the system S_2. TLC: R_F 0·39 (S_3). ^{1}H NMR spectrum ($CDCl_3$): 8·60 bs, 1 H (NH); 8·01—7·91 m, 2 H (benzoyl); 7·54—7·30 m, 3 H (benzoyl); 7·22 d, 1 H (J(6, 5) = 8·0, H-6); 5·92 d, 1 H (J(1', 2') = 4·8, H-1'); 5·73 dd, 1 H (J(5, 6) = 8·0; J(5, NH) = 2·0, H-5); 5·41 dd, 1 H (J(2', 1') = 4·8; J(2', 3') = 6·0, H-2'); 5·33 dd, 1 H (J(3', 2') = 6·0; J(3', 4') = 5·0, H-3'); 4·20 m, 1 H (H-4'); 4·08 dq, 2 H (J(H, Me) = 7·0; J(H, P) = 8·0, POCH_2·Me); 4·07 dq, 2 H (J(H, Me) = 7·0; J(H, P) = 8·0; POCH_2Me); 2·14—1·73 m, 4 H (PCH_2CH_2); 2·01 s, 3 H (Ac); 1·30 t, 3 H (J(H, H) = 7·0, POCH_2*Me*), 1·29 t, 3 H (J(H, H) = 7·0, POCH_2*Me*). For $C_{23}H_{29}N_2O_{10}P$ (524·5) calculated: 52·67% C, 5·57% H, 5·34% N; found: 52·31% C, 5·33% H, 5·21% N. Further, elution with the system S_2 yielded 3-(2-O-acetyl-3-O-benzoyl-5,6-dideoxy-6-diethylphosphono-β-D-*ribo*-hexofuranosyl)uracil (0·15 g, 10%) as a foam. TLC: R_F 0·27 (S_3). ^{1}H NMR spectrum ($CDCl_3$): 10·08 bs, 1 H (NH); 8·08—7·90 m, 2 H (benzoyl); 7·60—7·40 m, 3 H (benzoyl); 7·26 d, 1 H (J(6, 5) = 8·0, H-6); 6·39 d, 1 H (J(1', 2') = 2·5, H-1'); 5·92 dd, 1 H (J(2', 1') = 2·5; J(2', 3') = 6·0, H-2'); 5·75 m, 1 H (H-3'); 5·70 d, 1 H (J(5, 6) = 8·0, H-5); 4·26—3·96 m, 5 H (H-4', 2 × POCH_2Me); 2·20—1·84 m, 4 H (PCH_2CH_2); 2·02 s, 3 H (Ac); 1·35 t, 6 H (J(H, H) = 7·0, 2 × CH_2*Me*).

Glycosylation of *Va* in the Presence of Trimethylsilyl Trifluoromethanesulfonate

2,4-Bis-(trimethylsilyl)uracil (3 mmol), prepared as described in the preceding experiment, starting from uracil (336 mg, 3 mmol), 1,1,1,3,3,3-hexamethyldisilazane (3·8 ml) and pyridine (3·8 ml), were condensed with compound *Va* (944 mg, 2 mmol) in 1,2-dichloroethane (20 ml), in the presence of 1M trimethylsilyl trifluoromethanesulfonate in 1,2-dichloroethane (3·2 ml), for 16 h at 20°C. The reaction mixture was treated as described in the preceding experiment and N^1-ethyluracil (100 mg, 36%) was isolated from the organic layer chromatography on silica gel (50 g) in the S_1 system. M.p. 146—147°C (reported[28] m.p. 146—147·5°C). Further, elution with system S_2 yielded the nucleoside *VIa* (314 mg, 30%).

N^6-Benzoyl-9-(2-O-acetyl-3-O-benzoyl-5,6-dideoxy-6-diethylphosphono-β-D-*ribo*-hexofuranosyl)adenine (*VIb*)

The condensation of *Va* (1·1 g, 2·3 mmol) and bis-(trimethylsilyl)-N^6-benzoyladenine (3·1 mmol), prepared from N^6-benzoyladenine (740 mg, 3·1 mmol), 1,1,1,3,3,3-hexamethyldisilazane (6 ml) and pyridine (6 ml), was carried out in 30 ml 1,2-dichloroethane in the presence of 1M tin tetrachloride solution in 1,2-dichloroethane (3·0 ml) at 20°C for 16 h. Nucleotide *VIb* (1·2 g, 80%) was isolated as a foam. TLC: R_F 0·46 (S_3). ^{1}H NMR spectrum ($CDCl_3$): 8·99 bs, 1 H (NH); 8·79 s, 1 H (H-8); 8·11 s, 1 H (H-2); 8·09—8·01 m, 4 H (benzoyl); 7·64—7·36 m, 6 H (benzoyl); 6·22 d, 1 H (J(1', 2') = 5·0, H-1); 6·14 t, 1 H (J(2', 1') = J(2', 3') = 5·0, H-2'); 5·77 dd, 1 H (J(3',

2') = 5·0; J(3', 4') = 4·5, H-3'); 4·46 m, 1 H (H-4'); 4·11 dq, 2 H (J(H, H) = 7·0; J(H, P) = 8·0, POCH_2Me); 4·10 dq, 2 H (J(H, H) = 7·0, J(H, P) = 8·0, POCH_2Me); 2·41–1·73 m, 4 H (PCH_2CH_2); 2·03 s, 3 H (Ac); 1·34 t, 6 H (J(H, H) = 7·0, 2 × CH_2*Me*). For $C_{31}H_{34}N_5O_9P$ (651·6) calculated: 57·14% C, 5·26% H, 10·75% N; ound: 56·85% C, 5·01% H, 10·48% N.

1-(5,6-Dideoxy-6-phosphono-β-D-*ribo*-hexofuranosyl)uracil (*VIIa*)

Bromotrimethylsilane (2·5 ml, 19·3 mmol) was added to a solution of the nucleotide *VIa* (0·9 g, 1·7 mmol) in dry 1,2-dichloroethane (12 ml). The solution was allowed to stand for 16 h at 20°C and then evaporated in vacuo to dryness. Water (17 ml) and pyridine (7 ml) were added to the residue, the solution was allowed to stand for 1 h at 20°C, washed with ether (20 ml) and the aqueous layer was evaporated in vacuo to dryness. The pyridinium salt of *VIc* (0·92 g) was isolated as a foam. TLC: R_F 0·47 (S_4). ^{1}H NMR spectrum (D_2O): 8·78–8·48 m, 5 H (pyridine); 8·15–7·94 m, 2 H (benzoyl); 7·70 d, 1 H (J(6, 5) = 8·0, H-6); 7·70–7·45 m, 3 H (benzoyl); 6·05 d, 1 H (J(1', 2') = 4·5, H-1'); 5·90 d, 1 H (J(5, 6) = 8·0, H-5); 5·66 dd, 1 H (J(2', 1') = 4·5; J(2', 3') = 6·0, H-2'); 5·50 dd, 1 H (J(3', 2') = 6·0; J(3', 4') = 5·5, H-3'); 4·56–4·36 m, 1 H (H-4'); 2·04 s, 3 H (Ac); 2·02–1·80 m, 4 H (PCH_2CH_2).

A solution of *VIc* (0·92 g) in 5M ammonia in methanol (30 ml) was allowed to stand for 16 h at 20°C, the crystalline material was filtered off, washed with methanol and ether, and dried. Thus, the ammonium salt of *VIIc* (0·54 g, 90%) was isolated. TLC: R_F 0·11 (S_4). UV spectrum, pH 1–7: λ_{max} 260 nm (ε 9 800); pH 13: λ_{max} 260 nm (ε 7 800). CD spectrum, pH 7: λ_{max} 270 nm (Δε +1·18), 240 nm (Δε −0·57), crossover 253 nm. ^{1}H NMR spectrum (D_2O): 7·65 d, 1 H (J(6, 5) = 8·0, H-6); 5·88 d, 1 H (J(5, 6) = 8·0, H-5); 5·84 d, 1 H (J(1', 2') = 4·8, H-1'); 4·45 to 4·00 m, 3 H (H-2', 3', 4'); 2·14–1·80 m, 4 H (PCH_2CH_2). ^{31}P NMR spectrum (D_2O): +23·0.

9-(5,6-Dideoxy-6-phosphono-β-D-*ribo*-hexofuranosyl)adenine (*VIIb*)

Compound *VIIb* in a form of ammonium salt was synthesized in the same manner as *VIIa*, starting from *VIb* (0·1 g, 0·15 mmol). Yield 47 mg (80%). TLC: R_F 0·29 (S_4). For AMP, R_F 0·30 (S_4). UV spectrum pH, 7: λ_{max} 260 nm (ε 14 500); pH 1: λ_{max} 258 nm (ε 14 200), CD spectrum, pH 7: λ_{max} 265 nm (Δε −0·31), 235 nm (Δε +0·22), crossover 250 nm and 228 nm. ^{1}H NMR spectrum (D_2O): 8·31 s, 1 H (H-8); 8·22 s, 1 H (H-2); 6·05 d, 1 H (J(1', 2') = 6·0, H-1'); 4·70–4·20 m, 3 H (H-2', 3', 4'); 2·20–1·53 m, 4 H (PCH_2CH_2). ^{31}P NMR spectrum (D_2O): +24·8.

1-(2-O-Acetyl-3,6-di-O-benzoyl-5-deoxy-β-D-*ribo*-hexofuranosyl)uracil (*VIe*)

Condensation of *Vb* (1·4 g, 3·0 mmol) and 2,4-bis-(trimethylsilyl)uracil (4 mmol), prepared from uracil (448 mg, 4 mmol), 1,1,1,3,3,3-hexamethyldisilazane (5 ml) and pyridine (5 ml) as described for *VIa*, was carried out in 1,2-dichloroethane (40 ml), in the presence of 1M trimethylsilyl trifluoromethanesulfonate in 1,2-dichloroethane (4 ml) at 20°C during 16 h. Reaction mixture was then treated as described for *VIa* and the product *VIe* was isolated from the organic layer by column chromatography on silica gel (70 g) in the system S_2. Yield 1·41 g (91%). TLC: R_F 0·57 (S_3). ^{1}H NMR spectrum ($CDCl_3$): 9·16 bs, 1 H (NH); 8·02–7·88 m, 4 H (benzoyl); 7·52–7·30 m, 6 H (benzoyl);7·25 d, 1 H (J(6, 5) = 8·0, H-6); 5·90 d, 1 H (J(1', 2') = 4·5, H-1'); 5·70 d, 1 H (J(5, 6) = 8·0, H-5); 5·56–5·46 m, 2 H, (H-2', 3'); 4·54–4·10 m, 3 H (H-4', 6, 6'); 2·40–2·20 m, 2 H (H-5, 5'); 2·08 s, 3 H (Ac). For $C_{26}H_{24}N_2O_9$ (508·5) calculated: 61·41% C, 4·76% H, 5·51% N; found: 61·23% C, 4·58% H, 5·33% N.

N^6-Benzoyl-9-(2-O-acetyl-3,6-di-O-benzoyl-5-deoxy-β-D-*-ribo*-hexofuranosyl)adenine (*VIf*)

Condensation of *Vb* (1·4 g, 3·0 mmol) and bis-(trimethylsilyl)-N^6-benzoyladenine (4·0 mmol), prepared from N^6-benzoyladenine (960 mg, 4 mmol), 1,1,1,3,3,3-hexamethyldisilazane (8 ml) and pyridine (8 ml), was carried out in 50 ml 1,2-dichloroethane (reflux, 1·5 h), in the presence of 1M trimethylsilyl trifluoromethanesulfonate in 1,2-dichloroethane (4·5 ml). The reaction mixture was treated as described for *VIa* and the product *VIf* was isolated as a foam by column chromatography on silica gel (70 g) in the system S_2. Yield 1·32 g (72%). TLC: R_F 0·72 (S_3). ^{1}H NMR spectrum ($CDCl_3$): 8·88 bs, 1 H (NH); 8·74 s, 1 H (H-8); 8·06 s, 1 H (H-2); 8·10 to 7·93 m, 6 H (benzoyl); 7·70–7·28 m, 9 H (benzoyl); 6·18 m, 2 H (H-1', 2'); 5·83 m, 1 H (H-3'); 4·62–4·40 m, 3 H (H-4', 6', 6''); 2·10–1·95 m, 2 H (H-5', 5''); 1·98 s, 3 H (Ac). For $C_{34}H_{29}N_5O_8$ (635·6) calculated: 64·25% C, 4·60% H, 11·02% N; found: 63·88% C, 4·31% H, 10·86% N.

1-(5-Deoxy-β-D-*ribo*-hexofuranosyl)uracil (*VIIc*)

A solution of *VIe* (1 g, 1·97 mmol) in 0·1M MeONa in methanol (25 ml) was allowed to stand for 2 h at room temperature and evaporated to dryness. The residue was dissolved in a mixture of chloroform (20 ml) and water (20 ml), the aqueous layer was separated and passed through a column with Dowex-50 (H^+-form, 20 ml) and then the column was washed with water. The combined eluents were evaporated to dryness. Yield 0·5 g (98%). M.p. 105–107°C (ethanol). TLC: R_F 0·60 (S_4). UV spectrum, pH 1–7: λ_{max} 260 nm (ε 10 000); pH 13: λ_{max} 260 nm (ε 8 000). CD spectrum, pH 7: λ_{max} 270 nm (Δε +1·25), 240 nm (Δε −0·53), crossover 253 nm. ^{1}H NMR spectrum (D_2O): 7·66 d, 1 H (J(6, 5) = 8·0, H-6); 5·88 d, 1 H (J(5, 6) = 8·0, H-5); 5·63 d, 1 H (J(1', 2') = 4·0, H-1'); 4·45 dd, 1 H (J(2', 1') = 4·0; J(2', 3') = 5·0, H-2'); 4·31–4·11 m, 2 H (H-3', 4'); 3·85 t, 2 H (J(6', 5') = 6·5; H-6', 6''); 2·22–1·97 m, 2 H (H-5', 5'').

9-(5-Deoxy-β-D-*ribo*-hexofuranosyl)adenine (*VIId*)

Deblocking of *VIf* (1 mmol) was performed in a solution of 5M ammonia in methanol (15 ml). After usual processing and recrystallization from ethanol nucleoside *VIId* was obtained in a 79% yield. M.p. 232°C (decomp.). Reported[15] m.p. 231·5–232·5°C). TLC: R_F 0·55 (S_4). UV spectrum, pH 7: λ_{max} 260 nm (ε 15 000), pH 1: λ_{max} 258 nm (ε 14 600). CD spectrum, pH 7: λ_{max} 265 nm (Δε −0·28), 233 nm (Δε +0·19), crossover 243 nm and 226 nm. ^{1}H NMR spectrum (D_2O): 8·30 s, 1 H (H-8); 8·25 s, 1 H (H-2); 6·06 d, 1 H (J(1', 2') = 5·0, H-1'); 4·60–4·20 m, 3 H (H-2', 3', 4'); 3·76 t, 2 H (J(6', 5') = 6·5. H-6', 6''); 2·16–1·95 m, 2 H (H-5', 5'').

REFERENCES

1. Engel R.: Chem. Rev. *77*, 349 (1977).
2. Jones G. H., Moffatt J. G.: J. Am. Chem. Soc. *90*, 5337 (1968).
3. Hampton A., Kappler F., Perini F.: Bioorg. Chem. *5*, 31 (1976).
4. Montgomery J. A., Laseter A. G., Hewson K.: J. Heterocycl. Chem. *11*, 211 (1974).
5. Fuertes M., Witkowski J. T., Steeter D. G., Robins R. K.: J. Med. Chem. *17*, 642 (1974).
6. Hollman J., Schlimme E.: Liebigs Ann. Chem. *1984*, 98.
7. Albrecht H. P., Jones G. H., Moffatt J. G.: Tetrahedron *40*, 79 (1984).
8. Morr M., Ernst L., Grotjahn L.: Z. Naturforsch., B *38*, 1665 (1983).
9. Montgomery J. A., Hewson K.: Chem. Commun. *1969*, 15.
10. Mazur A., Tropp B. E., Engel R.: Tetrahedron *40*, 3949 (1984).
11. Montgomery J. A.: Carbohydr. Res. *33*, 184 (1974).

12. Padyukova N. Sh., Karpeiskii M. Ya., Kolobushkina L. I., Mikhailov S. N.: Tetrahedron Lett. *28*, 3623 (1987).
13. Etzold G., Kowollik G., Langen P.: Chem. Commun. *1968*, 422.
14. Lassota P., Kusmierek J. T., Stolarski R., Sugar D.: Z. Naturforsch., C *42*, 589 (1987).
15. Ryan K. J., Arzoumanian H., Acton E. M., Goodman L.: J. Am. Chem. Soc. *86*, 2503 (1964).
16. Montgomery J. A., Hewson K.: J. Med. Chem. *9*, 234 (1966).
17. David S., de Sennyey G.: Carbohydr. Res. *77*, 79 (1979).
18. Gramera R. E., Ingle T. R., Whistler R. L.: J. Org. Chem. *29*, 2074 (1964).
19. Holý A., Souček M.: Tetrahedron Lett. *1971*, 185.
20. Reist E. J., Spencer R. R., Baker B. R.: J. Org. Chem. *23*, 1757 (1958).
21. Stevens J. D.: *Methods in Carbohydrate Chemistry*, Vol. VI, p. 123. Academic Press, New York 1972.
22. Beigelman L. N., Ermolinskii B. S., Gurskaya G. V., Tsapkina E. N., Karpeiskii M. Ya., Mikhailov S. N.: Carbohydr. Res. *166*, 219 (1987).
23. Verheyden J. P. H., Moffatt J. G.: J. Org. Chem. *37*, 2289 (1972).
24. Vorbrüggen H.: *Nucleoside Analogues. Chemistry, Biology and Medical Application*, Vol. 26, p. 35. NATO ASI Series A. Plenum Press, New York 1980.
25. Morita T., Okamoto Y., Sakurai H.: Bull. Chem. Soc. Jpn. *51*, 2169 (1978).
26. Miles D. W., Inskeep W. H., Robins M. J., Winkley M. W., Robins R. K., Eyring H.: J. Am. Chem. Soc. *92*, 3872 (1970).
27. Ingwall J. S.: J. Am. Chem. Soc. *94*, 5487 (1972).
28. Tanabe T., Yamauchi K., Kinoshita N.: Bull. Chem. Soc. Jpn. *50*, 3021 (1977).