SYNTHESIS OF 1-β-D-PSICOFURANOSYLURACIL AND 1-β-D-PSICOFURANOSYLCYTOSINE*

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Nucleosides *I* and *II* have been prepared by the alkaline methanolysis of protected nucleosides *VI* and *VIII*, obtained by reaction of the halogenose *V* with the corresponding silylated bases. The β-configuration of compound *I* has been established by an alternative synthesis starting from the nucleoside *IX* of the known configuration. The β-configuration of compound *II* is inferred from the fact that the nucleoside was obtained by the alkaline methanolysis of the protected nucleoside *XII* of a known configuration. In this reaction, the resulting compound *II* is accompanied by a considerable amount of an anhydro nucleoside which was ascribed the alternative structures *XIIIa* or *XIIIb*. The alkaline methanolysis of compound *IX* leads to the anhydro nucleoside *XVa* or *XVb* as the single product.

In an earlier paper[1] of this Series, the synthesis of some pyrimidine nucleosides derived from 1-deoxy-D-psicose has been reported. In connection with chiroptical and biological investigations on compounds of this type, the preparation of analogous nucleosides derived from D-psicose has been attempted. In the present paper we wish to report the synthesis of 1-β-D-psicofuranosyluracil (*I*) and 1-β-D-psicofuranosylcytosine (*II*).

In the synthesis of compounds *I* and *II*, D-psicose[2-5] has been used as the starting material. D-Psicose has been obtained in 80% yield by the action of aqueous 0·1M perchloric acid on 3,4,5,6-tetra-O-acetyl-1-deoxy-1-diazo-D-psicose. This procedure afforded markedly higher yields than the original method of Wolfrom[2] which requires the isolation of the intermediary 1,3,4,5,6-penta-O-acetyl-D-psicose of a low crystallisation ability. D-Psicose was converted by the action of methanolic hydrogen chloride to a mixture of anomeric methyl D-psicofuranosides (*IIa* and *IIb*) which were separated in the form of the *p*-toluates *IIIa* and *IIIb*; only the predominant methyl 1,3,4,6-tetra-O-*p*-toluyl-β-D-psicofuranoside (*IIIb*) was, however, obtained in the pure form by chromatography on silica gel. Ammonolysis of the *p*-toluyl groups of compound *IIIb* led to the glycoside *IIb*, the optical rotation of which was in accordance with that of a specimen[6] of *IIb* obtained on chromatography of the

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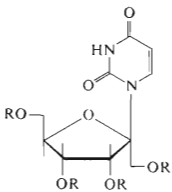
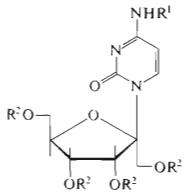
anomeric mixture over cellulose. The sirupous glycoside *IIb* was characterised as the crystalline phenyl boronate *IV*.

Analogously to the earlier paper[1], the preparation of nucleosides *I* and *II* was now effected with the use of the silylation process. Reaction of 2,4-bis(trimethylsilyloxy)-pyrimidine with the halogenose *V* in the presence of mercuric acetate in acetonitrile afforded 1-(1,3,4,6-tetra-O-*p*-toluyl-β-D-psicofuranosyl)uracil (*VI*) from which the free nucleoside *I* was obtained by the alkaline methanolysis. The nucleoside *I* was characterised as the crystalline 1-(1,3,4,6-tetra-O-acetyl-β-D-psicofuranosyl)uracil (*VII*).

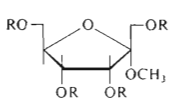


I; R = H
VI; R = *p*-$CH_3C_6H_4CO$
VII; R = Ac

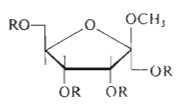


II; $R^1 = R^2 = H$
VIII; R^1 = Ac, R^2 = *p*-$CH_3C_6H_4CO$

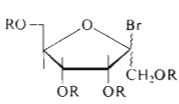
An analogous reaction of the halogenose *V* with 2-trimethylsilyloxy-4-(N-trimethylsilylacetamido)pyrimidine led to 1-(1,3,4,6-tetra-O-*p*-toluyl-β-D-psicofuranosyl)-4-acetamido-1,2-dihydro-2-pyrimidinone (*VIII*) which underwent the alkaline methanolysis under the formation of the nucleoside *II*.



IIa; R = H
IIIa; R = *p*-$CH_3C_6H_4CO$



IIb; $R^1 = R^2 = H$
IIIb; $R^1 = R^2$ = *p*-$CH_3C_6H_4CO$
IV; R^1 = H, 2 $R^2 = C_6H_5B$

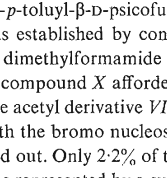


V; R = *p*-$CH_3C_6H_4CO$

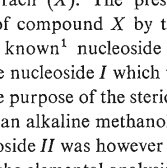
In the paper[1] on the synthesis of pyrimidine nucleosides derived from 1-deoxy-D-psicose, the configuration at the anomeric center has been ascribed on the basis of the Baker rule. In the case of nucleosides derived from D-psicose, however, this rule appears less reliable since the acyl group on the hydroxylic function at position 1 of the halogenose derived from keto sugars could participate on the formation of the

orthoester ion. By participation of this acyl group is explained by Baker and co-workers[7] the formation of 6-benzamido-9-(1,3,4,5-tetra-O-benzoyl-β-D-fructopyranosyl)purine which accompanies the α-anomer in the reaction of 1,3,4,5-tetra-O-benzoyl-D-fructopyranosyl bromide with 6-benzamidopurine chloromercuri salt. On the other hand, the reaction[7] of 1,3,4,6-tetra-O-benzoyl-D-fructofuranosyl bromide with 6-benzamidopurine chloromercuri salt as well as the analogous reaction of 1,3,4,6-tetra-O-benzoyl-D-psicofuranosyl bromide[6] afford exclusively nucleosides of the *trans* configuration at positions 2′,3′. In spite of the fact that the formation of an α-anomer in the reaction of the halogenose *V* with silylated bases in the presence of mercuric salts appears by analogy to the above mentioned reactions of furanosyl halides less probable, it was considered desirable with respect to the exception in the rule with pyranosyl halides to correlate the configuration at the anomeric center of compounds *I* and *II* with that of pyrimidine nucleosides derived from 1-deoxy-D-psicose which are known to obey the Baker rule without any exception.

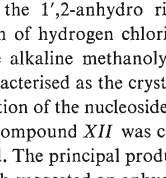
Consequently, the earlier reported[1] nucleoside *IX* was converted by the action of lithium azide in hexamethylphosphoric triamide into 1′,2-anhydro-1-(3,4,6-tri-O-*p*-toluyl-β-D-psicofuranosyl)uracil (*X*). The presence of the 1′,2-anhydro ring was established by conversion of compound *X* by the action of hydrogen chloride in dimethylformamide into the known[1] nucleoside *XI*. The alkaline methanolysis of compound *X* afforded the free nucleoside *I* which was characterised as the crystalline acetyl derivative *VII*. For the purpose of the steric correlation of the nucleoside *II* with the bromo nucleoside *XII*, an alkaline methanolysis of compound *XII* was carried out. Only 2·2% of the nucleoside *II* was however obtained. The principal product was represented by a substance, the elemental analysis of which suggested an anhydro nucleoside resulting from the protected nucleoside *XII* on removal of three *p*-toluyl groups and one hydrogen bromide molecule. On the basis of UV and IR spectra corresponding to 1-substituted derivatives of cytosine and because of the absence of the *cis*-diol grouping inferred from titration with periodic acid, a nucleoside might



X; R = *p*-$CH_3C_6H_4CO$



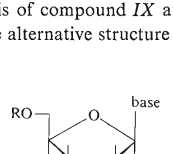
IX; R = *p*-$CH_3C_6H_4CO$, X = Br
XI; R = *p*-$CH_3C_6H_4CO$, X = Cl
XIV; R = H, X = Cl
XVII; R = Ac, X = Cl

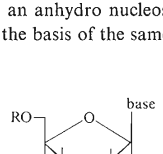


XII, R = *p*-$CH_3C_6H_4CO$

be involved, derived from an anhydro sugar and possessing the structure *XIIIa* or *XIIIb*. This assumption is supported by NMR spectrum which, however, did not allow to decide between the two alternatives.

In connection with the unexpected results obtained in the alkaline methanolysis of compound *XII*, it appeared desirable to examine also the analogous derivatives *IX* and *XI* in this respect. Thus, in the case of the chloro derivative *XI*, the expected chloro nucleoside *XIV* was obtained as the single product. On the other hand, the methanolysis of compound *IX* afforded exclusively an anhydro nucleoside which is ascribed the alternative structure *XVa* and *XVb* on the basis of the same evidence as above.





XIIIa; R = H, Base = cytosine
XVa; R = H, Base = uracil
XVIa; R = Ac, Base = uracil

XIIIb; R = H, Base = cytosine
XVb; R = H, Base = uracil
XVIb; R = Ac, Base = uracil

An analogous intramolecular cyclisation has been observed by Horwitz and co-workers[8] in the treatment of 2,3′-anhydro-1-(2-deoxy-5-O-methanesulfonyl-β-D--*threo*-pentofuranosyl)thymine with 0·1M-NaOH. According to the authors, the first step of the reaction consists in hydrolysis of the 2,3′-anhydro bond which is then followed by the intramolecular cyclisation of the intermediate to afford 1-(2-deoxy--3,5-anhydro-β-D-*threo*-pentofuranosyl)thymine.

EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block). Analytical samples were dried for 8 h at 25°C/0·01 Torr. Descending paper chromatography was performed on paper Whatman No 1 in the solvent systems S_1, 1-butanol–-ethanol–water (40 : 11 : 19), and S_2, 2-propanol–30% aqueous ammonia–water (7 : 1 : 2). Electrophoresis was carried out on paper Whatman No 1 at 40 V/cm for 2 h in the buffer solutions E_1, 0·05M triethylammonium borate (pH 7·5), and E_2, 0·05M sodium hydrogen citrate. UV spectra were taken on an Optica Milano CF-4 apparatus and IR spectra on a Zeiss Model UR 10 apparatus. CD spectra were measured on a Rousel-Jouan Dichrograph II Model CD 185 spectropolarimeter. NMR spectra were recorded on a Varian HA 100 apparatus at 100 MHz.

D-Psicose

A solution of 3,4,5,6-tetra-O-acetyl-1-deoxy-1-diazo-D-psicose[2] (3·58 g; 10 mmol) in methanol (6 ml) was poured with stirring into a hot (60°C) aqueous 0·1M perchloric acid (100 ml), the whole kept at 60°C for 10 h, cooled down, and neutralised with Zerolite FF (carbonate) ion exchange resin. The resin was then filtered off and washed with water (100 ml). The washings and filtrate were evaporated under diminished pressure and the residue was dried over phosphorus pentoxide at 20°C/15 Torr for 2 days. Yield, 1·46 g (81%) of the chromatographically homogene-

ous sirupous D-psicose. Optical rotation: $[\alpha]_D^{25}$ +2·6° (*c* 1·0; water). The chromatographical mobility on paper in the solvent system S_1 is identical with that of D-fructose (R_F 0·35). Osotriazole: m.p. 134·5—135·0°C (reported[2], m.p. 132—134°C).

Methyl 1,3,4,6-Tetra-O-*p*-toluyl-β-D-psicofuranoside (*IIIb*)

A solution of D-psicose (3·60 g; 20 mmol) in 0·1M methanolic hydrogen chloride (250 ml) was kept at room temperature for 4 h and then neutralised with silver carbonate. The precipitate was filtered off, washed with two 20 ml portions of methanol, the filtrate and washings combined, and evaporated under diminished pressure. The residue was dissolved in pyridine (35 ml) and the solution treated with stirring and cooling in ice bath with *p*-toluyl chloride (15 ml). After 2 days at room temperature, the mixture was poured onto ice and the *p*-toluylated glycosides extracted with ether (100 ml). The extract was washed with 5% aqueous phosphoric acid until the aqueous layer remained acid and then with saturated aqueous sodium hydrogen carbonate (50 ml), dried over anhydrous magnesium sulfate, and evaporated under diminished pressure. The residue was chromatographed on a column of silica gel (600 g; particle size, 60—120 micron) in 92 : 8 benzene–ethyl acetate to afford 6·32 g of a mixture of anomeric *p*-toluylated methyl glycosides *IIIa* and *IIIb*. For $C_{39}H_{38}O_{10}$ (666·7) calculated: 70·26% C, 5·75% H; found: 70·06% C, 5·75% H. The mixture (1 g) was rechromatographed on a column of silica gel (100 g; particle size, 60—120 micron) in the above solvent system to afford 450 mg of the more mobile, chromatographically homogeneous β-anomer *IIIb*, $[\alpha]_D^{25}$ −46·9° (*c* 0·62; ethyl acetate). For $C_{39}H_{38}O_{10}$ (666·7) calculated: 70·26% C, 5·75% H; found: 70·36% C, 5·67% H.

Methyl β-D-Psicofuranoside (*IIb*)

A solution of the methyl glycoside *IIIb* (333 mg; 0·5 mmol) in saturated methanolic ammonia (10 ml) was kept at room temperature for 3 days and then evaporated under diminished pressure. The residue was chromatographed on a column of silica gel in the solvent system 5 : 1 : 1 : 1 ethyl acetate–acetone–ethanol–water to afford 70 mg of the chromatographically homogeneous sirupous compound *IIb*, $[\alpha]_D^{25}$ −38·0° (*c* 0·46; methanol); reported[6], $[\alpha]_D$ −40·2° (methanol).

Methyl β-D-Psicofuranoside 3,4-Phenylboronate (*IV*)

From a mixture of compound *IIb* (120 mg), phenylboronic acid (66 mg), and benzene (15 ml) there was removed by distillation 5 ml of the distillate in the course of 1 h. The remaining benzene was evaporated under diminished pressure and the residue was triturated with light petroleum (5 ml). The solid portion was filtered off and crystallised from diisopropyl ether to afford 114 mg of compound *IV*, m.p. 123—124°C. Optical rotation: $[\alpha]_D^{25}$ −136° (*c* 0·51; benzene). IR spectrum (chloroform): 3595 cm^{-1}, 3447 cm^{-1} (OH). For $C_{13}H_{17}BO_6$ (280·1) calculated: 55·75% C, 6·12% H, 3·86% B; found: 55·59% C, 6·22% H, 4·08% B.

1-(1,3,4,6-Tetra-O-*p*-toluyl-β-D-psicofuranosyl)uracil (*VI*)

To a mixture of the methyl glycosides *IIIa* and *IIIb* (10 g; 15 mmol) in dichloromethane (50 ml) precooled to 0°C there was added a 30% solution of hydrogen bromide in acetic acid (50 ml) and the whole was kept for 30 min at 0°C and for 20 min at room temperature. The mixture was then diluted with dichloromethane (75 ml) and poured onto ice. The organic layer was washed with water (20 ml) and three 50 ml portions of precooled (0°C) saturated aqueous sodium hydrogen carbonate, dried over magnesium sulfate, and evaporated under diminished pressure.

The residue was dissolved in acetonitrile (25 ml), the solution treated with 2,4-bis(trimethylsilyloxy)pyrimidine (7·70 g; 30 mmol) and mercuric acetate (4·30 g; 15 mmol), the whole stirred for 12 h at room temperature and for 10 min at 60°C, allowed to cool, and diluted with chloroform (100 ml). The solid portion was removed by filtration and washed with three 10 ml portions of chloroform. The filtrate and washings were combined, washed with three 50 ml portions of 10% aqueous potassium iodide and two 50 ml portions of water, dried over anhydrous magnesium sulfate, and evaporated under diminished pressure. The residue was chromatographed on a column of silica gel (250 g; particle size, 30—60 micron) in the solvent system benzene–ethyl acetate (3 : 1). Crystallisation from ethanol afforded 2·22 g (20%) of compound *VI*, m.p. 149—150°C; $[\alpha]_D^{25}$ −65·0° (*c* 0·50; ethyl acetate). IR spectrum (chloroform): 1725 cm^{-1}, 1694 cm^{-1} (CO), 3382 cm^{-1} (NH). For $C_{42}H_{38}N_2O_{11}$ (746·8) calculated: 67·55% C, 5·13% H, 3·75% N; found: 67·84% C, 5·30% H, 3·58% N.

1-β-D-Psicofuranosyluracil (*I*)

A solution of compound *VI* (500 mg; 0·67 mmol) in 0·2M methanolic barium methoxide (20 ml) was kept at 0°C for 12 h, saturated with carbon dioxide, and made alkaline by the addition of one drop of conc. aqueous ammonia. After 15 min, the precipitate was filtered off and washed with two 2 ml portions of methanol. The filtrate and washings were combined and evaporated under diminished pressure. The residue was dissolved in water (20 ml) and the solution was inoculated with methyl *p*-toluate to deposit crystals which were removed by filtration. The filtrate was evaporated, the residue dissolved in water (10 ml), and the solution chromatographed on a 1·5 × 28 cm column of Dowex 1 (formate) ion exchange resin. The elution (with water) was checked by ultraviolet absorption of the eluate. Evaporation of the absorbing fraction afforded 111 mg (60%) of the amorphous nucleoside *I*. UV spectrum (water): λ_{max} 264 nm (log ε 3·92). CD spectrum (water): 264 nm (+3277), 219 nm (+1582), 196 nm (−15142). Periodic acid uptake (pH 6·8): 1·00 mol after 1 h. For $C_{10}H_{14}N_2O_7$ (274·2) calculated: 43·80% C, 5·15% H, 10·22% N; found: 44·19% C, 5·69% H, 9·88% N.

1-(1,3,4,6-Tetra-O-acetyl-β-D-psicofuranosyl)uracil (*VII*)

A solution of 1-β-D-psicofuranosyluracil (*I*) (50 mg) in pyridine (2 ml) and acetic anhydride (1 ml) was allowed to stand for 12 h at room temperature and diluted with ethanol (2 ml). After additional 2 h, the mixture was evaporated under diminished pressure, the residue coevaporated with toluene, and crystallised from a 10 : 1 mixture of di-n-propyl ether and methanol to afford 48 mg of compound *VII*, m.p. 140·5—141·5°C, $[\alpha]_D^{25}$ −2·5° (*c* 0·32; ethyl acetate). UV spectrum (ethanol): λ_{max} 259 nm (log ε 3·99). For $C_{18}H_{22}N_2O_{11}$ (442·4) calculated: 48·87% C, 5·01% H, 6·33% N; found: 49·11% C, 4·92% H, 6·38% N.

1-(1,3,4,6-Tetra-O-*p*-toluyl-β-D-psicofuranosyl)-4-acetamido-1,2-dihydro-2-pyrimidinone (*VIII*)

To a solution of psicofuranosyl bromide *V* (15 mmol) in acetonitrile (25 ml) there was added 2-trimethylsilyloxy-4-(N-silylacetamido)pyrimidine (7·80 g; 30 mmol) and then (when the silyl compound dissolved) mercuric acetate (4·30 g; 15 mmol). The whole mixture was stirred at room temperature for 12 h and diluted with chloroform (100 ml). The insoluble portion was filtered off and washed with three 10 ml portions of chloroform. The filtrate and washings were combined, evaporated under diminished pressure, and the residue dissolved in chloroform (100 ml). The solution was washed with three 50 ml portions of 10% aqueous potassium iodide and two 50 ml

portions of water, dried over anhydrous magnesium sulfate, and evaporated under diminished pressure. The residue was chromatographed on a column of silica gel (250 g; particle size, 30—60 micron) in the solvent system benzene–ethyl acetate (1 : 1). Crystallisation from ethanol afforded 1·83 g (15·5%) of compound *VIII*, m.p. 207·5—209·0°C, $[\alpha]_D^{25}$ —60·7° (*c* 0·50; ethyl acetate). For $C_{44}H_{41}N_3O_{11}$ (787·8) calculated: 67·08% C, 5·25% H, 5·33% N; found: 66·86% C, 5·14% H, 5·31% N.

1-β-D-Psicofuranosylcytosine (*II*)

A solution of the protected nucleoside *VIII* (500 mg; 0·66 mmol) in 0·2M methanolic barium methoxide (20 ml) was kept at 0°C for 12 h, saturated with carbon dioxide, made alkaline by the addition of one drop of conc. aqueous ammonia, and evaporated under diminished pressure. The residue was dissolved in hot water (4 ml) and the insoluble portion filtered off. The filtrate was cooled down to deposit crystals which were collected with suction and washed with ethanol (1 ml). Crystallisation from water afforded 122 mg (70·5%) of compound *II*, m.p. 207—208°C (water). UV spectrum in water: sh 227 nm (log ε 3·86), λ_{max} 273 nm (log ε 3·89); in 0·1M-HCl: λ_{max} 215 nm and 281 nm (log ε 3·89 and 4·06, resp.). IR spectrum (KBr): 1 659 cm^{-1}, 1 644 cm^{-1} (CO, NH_2), 1 633 cm^{-1} (C=C). CD spectrum (water); 271 nm (+3083), 234 nm (—2312), 219 nm (+1349). Periodic acid uptake (pH 6·8): 0·95 mol after 1 h. For $C_{10}H_{15}N_3O_6$ (273·25) calculated: 43·96% C, 5·53% H, 15·38% N; found: 44·26% C, 5·51% H, 15·38% N.

1′,2-Anhydro-1-(3,4,6-tri-O-*p*-toluyl-β-D-psicofuranosyl)uracil (*X*)

A solution of compound[1] *IX* (692 mg; 1 mmol) and lithium azide (200 mg) in hexamethylphosphoric triamide (12 ml) was kept at room temperature for 48 h, diluted with water (100 ml), and extracted with dichloromethane (two 50 ml portions). The extract was washed with three 100 ml portions of water, dried over anhydrous magnesium sulfate, and evaporated under diminished pressure. The residue was chromatographed on a column of silica gel (75 g; 30—60 micron) in the solvent system benzene–acetone (3 : 2). Crystallisation from a mixture of diisopropyl ether and ethanol afforded 455 mg (74·5%) of compound *X*, m.p. 188·5—189·5°C; $[\alpha]_D^{25}$ —177·8° (*c* 0·40; ethyl acetate). IR spectrum (chloroform): 1 651 cm^{-1} (CO). For $C_{34}H_{30}N_2O_9$ (610·6) calculated: 66·88% C, 4·95% H, 4·59% N; found: 66·82% C, 5·00% H, 4·58% N.

Reaction with hydrogen chloride. A solution of compound *X* (61 mg; 0·1 mmol) in 1M hydrogen chloride in dimethylformamide (2·4 ml) was heated at 100°C for 30 min, cooled down, poured into saturated aqueous sodium hydrogen carbonate (20 ml), and extracted with two 10 ml portions of dichloromethane. The extract was washed with two 15 ml portions of water, dried over anhydrous magnesium sulfate, and evaporated under diminished pressure. Crystallisation of the residue from ethanol afforded 56 mg (86·5%) of a substance, m.p. 185—186°C, undepressed on admixture with the chloro nucleoside[1] *XI*.

Methanolysis. Compound *X* (183 mg; 0·3 mmol) was methanolysed with 0·2M methanolic barium methoxide analogously to compound *VI*. The product was dissolved in water (2 ml) and the solution applied to a column (1 × 20 cm) of Dowex 1 (formate) ion exchange resin. The column was eluted with water and the UV-absorbing effluent fraction evaporated to afford 65 mg (71%) of a substance, the IR spectrum (KBr) of which was identical with that of the nucleoside *I*. The subsequent acetylation of this substance (50 mg) with acetic anhydride (1 ml) in pyridine (2 ml) and crystallisation from a mixture (10 : 1) of di-n-propyl ether and methanol afforded a substance, m.p. 140—141°C, undepressed on admixture with the acetylated nucleoside *VII*.

1-(1,3- or 1,4-Anhydro-β-D-psicofuranosyl)cytosine (*XIIIa,b*)

The nucleoside derivative[1] *XII* (733 mg; 1 mmol) was methanolysed with methanolic barium methoxide analogously to compound *IX*. The product was dissolved in water (10 ml) and the solution applied to a column (1·5 × 30 cm) of IRC-50 ion exchange resin (pre-washed with 1M-NaOH, water, 1M ammonium formate adjusted with formic acid to pH 3·4, and finally with water until the effluent was neutral). The column was eluted with water to afford two UV-absorbing fractions. The first fraction was identified as *p*-toluic acid. The second fraction was evaporated and the residue crystallised from water to afford 142 mg (56%) of compound *XIIIa,b*, m.p. 214°C (decompn.). UV spectrum in water: λ_{max} 239 nm and 266 nm (log ε 3·93 and 3·94, resp.); in 0·1M-HCl: λ_{max} 213 and 276 nm (log ε 3·92 and 4·08, resp.). NMR spectrum in dimethyl sulfoxide (hexamethyldisiloxane as internal standard, recalculated to tetramethylsilane; chemical shifts in p.p.m.): 4·57–4·97 (2 d, 2 H, J_{gem} = 8 Hz, $H_{1'a}$, $H_{1'b}$); 5·80–6·83 (2 d, 2 H, $J_{5,6}$ = = 8 Hz, H_5, H_6). For $C_{10}H_{13}N_3O_5$ (255·2) calculated: 47·06% C, 5·13% H, 16·47% N; found: 47·22% C, 5·08% H, 16·80% N.

After the elution of compound *XIIIa, b* with water, the column was eluted with 0·05M formic acid. The UV-absorbing fraction was evaporated and the residue crystallised from water to afford 6 mg of compound *II*, m.p. 206–207°C, undepressed on admixture with an authentic sample.

1-(2,3- or 1,4-Anhydro-β-D-psicofuranosyl)uracil (*XVa, b*)

A mixture of compound *IX* (1·03 g; 1·5 mmol) and 0·2M methanolic barium methoxide (40 ml) was kept at 0°C for 5 h under occasional stirring, saturated with carbon dioxide, and made alkaline by the addition of one drop of conc. aqueous ammonia. After 15 min at room temperature, the precipitate was filtered off and washed with two 5 ml portions of water. The filtrate and washings were combined and evaporated under diminished pressure. The residue was dissolved in water (3 ml) and the solution seeded to deposit crystalline methyl *p*-toluate which was filtered off and washed with two 1 ml portions of water. The filtrate and washings were combined and applied to a column (1·5 × 30 cm) of Dowex 1 (acetate) ion exchange resin. Elution with water and evaporation of the UV-absorbing fraction afforded 339 mg (88%) of compound *XVa, b* in the form of a solid foam. UV spectrum (water): λ_{max} 257 nm (log ε 3·85). IR spectrum (KBr): 1728 cm^{-1}, 1690 cm^{-1} (CO), 1626 cm^{-1} (C=C), 3080 cm^{-1} (CH heterocycl.). NMR spectrum in a mixture of deuteriochloroform and dimethyl sulfoxide (hexamethyldisiloxane as internal standard, recalculated to tetramethylsilane; chemical shifts in p.p.m.): 3·63 (2 d, 2 H, $J_{5',6'a}$ = = 4 Hz, $J_{5',6'b}$ = 1 Hz, J_{gem} = 11 Hz, $H_{6'a}$, $H_{6'b}$); 3·86 (m, 1 H, $H_{5'}$); 4·18 (m, 1 H, $J_{3',4'}$ = = 1 Hz, $H_{4'}$), 5·30 (m, 1 H, $H_{3'}$), 4·64–5·05 (2 d, 2 H, J_{gem} = 8 Hz, $H_{1'a}$, $H_{1'b}$); 5·60–7·11 (2 d, 2 H, $J_{5,6}$ = 8 Hz, H_5, H_6). For $C_{10}H_{12}N_2O_6$ (256·2) calculated: 46·88% C, 4·72% H, 10·93% N; found: 46·38% C, 5·13% H, 10·74% N.

1-(4,6- or 3,6-Di-O-acetyl-1,3- or 1,4-anhydro-β-D-psicofuranosyl)uracil (*XVIa, b*)

A solution of the anhydro compound *XVa, b* (50 mg) in pyridine (2 ml) and acetic anhydride (1 ml) was allowed to stand at room temperature for 2 days, diluted with ethanol (2 ml), kept for additional 2 h, and evaporated under diminished pressure. The residue was coevaporated with three 4 ml portions of toluene and chromatographed on a column of silica gel in the solvent system benzene–acetone (1 : 1) to afford 51 mg of compound *XVIa, b* in the form of a solid foam. UV spectrum (ethanol): λ_{max} 256 nm (log ε 3·94). IR spectrum (chloroform): 3380 cm^{-1}, 3195 cm^{-1} (NH), 1742 cm^{-1} (CO acetate), 1693 cm^{-1}, 1704 cm^{-1} (CO uracil), 1632 cm^{-1} (C=C). NMR spectrum in deuteriochloroform (tetramethylsilane as internal standard, chemical shifts

in p.p.m.): 2·08 (s, 3 H, CH_3CO); 2·13 (s, 3 H, CH_3CO); 4·38 (m, 2 H, $J_{5',6'a} = 6·1$ Hz, $J_{5',6'b} = 2·4$ Hz, J_{gem} 12·5 Hz, $H_{6'a,6'b}$); 4·64 (m, 1 H, $H_{5'}$); 4·75—5·13 (2 d, 2 H, $J_{gem} = 7·5$ Hz, $H_{1'a}$, $H_{1'b}$); 5·20 (q, 1 H, $J_{3',4'} = 4·0$ Hz, $J_{4',5'} = 8·1$ Hz, $H_{4'}$); 5·70 (d, 1 H, $H_{3'}$), 5·80—6·94 (2 d, 2 H, $J_{5,6} = 7·9$ Hz, H_5, H_6). For $C_{14}H_{16}N_2O_8$ (340·3) calculated: 49·41% C, 4·74% H, 8·23% N; found: 49·02% C, 4·96% H, 7·87% N.

1-(1-Chloro-1-deoxy-β-D-psicofuranosyl)uracil (*XIV*)

Methanolysis of the protected nucleoside *XI* (1·29 g; 2 mmol) with 0·2M methanolic barium methoxide (45 ml) and the subsequent chromatography on a column of silica gel (75 g; particle size, 60—120 micron) in the solvent system ethyl acetate–acetone–ethanol–water (4 : 1 : 1 : 1) afforded 375 mg (64%) of compound *XIV* as a chromatographically homogeneous sirup. UV spectrum (water): λ_{max} 207 nn and 262 nm (log ε 3·87 and 4·00, resp.). CD spectrum (water): 255·5 nm (—1 900), sh 235 nm (—280), 215 nm (+4 760). For $C_{10}H_{13}ClN_2O_6$ (292·7) calculated: 41·04% C, 4·48% H, 9·57% N, 12·11% Cl; found: 41·46% C, 4·60% H, 9·22% N, 11·80% Cl.

1-(3.4.6-Tri-O-acetyl-1-chloro-1-deoxy-β-D-psicofuranosyl)uracil (*XVII*)

A solution of the chloro compound *XIV* (50 mg) in pyridine (2 ml) and acetic anhydride (1 ml) was kept at room temperature for 12 h, diluted with methanol (2 ml), kept for additional 2 h, and evaporated under diminished pressure. The residue was coevaporated with three 4 ml portions of toluene and crystallised from a mixture (10 : 1) of di-n-propyl ether and methanol to afford 52 mg of compound *XVII*, m.p. 187·5—189°C, $[\alpha]_D^{25}$ +23·3° (*c* 0·50; ethyl acetate). UV spectrum (ethanol): λ_{max} 213 nm and 259 nm (log ε 3·79 and 4·01, resp.); CD spectrum (ethanol): 272·5 nm (+1 430), 216·5 nm (+9 160), 195 nm (—16 180). For $C_{16}H_{19}ClN_2O_9$ (418·8) calculated: 45·89% C, 4·57% H, 6·69% N, 8·47% Cl; found: 46·11% C, 4·74% H, 6·54% N, 8·37% Cl.

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