NUCLEIC ACID COMPONENTS AND THEIR ANALOGUES. CLVI.* PREPARATION OF ENANTIOMETRIC 1-(α-XYLOFURANOSYL), 1-(α-LYXOFURANOSYL), AND 1-(2-DEOXY-α-LYXOFURANOSYL) DERIVATIVES OF URACIL AND CYTOSINE

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D- and L-xylose react with cyanamide under the formation of the 2′-amino-1,2-oxazoline derivative *I* which on treatment with methyl propiolate affords the $O^{2,2'}$-anhydro derivative of 1-(α-xylofuranosyl)uracil (*II*). Alkaline hydrolysis of the anhydro compound *II* leads to 1-(α-xylofuranosyl)uracil (*III*). On treatment with acetone and triethyl orthoformate, compound *II* affords the 3′,5′-O-isopropylidene derivative *IV* which is converted in alkaline media to 1-(3,5-O-isopropylidene-α-xylofuranosyl)uracil (*V*). When treated with hydrogen chloride in dimethylformamide, the 3′,5′-dibenzoate *VI* (obtained on benzoylation of compound *II*) affords a mixture of the α-lyxofuranosyl derivatives *VII* and *VIII*, or, with the use of an excess of the agent, the 2′-deoxy-2′-chloro derivative *XI*. Deblocking of compounds *VII* and *VIII* leads to the free 1-(α-lyxofuranosyl)uracil (*X*). Reductive dehalogenation of compound *XI* with tri-n-butyltin hydride affords the 3′,5′-di-O-benzoyl-2′-deoxy-α-lyxofuranosyl derivative *XII*, the alkaline deblocking of which leads to the free 1-(2-deoxy-α-lyxofuranosyl)uracil (*XIII*). The cytosine analogue *XIV* was prepared from compound *XI* by a successive treatment with phosphorus pentasulfide and ammonia. None of the nucleosides *III*, *X*, *XIII* and *XIV* exhibits any bacteriostatic activity on *Escherichia coli*.

Since the discovery of the biochemical activity of 1-(β-D-arabinofuranosyl)cytosine, considerable attention has been paid to nucleoside analogues with a modified sugar moiety. Because of the difficult accessibility of these analogues, however, the corresponding biological assays are far from being systematic in spite of the use of various bacterial and animal systems. In some earlier papers[1,2], we have described the L-enantiomers of the naturally occurring nucleosides as well as some α-ribonucleosides and their 2′-deoxy derivatives[3]. The preparation and properties of nucleoside analogues of the α-xylofuranosyl, α-lyxofuranosyl, and 2-deoxy-α-lyxofuranosyl type which are closely related to ribonucleosides, have been investigated so far to a very limited extent.

The recently reported[4] synthesis of pyrimidine nucleosides comprises condensation of free aldoses with cyanamide and addition of an acetylenic derivative under the formation of a pyrimidine cyclonucleoside. This route has been successfully used in the preparation of L-*ribo* and L-*arabino* derivatives[5–7], α-*ribo* nucleosides[3] as well as in the synthesis of the corresponding 2-deoxy derivatives of pyrimidine nu-

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cleosides[3,5,8]. It was therefore desirable to apply the novel procedure also in the xylose series. The present paper reports on the preparation of compounds of both enantiomeric types starting from $O^{2,2'}$-anhydro-1-(α-xylofuranosyl)uracil (*II*) and comprising particularly the α-xylofuranosyl, α-lyxofuranosyl, and 2-deoxy-α-lyxofuranosyl derivatives. Compounds of the L-lyxose series are closely related to the naturally occurring β-D-ribonucleosides: both types of these compounds differ by configuration of the primary alcoholic function at the carbon atom 4'. This difference is of little importance[9] for some reactions *in vitro* but represents the determining factor for penetration into the bacterial cell[1].

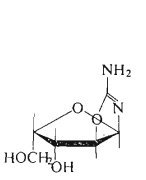
Both D-xylose and L-xylose react readily with cyanamide in aqueous-methanolic ammonia under the formation of the 1,2-oxazoline *I*. On treatment with methyl propiolate, compound *I* is converted to $O^{2,2'}$-anhydro-1-(α-xylofuranosyl)uracil* (*II*) which is readily hydrolysed in aqueous alkali (attack of hydroxylic ion at position $C_{(2)}$) under the formation of 1-(α-xylofuranosyl)uracil (*III*). The anhydro bond in the cyclonucleoside *II* is considerably stable towards hydrolysis both in alkaline and acidic media. Reaction of compound *II* with acetone and triethyl orthoformate[10] afforded the 3',5'-O-isopropylidene derivative *IV* which is slowly converted by alkaline hydrolysis into the 3',5'-isopropylidene derivative *V*, identical with a specimen prepared by an analogous route from the xylofuranoside *III*. Compounds *IV* and *V* may be readily recrystallised and are therefore suitable for the purification of the crude substances *II* and *III* on a larger scale.

The derivatives of 2-deoxylyxose were prepared analogously to the conversion of $O^{2,2'}$-anhydro derivatives of the β-*arabino* and α-*ribo* configuration[3,5,8]. On treatment with benzoyl cyanide[11], the anhydro derivative *II* was transformed into the 3',5'-di-O-benzoyl derivative *VI* which was then heated with hydrogen chloride in dimethylformamide. In contrast to the above mentioned analogous treatments, compound *VI* is converted only to a small extent into the required 2'deoxy-2'-chloro-derivative *XI*. The reaction product is reprensented by three isomeric dibenzoates *VII–IX* which were isolated in a pure state and ascribed the corresponding structure on the basis of elemental analysis, NMR spectra, and results of the alkaline deblocking to free nucleosides. The 1-(3,5-di-O-benzoyl-α-xylofuranosyl)uracil (*IX*) which is present in the mixture only in a small amount, is obviously formed by hydrolysis of the anhydro derivative *VI*. The 2',5'-dibenzoyl (*VII*) and 3',5'-dibenzoyl (*VIII*) derivatives of 1-(α-lyxofuranosyl)uracil are obtained as principal products. Compounds *VII* and *VIII* are obviously formed by opening of the anhydro bond in compound *VI* under participation of the benzoyl group at position 3'. From the formal point of view, the 3'-benzoyl group is isomerised into the 2'-benzoyl group, but the occurrence of the 2',5'- and 3',5'-isomeric dibenzoates is obviously due to ring

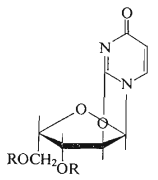
* Unless stated otherwise, the formulae in Schemes refer to L-enantiomers. The enantiomers are differentiated by a prefix before the formula number.

opening of the cyclic orthobenzoate intermediate[12]. Removal of protecting groups from the dibenzoates *VII–IX* led to the free nucleosides *II* and *X*.

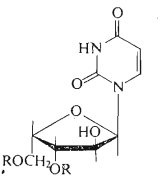
The use of a great excess of hydrogen chloride leads to an exclusive formation of a 2′-deoxy-2′-chloro derivative which was ascribed on the basis of NMR spectra the structure *XI* with the chloro atom in the configuration *lyxo*. This finding simultaneously proves the sterically uniform course of the opening of the anhydro bond in cyclonucleosides of the *xylo* configuration; this opening also proceeds by the S_N2



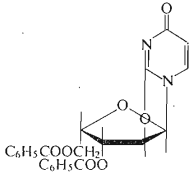
I



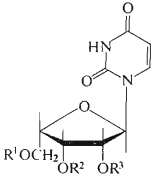
II, R = H
IV, R—R = $>C(CH_3)_2$



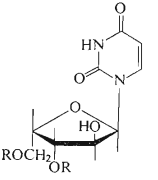
III, R = H
V, R—R = $C(CH_3)_2$



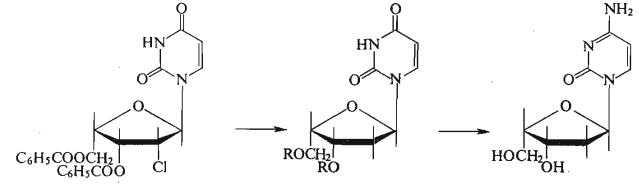
VI



VII, $R^1 = R^2 = C_6H_5CO$, $R^3 = H$
VIII, $R^1 = R^3 = C_6H_5CO$, $R^2 = H$
X, $R^1 = R^2 = R^3 = H$



IX, R = C_6H_5CO
III, R = H



XI

XII, R = C_6H_5CO
XIII, R = H

XIV

mechanism. The reductive dehalogenation of compound *XI* with tri-n-butyltin hydride[5,8] affords a high yield of 1-(3,5-di-O-benzoyl-2-deoxy-α-lyxofuranosyl)uracil (*XII*). The alkaline deblocking leads to the free 2'-deoxynucleoside *XIII*. On treatment with phosphorus pentasulfide in dioxane and ammonolysis of the resulting 4-thio derivative, compound *XII* is converted to 1-(2-deoxy-α-lyxofuranosyl)cytosine (*XIV*).

The present methods represent not only an easy approach to the preparation of novel 2-deoxy-α-lyxofuranosyl derivatives, *i.e.*, analogues of 2'-deoxyribonucleosides with an inversed configuration on the carbon atom at position 4', but also constitute an advantageous route for the synthesis of α-lyxofuranosides which does not require the use of lyxose as the starting compound.

Bacteriostatic assays of the nucleosides *III*, *X*, *XIII* and *XIV* did not meet with positive results even at concentrations of 1 000 μg/ml (*E. coli* on synthetic medium[13]). The negative result with the 2'-deoxynucleosides L-*XIII* and L-*XIV* is not surprising since the corresponding α-L-lyxofuranosides have been recently shown not to penetrate the cell-wall of *E. coli*[1]. Also the L-ribonucleosides are not accepted by permeases for penetration through the cell-wall; such an activity can be therefore hardly expected with compounds D-*X*, D-*XIII* and D-*XIV* in which two determining factors for the specificity of enzymatical systems mentioned had been changed. An unequivocal confirmation of these ideas could be obtained with the use of the corresponding labelled compounds and investigations of their ability to penetrate the bacterial cell-walls.

EXPERIMENTAL

Unless stated otherwise, the solutions were taken down on a rotatory evaporator at 35°C/15 Torr. The substances were dried over phosphorus pentoxide at 0·1 Torr.

Methods

Descending chromatography was performed on paper Whatman No 1 (preparative runs on paper Whatman No 3 MM) in the solvent systems S_1, 2-propanol–concentrated aqueous ammonia–water (7 : 1 : 2); S_2, 1-butanol saturated with water; and S_3, 1-butanol–ethanol–water (40 : 11 : 19). Paper electrophoresis was performed on paper Whatman No 3 MM in the buffer solution E_1, 0·1M triethylammonium borate (pH 7·5) at 20 V/cm by the technique of Markham and Smith[14]. For the R_F values and electrophoretical mobilities see Table I. Thin-layer chromatography on silica gel was performed on ready-for-use indicator-containing Silufol UV_{254} plates (Kavalier Glass Works, Votice, Czechoslovakia) in the solvent systems S_4, ethanol–chloroform (5 : 95), and S_5, ethyl acetate–benzene (1 : 1). Preparative runs were performed on 60 × 16 × 0·3 cm layers of an indicator containing silica gel (30—60 mesh), produced by Service Laboratories of our Institute; products were eluted with methanol.

Ultraviolet absorption spectra were taken on a Beckman DU spectrophotometer in 0·01M-HCl. Quantitative determinations were performed with the use of the following molar extinction coefficients at 260 nm: uracil derivatives, 10000; cytosine derivatives, 6800. CD-spectra were measured on a Jouan Model CD-185 Dichrograph spectrophotometer in aqueous solutions. NMR spectra were measured in deuteriochloroform with the use of hexamethyldisiloxane as internal standard.

Reagents. Cyanamide was prepared according to ref.[15]. Tri-n-butyltin hydride was prepared according to ref.[8] and stored as a 25% solution in benzene at 0°C.

TABLE I

Chromatography (R_F values in S_1—S_5) and Electrophoresis (E_u values in E_1)

Compound	S_1	S_2	S_3	S_4	S_5	E_1[a]
Uridine	0·50	0·17	0·32	—	—	1·00
2′-Deoxyuridine	0·60	0·32	0·47	—	—	0
2′-Deoxycytidine	0·62	—	—	—	—	0
II	0·60	0·13	0·27	—	—	0·86
III	0·57	0·22	0·40	—	—	0·70
IV	0·74	—	—	0·18	—	0
V	0·74	—	—	0·27	—	0
VI	—	—	—	0·15	—	—
VII	—	—	—	0·17	0·18	—
VIII	—	—	—	0·20	0·44	—
IX	—	—	—	0·18	0·35	—
X	0·46	0·12	0·27	—	—	1·10
XI	—	—	—	0·40	0·55	—
XII	—	—	—	0·30	0·40	—
XIII	0·58	—	—	—	—	0·45
XIV	0·60	—	—	—	—	0·26
XV						

[a]Referred to uridine.

Reaction of Xylose with Cyanamide

A mixture of D- or L-xylose (75 g; 0·5 mol), cyanamide (40 g), methanol (125 ml), and 6M-NH_3 (25 ml) was stirred for 3 h, the resulting solution kept at room temperature for 3 days, and evaporated under diminished pressure. The residue was coevaporated with three 100 ml portions of ethanol and the foam kept under ethanol (100 ml) overnight to deposit crystals. The solid was dissolved in refluxing ethanol (400 ml), the solution cooled, and diluted with acetone (500 ml) to deposit the product which was collected with suction, washed with acetone (500 ml) and ether, and dried. Yield 74 g (85%) of compound L-*I*, m.p. 162 °C, $[\alpha]_D^{25}$ +30·8° (*c* 0·5, dimethylformamide). For $C_6H_{10}N_2O_4$ (174·1) calculated: 41·34% C, 5·78% H, 16·08% N; found: 40·56% C, 6·10% H, 15·84% N. A similar procedure was used for the preparation (yield, 80%) of D-*I* enantiomer, m.p. 164 °C, $[\alpha]_D^{25}$ −31·5° (*c* 0·5, dimethylformamide). Found: 41·94% C, 5·95% H, 16·65% N.

$O^{2,2'}$-Anhydro-1-(α-L-xylofuranosyl)uracil (L-*II*)

A mixture of compound L-*I* (15 g; 86 mmol), methyl propiolate (25 g), and 50% aqueous ethanol (200 ml) was refluxed for 6 h, cooled, and evaporated under diminished pressure. The residue

was coevaporated with two 50 ml portions of ethanol, dissolved in hot ethanol (50 ml), and the solution diluted with acetone (300 ml) to deposit crystals which were collected with suction, washed with acetone and ether, and dried under diminished pressure. Yield, 8·9 g (46%) of compound L-*II* which does not melt up to 250°C, $[\alpha]_D^{25}$ −80·1° (*c* 0·5, dimethylformamide. Ultraviolet spectrum (in water): λ_{max} 233, 248 nm; λ_{min} 235 nm, ε_{248} 7500, ε_{233} 7800, ε_{260} 5500; $A_{250/260}$ 1·36, $A_{280/260}$ 0·05. For $C_9H_{10}N_2O_5$ (226·2) calculated: 47·78% C, 4·45% H, 12·38% N; found: 47·99% C, 4·83% H, 12·21% N. The enantiomer D-*II* (does not melt up to 250°C) was prepared similarly in 48% yield. Optical rotation: $[\alpha]_D^{25}$ +69·7° (*c* 0·5, dimethylformamide). Found: 48·02% C, 4·54% H, 12·16% N.

1-(α-L-Xylofuranosyl)uracil (L-*III*)

A solution of compound *L-II* (1·0 g; 4·4 mmol) in 5% aqueous ammonia was kept at room temperature overnight, evaporated to dryness under diminished pressure, the residue coevaporated with ethanol (50 ml), dissolved in hot ethanol (50 ml), the solution filtered while hot through a thin layer of Hyflo Super Cel, the filtrate treated with ether until turbid, and then kept in a refrigerator to deposit crystals. Yield, 0·9 g (84%) of compound L-*III*, m.p. 202—204°C. Ultraviolet spectrum (H_2O): λ_{max} 230 nm, λ_{min} 230 nm, ε_{260} 9850, $A_{250/260}$ 0·71, $A_{280/290}$ 0·47, $A_{290/260}$ 0·10. For $C_9H_{12}N_2O_6$ (244·2) calculated: 44·26% C, 4·95% H, 11·47% N; found: 44·85% C, 5·02% H, 11·56% N. A similar procedure was used for preparing (yield, 76%) of the enantiomer D-*III*, m.p. 208 °C. Found: 44·23% C, 4·57% H, 11·85% N. NMR spectrum: $H_{1'}$ (d, 1 H) 6·10, $J_{1',2'}$ 2·5; $H_{2'}$ + $H_{3'}$ (m, 2 H) 4·10; $H_{4'}$ (m, 1 H) 4·30; 2 $H_{5'}$ (m, 2 H) 3·68; H_5 (d, 1 H) 5·54, $J_{5,6}$ 8·0; H_6 (d, 1 H) 7·47, $J_{6,5}$ 8·0; OH (bs, 3 H) 5·20.

3′,5′-O-Isopropylidene-$O^{2,2'}$-anhydro-1-(α-D-xylofuranosyl)uracil (D-*IV*)

Compound D-*I* (30 mmol) was converted to the crude D-*II* which was (without purifying by precipitation with acetone) dried over phosphorus pentoxide under diminished pressure and then treated with dimethylformamide (40 ml), triethyl orthoformate (20 ml), acetone (8 ml), and 6M-HCl in dimethylformamide (3 ml). The reaction mixture was kept at room temperature overnight, diluted with triethylamine (5 ml), collected with suction, the filtrate rapidly evaporated at 40°C/0·1 Torr, and the residue coevaporated under the same conditions with five 50 ml portions of toluene. The final residue was crystallised from ethanol to afford 3·4 g (42%) of compound D-*IV*, m.p. 308°C, $[\alpha]_D^{25}$ 0·6° (*c* 0·5, dimethylformamide). For $C_{12}H_{14}N_2O_5$ (266·3) calculated: 54·07% C, 5·29% H, 10·52% N; found: 53·93% C, 5·58% H, 10·50% N. NMR spectrum: $H_{1'}$ (d, 1 H) 6·42 p.p.m., $J_{1',2'}$ 5·5; $H_{2'}$ (d, 1 H) 5·25, $J_{2',1'}$ 5·5, $J_{2',3'}$ 0; $H_{3'}$ (d, 1 H) 4·69, $J_{3',2'}$ 0, $J_{3',4'}$ 2·0; $H_{4'}$ (m, 1 H) 3·94; $H_{5'}$ (dd, 1 H) 4·20, $J_{5',4'}$ 2·0, J_{gem} 13·5; H_5 (d, 1 H) 5·93, $J_{5,6}$ 7·5; H_6 (d, 1 H) 7·83, $J_{6,5}$ 7·5; CH_3 (2s, 6 H) 1·32 and 1·47.

3′,5′-Isopropylidene-1-(α-D-xylofuranosyl)uracil (*D-V*)

A. A mixture of compound D-*III* (2·44 g; 10 mmol), dimethylformamide (25 ml), triethyl orthoformate (10 ml), acetone (5 ml), and 6M-HCl in dimethylformamide (1 ml) was kept at room temperature overnight and then processed as in the case of compound D-*IV*. Crystallisation from ethanol (the solution was treated with cyclohexane until turbid) afforded 2·4 g (86%) of compound D-*V*, m.p. 243°C, $[\alpha]_D^{25}$ −85·5° (*c* 0·5, dimethylformamide). For $C_{12}H_{16}N_2O_6$ (284·2) calculated: 50·69% C, 5·67% H, 9·85% N; found: 51·04% C, 5·73% H, 10·02% N. NMR spectrum: $H_{1'}$ (d, 1 H) 6·11 p.p.m., $J_{1',2'}$ 3·0; $H_{2'}$ (m, 1 H) 4·19; $H_{3'}$ + $H_{4'}$ + 2 $H_{5'}$ (m, 4 H) 3·80—4·40; H_5 (d, 1 H) 5·54, $J_{5,6}$ 8·0; H_6 (d, 1 H) 7·47, $J_{6,5}$ 8·0; $C_{2'}$—OH (bs, 1 H) 5·80; NH (bs, 1 H) 11·19; CH_3 (2 s, 6 H) 1·30 and 1·42 p.p.m.

B. A solution of compound D-*IV* (1·0 g; 3·8 mmol) in ethanol (50 ml) was treated with triethylamine (0·5 ml) and then refluxed until the reaction was quantitative (for about 2 h) as shown by thin-layer chromatography in the solvent system S_4. The reaction mixture was evaporated to dryness under diminished pressure, the residue coevaporated with two 10 ml portions of ethanol, and crystallised from ethanol (cyclohexane was added to the solution until turbid). Yield, 0·8 g (75%) of compound D-*V*, m.p. 243°C, identical with the specimen obtained by the procedure *A*.

3′,5′-Di-O-benzoyl-$O^{2,2'}$-anhydro-(1-α-L-xylofuranosyl)uracil (L-*VI*)

Triethylamine (5 ml) was added under stirring to a mixture of compound L-*II* (9·1 g; 40 mmol), benzoyl cyanide (11·8 g; 90 mmol), and acetonitrile (60 ml). When the exothermic reaction subsided, the mixture was stirred for additional 1 h, evaporated to dryness under diminished pressure, the residue dissolved in ethanol (100 ml), the solution filtered with active charcoal (0·5 g), the filtrate concentrated under diminished pressure, and the concentrate (about 50 ml) kept in a refrigerator overnight to deposit crystals which were collected with suction, washed with ethanol and ether, and dried. Yield, 12 g (69%) of compound L-*VI*, m.p. 118°C, $[\alpha]_D^{25}$ −91·2° (*c* 0·5, dimethylformamide). For $C_{23}H_{18}N_2O_7$ (434·4) calculated: 63·59% C, 4·17% H, 6·45% N; found: 64·00% C, 4·31% H, 6·54% N. NMR spectrum: $H_{1'}$ (d, 1 H) 6·53, $J_{1',2'}$ 5·5; $H_{2'}$ (d, 1 H) 5·55, $J_{2',1'}$ 5·5; $H_{3'}$ (m, 1 H) 5·88, $J_{3',2'}$ 0·5, $J_{3',4}$ 2·5; $H_{4'}$ + $H_{5'}$ (m, 3 H) 4·55—4·75; H_5 (d, 1 H) 6·06, $J_{5,6}$ 8·0; H_6 (d, 1 H) 7·59, $J_{6,5}$ 8·0; arom. (m, 6 H) 7·30—7·70; arom. (m, 4 H) 7·90—8·10. A similar procedure was used in the preparation (yield, 85%) of the enantiomer D-*VI*, m.p. 119°C (ethanol); $[\alpha]_D^{25}$ +89·3° (*c* 0·5, dimethylformamide).

1-(α-L-Lyxofuranosyl)uracil (L-*X*)

A solution of compound L-*VI* (5·0 g; 11·5 mmol) in dimethylformamide (40 ml) was treated with 6M-HCl in dimethylformamide (5 ml) and the whole heated at 110°C for 1 h. The mixture was poured into water (500 ml), the precipitate dissolved in chloroform (100 ml), the solution dried over magnesium sulfate, filtered, and the filtrate evaporated under diminished pressure. The residue was chromatographed on 3 plates of silica gel in the solvent system S_5 (double elution). Bands of products *VII*—*IX* were separately eluted with methanol, the eluates evaporated under diminished pressure, and the residues dried over phosphorus pentoxide *in vacuo* to afford 3·1 g (60%) of the dibenzoates *VII* and *VIII* (ratio, 1 : 1·5) and 0·5 g (10%) of compound L-*IX*. NMR spectrum of L-*IX*: $H_{1'}$ (d, 1 H) 6·34, $J_{1',2'}$ 3·5; $H_{2'}$ (q, 1 H) 4·51, $J_{2',3'}$ 1·5; $H_{3'}$ (m, 1 H) 5·65, $J_{3',4'}$ 3·2; $H_{4'}$ (sextet, 1 H) 5·0, $J_{4',5'}$ 5·5; 2 $H_{5'}$ (m, 2 H) 4·61; H_5 (d, 1 H) 5·68, $J_{5,6}$ 8·0; H_6 (d, 1 H) 7·57; arom. (m, 6 H) 7·25—7·65, arom. (m, 4 H) 7·90—8·10; OH (brs, 1 H) 5·25; NH (brs, 1 H) 10·34. For $C_{23}H_{20}N_2O_8$ (452·4) calculated: 61·06% C, 4·45% H, 6·19% N; found, *VII*: 61·52% C, 4·52% H, 6·38% N; *VIII*: 61·12% C, 4·50 %H, 6·32% N; *IX*: 61·35% C, 4·60% H, 6·42% N.

Deblocking. The residual mixture of compounds *VII*—*IX* (0·1 g) was kept at 50°C in 0·1M methanolic sodium methoxide (5 ml) for 3 h and subjected to electrophoresis in the buffer solution E_1 to show the ratio of isomeric L-*III* and L-*X* equal to 1 : 9. The mixture of compounds L-*VII* and L-*VIII* (3·0 g; 6·7 mmol) in 0·1M methanolic sodium methoxide (50 ml) was kept at room temperature overnight, evaporated under diminished pressure, the residue dissolved in water (100 ml), and the solution neutralised with Dowex 50 (H^+) ion exchange resin. The resin was filtered off, washed with water, the filtrate and washings combined, washed with two 25 ml portions of ether, the aqueous phase evaporated to dryness and the residue crystallised from water. Yield, 1·3 g (80%) of compound L-*X*, m.p. 202°C. For $C_9H_{12}N_2O_8$ (244·2) calculated:

44·26% C, 4·95% H, 11·47% N; found: 44·28% C, 4·92% H, 11·49% N. CD spectrum: 270·5 nm (+4090), 256 (0), 240·5 (−4750), 226·5 (min, −3370), 214·5 (−5570), 204 (0). A similar procedure was used in the preparation (yield, 45%, based of the starting D-*VI*) of the enantiomer D-*X*, m.p. 202−3°C. CD spectrum: 270·5 nm (−4070), 256·5 (0), 240·5 (+4710), 228·5 (min, +3640), 214·5 (+5580), 240 (0). NMR spectrum, D-*X*: $H_{1'}$, (d, 1 H) 5·82, $J_{1',2'}$ 6·5; $H_{2'} + H_{3'}$, (m, 2 H) 4·25−4·48; $H_{4'}$, (m, 1 H) 4·17; 2 $H_{5'}$, (m, 2 H) 3·50−3·85; $J_{4',5'}$ 5·0, J 6·0, J_{gem} 12·5; H_5 (d, 1 H) 5·63, $J_{5,6}$ 8·0; (d, 1 H) 7·58, $J_{6,5}$ 8·0.

1-(3,5-Di-O-benzoyl-2-deoxy-2-chloro-α-L-lyxofuranosyl)uracil (L-*XI*)

A solution of compound L-*VI* (10·0 g; 23 mmol) in dimethylformamide (80 ml) was treated with 6M-HCl in dimethylformamide (40 ml) and the whole heated at 100°C for 90 min. The mixture was poured into water (1000 ml), the precipitate collected with suction, washed with water (500 ml), and dissolved in chloroform (200 ml). The solution was dried over magnesium sulfate, evaporated, and the residue dried under diminished pressure. Yield, 10·2 g (95%) of the amorphous L-*XI*, homogeneous in the solvent systems S_4 and S_5; $[\alpha]_D^{25}$ −58·8° (*c* 0·5, dimethylformamide). For $C_{23}H_{19}ClN_2O_7$ (470·9) calculated: 58·67% C, 4·06% H, 7·53% Cl, 5·95% N; found: 58·27% C, 3·95% H, 8·02% Cl, 5·68% N. A similar procedure was used in the preparation (yield, 96·5%) of the enantiomer D-*XI*, $[\alpha]_D^{25}$ +57·1° (*c* 0·5, dimethylformamide). Found: 58·14% C, 4·20% H, 7·92% Cl, 6·21% N. NMR spectrum, D-*XI*: $H_{1'}$, (d, 1 H) 5·86, $J_{1',2'}$ 7·4; $H_{2'}$, (m, 1 H) 5·28, $J_{2',1'}$ 7·4, $J_{2',3'}$ 4·5; $H_{3'}$ (t, 1 H) 6·10, $J_{3',2'}$ 4·5; $H_{4'}$ (m, 1 H) 5·13, $J_{4',3'}$ 4·5; 2 $H_{5'}$ (dd, 2 H) 4·59; H_5 (d, 1 H) 7·23, $J_{5,6}$ 8·1; H_6 (d, 1 H) 5·72, $J_{6,5}$ 8·1; arom. (m, 6 H) 7·20−7·65; arom. (m, 4 H) 7·90−8·15; NH (brs, 1 H) 9·43.

1-(3,5-Di-O-benzoyl-2-deoxy-α-L-lyxofuranosyl)uracil (L-*XII*)

Azo-bisisobutyronitrile (0·2 g) was added to a mixture of compound L-*XI* (11·5 g; 24·4 mmol) and tri-n-butyltin hydride (24 g) in benzene (200 ml) and the whole refluxed for 1 h. The reaction was quantitative as indicated by chromatography in the solvent system S_5. The reaction mixture was evaporated under diminished pressure, the residue diluted with light petroleum (500 ml), the precipitate collected with suction, washed with light petroleum (500 ml), dissolved in ethanol (25 ml), and the solution added dropwise under stirring into light petroleum (300 ml). The product was collected with suction, washed with light petroleum (100 ml), and dried under diminished pressure. Yield, 7·9 g (75%) of compound L-*XII*, $[\alpha]_D^{25}$ −38·0° (*c* 0·5, dimethylformamide). For $C_{23}H_{30}N_2O_7$ (436·4) calculated: 63·29% C, 4·62% H, 6·42% N; found: 63·56% C, 4·75% H, 6·58% N. A similar procedure was used in the preparation (yield, 86%) of the enantiomer D-*XII*, $[\alpha]_D^{25}$ +41·4° (*c* 0·5, dimethylformamide). Found: 62·82% C, 5·08% H, 6·21% N.

1-(2-Deoxy-α-L-lyxofuranosyl)uracil (L-*XIII*)

A solution of compound L-*XII* (3·0 g; 6·9 mmol) in 0·1M methanolic sodium methoxide (50 ml) was heated at 50°C for 6 h, evaporated under diminished pressure, the residue dissolved in water (100 ml), and the solution neutralised with Dowex 50 (H^+) ion exchange resin. The resin was filtered off, washed with water (50 ml), the filtrate and washings combined, washed with two 25 ml portions of ether, and the aqueous phase evaporated under diminished pressure. As shown by electrophoresis in the buffer solution E_1, the residue contained a small amount (5%) of contaminants (uracil). The residue was dissolved in water (25 ml) and the solution chromatographed on a column (80 × 4 cm) of DEAE-cellulose (Cellex D in the borate cycle), the elution being performed (rate, 3 ml per min) with 2 l of water and then with the use of a gradient of 0−0·5M

triethylammonium borate pH 7·5 (2 l of water in the mixing chamber and 2 l of the buffer in the reservoir. The course of elution was checked continuously with the Uvicord apparatus. The 0·03—0·05M fraction of the product was evaporated under diminished pressure, the residue coevaporated with five 50 ml portions of methanol, and the final residue (homogeneous in E_1) applied to a column packed with 25 ml of Dowex 50 (H^+) ion exchange resin. The elution was performed with the use of the Uvicord apparatus. The ultraviolet-absorbing fraction was evaporated, the residue coevaporated with ethanol, and the final residue crystallised at room temperature from ethanol (25 ml) to deposit in the course of several days the product L-*XIII* which was collected with suction, washed with a little ethanol and ether, and dried under diminished pressure. Yield, 1·0 g (64%) of compound L-*XIII*, homogeneous on chromatography and electrophoresis; m.p. 162°C. For $C_9H_{12}N_2O_5$ (228·2) calculated: 47·38% C, 5·30% H, 12·27% N; found: 47·37% C, 5·33% H, 12·20% N. A similar procedure was used in the preparation (yield, 72%) of the enantiomer D-*XIII*, m.p. 161—162°C. Found: 47·25% C, 5·48% H, 12·12% N. CD spectrum, of L-*XIII*: 270·5 nm (+6750), 261·5 s (+5600), 249·5 (0), 236·5 (−3500), 223·5 min (−2600), 216 (−4000); D-*XIII*: 270·5 (−6800), 262 s (−5600), 249·5 (0), 236·5 (+3400), 223·5 min (+2400), 216 (+3800).

1-(2-Deoxy-α-L-lyxofuranosyl)cytosine (L-*XIV*)

A mixture of compound L-*XII* (2 g; 4·6 mmol), phosphorus pentasulfide (1·2 g), and dioxane (100 ml) was refluxed for 30 min, treated with additional 1·2 g of phosphorus pentasulfide, and refluxed for 30 min more. The mixture was filtered while hot, the material on the filter washed with dioxane (50 ml), the filtrate and washings combined, and evaporated under diminished pressure. The residue was dissolved in chloroform (300 ml), the solution washed with 100 ml portions of saturated aqueous sodium hydrogen carbonate and 100 ml of water, dried over magnesium sulfate, the solid filtered off and washed with chloroform, the filtrate and washings combined, and evaporated under diminished pressure. The residue was dissolved in 30% methanolic ammonia (200 ml), the solution placed into a glass ampoule, and this heated in an autoclave at 110°C for 9 h. After cooling, the solution was evaporated under diminished pressure, the residue dissolved in water (200 ml), the solution washed with two 50 ml portions of ether, the aqueous phase concentrated to the volume of about 50 ml, the concentrate adjusted with concentrated hydrochloric acid to pH 2·5—3·0 and applied to a column packed with 300 ml of Dowex 50 (H^+) ion exchange resin. The column was eluted (rate, 3 ml per min) with water to the loss of ultraviolet absorption (2 l) and then with 5% aqueous ammonia. The ultraviolet-absorbing fraction of the ammonia eluate was evaporated under diminished pressure and the residue chromatographed on a column of DEAE-cellulose in the borate cycle analogously to compound *XIII* in order to remove a small amount of the contaminating cytosine. The eluate of compound L-*XIV* was evaporated under diminished pressure, the residue coevaporated with five 50 ml portions of methanol, the final residue applied to a column (25 ml) of pyridinium Dowex 50 ion exchange resin, the column eluted with 100 ml of 30% aqueous pyridine, the eluate evaporated under diminished pressure, the residue coevaporated with ethanol, and finally crystallised from ethanol (20 ml). The solution was treated with ether until turbid and then kept at 0°C for several days to deposit crystals which were collected with suction, washed with ether, and dried under diminished pressure. Yield, 0·80 g (77%) of compound L-*XIV*, homogeneous on chromatography (S_1) and electrophoresis (E_1); m.p. 189—190°C. For $C_9H_{13}N_3O_4$ (227·2) calculated: 47·57% C, 5·76% H, 18·49% N; found: 48·20% C, 5·48% H, 18·76% N. A similar procedure was used in the preparation (yield, 82%) of the enantiomer D-*XIV*, m.p. 190—192°C. Found: 47·34% C, 5·98% H, 18·60% N. CD spectrum, L-*XIV*: 273·5 (+8300), 236 s (+800), 230 (0), 215·5 (−5600), 206·6 (0); D-*XIV*: 273 (−8250), 236 s (−750), 230 (0), 215·5 (+5600), 207 (0).

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