PREPARATION OF THE 1-(2,5-ANHYDRO-β-D-ARABINOFURANOSYL) DERIVATIVES OF CYTOSINE AND URACIL AND THEIR CLEAVAGE WITH HYDROGEN BROMIDE*

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Anhydronucleoside *Ia* was prepared from chloroarabinofuranosylcytosine *IIIc* or from 2,2′-anhydro-1-(5-chloro-5-deoxy-β-D-arabinofuranosyl)cytosine by the action of a strongly basic ion exchanger. The anhydro derivative *IIa* was prepared from 2,2′-anhydro-1-(5-chloro-5-deoxy-β-D-arabinofuranosyl)uracil by treatment with aqueous solution of sodium hydroxide. The action of hydrogen bromide in dimethylformamide on 2′,5′-anhydronucleosides *Ia* and *IIa* leads both to the cleavage of the anhydro bond under formation of the 5′-bromo derivatives *IIIa* and *IVa* and to the cleavage of nucleosidic bond. In case of the uracil derivative *IIa*, the α-arabinofuranosyl derivative *V* was also isolated after preceding acetylation. For unambiguous proof of the structure, an alternative synthesis of compound *V* was performed.

It is known from literature[1,2] that the 2′,5′-anhydro ring in the 2′,5′-anhydroarabinofuranosyl derivative of cytosine *Ia* and uracil *IIa* is very stable, in contrast to the 3′,5′-anhydro ring in 3′,5′-anhydroxylofuranosyluracil. Attempts at the cleavage of the 2′,5′-anhydro ring by acid have led to the cleavage of nucleosidic bond. The attempt to cleave this ring by treatment with the nucleophiles[2] such as iodide, azide, and benzylmercaptide was unsuccessful as well, despite the fact that in 3′,5′-anhydroxylofuranosyl nucleosides, the anhydro ring is attacked by such nucleophiles (*cf.* lit.[2] and references therein). However, there has been no report in the literature on an attempt to cleave the 2′,5′-anhydro ring with hydrogen bromide in polar aprotic solvent. The subject of this work is the cleavage of 2′,5′-anhydronucleosides *Ia* and *IIa* with hydrogen bromide in dimethylformamide.

The starting anhydronucleoside *Ia* was prepared either from 1-(5-chloro-5-deoxy-β-D-arabinofuranosyl)cytosine (*IIIc*) or 2,2′-anhydro-1-(5-chloro-5-deoxy-β-D-arabinofuranosyl)cytosine[3] by forming the 2′,5′-anhydro ring on the action of a strongly basic ion exchanger in carbonate cycle. The uracil analog *IIa* was prepared by the action of aqueous sodium hydroxide on 2,2′-anhydro-1-(5-chloro-5-deoxy-β-D-arabinofuranosyl)uracil[4]. Anhydronucleoside *Ia* was heated with 2·2M solution

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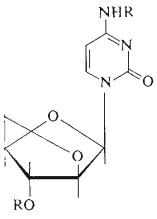
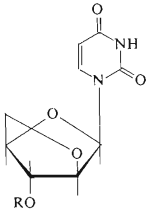
of hydrogen bromide in dimethylformamide at 120°C for 25 min. Along with cytosine, the 5′-bromo derivative *IIIa* was also isolated from the reaction mixture in a 48% overall yield. The proof of the structure of the bromo derivative was performed by transforming it to the anhydro derivative *Ia* by the action of Dowex I in carbonate form. Also, the ^{1}H NMR spectra of the acetate *IIIb* and those of the corresponding chloro derivative *IIIc* are practically identical, except for the shifts of $H_{5'}$ protons. The specific rotation value of *IIIa* (+140°) is in accordance with the proposed structure as well, because the rotation of the corresponding chloro derivative[3] amounts to +150°. A little more complicated is the course of cleavage of the 2′,5′-anhydro ring in the uracil derivative *IIa*. Compound *IIa* was heated in 2·2M solution of hydrogen bromide in dimethylformamide at 120°C for 5 min. Beside uracil, two bromo derivatives were isolated from the reaction mixture. Because of the easier isolation, they were obtained in the form of the acetates *IVb* and *V*. The chromatographically more mobile bromo derivative *IVb* was transformed to the anhydro derivative *IIa* on treatment with aqueous sodium hydroxide. The ^{1}H NMR spectrum of the bromo derivative *IVb* is practically identical, except for the shifts of $H_{5'}$ protons, with the spectrum of the corresponding chloro derivative *IVc*. All that is in agreement with the proposed structure. The UV spectrum of the chromatographically less mobile bromo derivative *V*, measured at pH 2 (260 nm, log ε 4·03) and pH 12 (262 nm, log ε 3·89), corresponds to that of 1-substituted uracil. Therefore, the 1→3 migration of ribosyl, which was observed during the reaction of 2,2′-anhydro-1-β-D-arabinofuranosyluracil-6-carboxamide with hydrogen bromide[5] and at the reaction of 2,2′-anhydro-1-β-D-arabinofuranosyluracil with liquid hydrogen fluoride[6], cannot be supposed in this case. The chemical shift (δ) of sugar proton $H_{1'}$ in the NMR spectrum of the bromo derivative *V* is 5·93 ppm while in the spectrum of *IVb* this value is 6·31 ppm. Similar differences were found between α- and β-arabinofuranosyluracil[7]. This would suggest that the chromatographically less mobile bromo derivative is of α-configuration. In order to obtain an unambiguous proof of the structure, it was decided to synthetize *V* in an unambiguous way. 1-α-D-Arabinofuranosyluracil[8] was tritylated with triphenylmethyl chloride in pyridine[9]. Acetylation of the trityl derivative *VI* with acetic anhydride in pyridine afforded trityl acetate *VII*. Detritylation was performed in 85% acetic acid[9] under formation of the diacetate *VIII*. Reaction of *VIII* with methanesulfonyl chloride in pyridine afforded the methylsulfonyl derivative *IX*. Nucleophilic substitution of methylsulfonyl group was performed by heating with tetrabutylammonium bromide in acetonitrile. NMR spectrum, IR spectrum, and specific rotation of the prepared bromo derivative *V* were identical with those of the chromatographically less moving bromo derivative obtained on cleavage of the anhydro derivative *II a*. On treatment with aqueous sodium hydroxide, both compounds afforded the single anhydronucleoside *X*.

The action of hydrogen bromide in dimethylformamide on the anhydronucleosides *Ia* and *IIa* leads to the cleavage of both the 2′,5′-anhydro ring and the nucleosidic

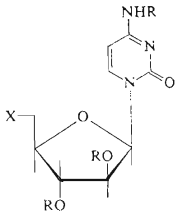
bond. With regard to a higher yield of the bromo derivative *IIIa* in comparison with the yield of *IVa*, a higher stability of the nucleosidic bond in cytosine derivative (in comparison with the uracil one) can be assumed. In the course of reaction of the anhydro derivative *IIa* with hydrogen bromide, uracil probably reacts with the formed bromo halogenose with the formation of both anomers *IVb* and *V*. The



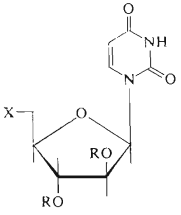
Ia, R = H
Ib, R = CH_3CO



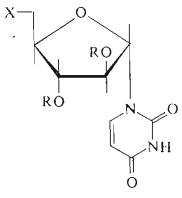
IIa, R = H
IIb, R = CH_3CO



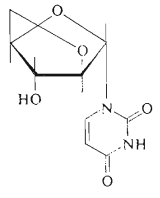
IIIa, R = H, X = Br
IIIb, R = CH_3CO, X = Br
IIIc, R = H, X = Cl
IIId, R = CH_3CO, X = Cl



IVa, R = H, X = Br
IVb, R = CH_3CO, X = Br
IVc, R = CH_3CO, X = Cl



V, R = CH_3CO, X = Br
VI, R = H, X = OTr
VII, R = CH_3CO, X = OTr
VIII, R = CH_3CO, X = OH
IX, R = CH_3CO, X = OMs



X

α-derivative *V* was obtained in higher yield than β-derivative *IVb*. Thus, the direction of the attack is probably governed by participation of hydroxyl in position 2 of the sugar derivative. The α-anomer of the cytosine bromo derivative was neither isolated nor detected in the reaction mixture. Nucleophility of the protonated cytosine is negligible and so the repeated bonding to the sugar cannot take place.

EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block). The ultraviolet spectra were recorded on a Specord apparatus. The infrared spectra were taken on a UR-20 (Carl Zeiss, Jena) apparatus. Optical rotations were measured on an automatic Perkin–Elmer 141 MC polarimeter. The ^{1}H NMR spectra were recorded on a Varian HA-100 (100 MHz) and a Tesla BS 467 (60 MHz) instruments, using tetramethylsilane as internal standard; chemical shifts (δ-values) are expressed in ppm and the coupling constant in Hz. Column chromatography was performed on the Pitra silica gel (particle size, 30—60 μm; produced by Service Laboratories of this Institute).

4-Amino-1-(2,5-anhydro-β-D-arabinofuranosyl)pyrimidin-2(1*H*)one (*Ia*)

A) A solution of 4-amino-1-(5-chloro-5-deoxy-β-D-arabinofuranosyl)pyrimidin-2-(1*H*)-one[3] (523 mg; 2 mmol) in water (40 ml) was heated to 50°C, Dowex 1 (CO_3^{2-}; 25 ml) was added and the mixture was stirred at 50°C for 6 h. The resin was filtered off, washed with water, and the combined filtrates were evaporated under diminished pressure. Crystallization of the residue from water afforded 310 mg (65%) of *Ia* in the form of a hemihydrate. Crystallization of the mother liquors residue yielded additional 105 mg (22%) of the same compound, m.p. 264—266°C (reported[2], 257—258°C, dec.). $[\alpha]_D^{25}$ +233° (*c* 0·50; water); reported[2], +232·3°. For $C_9H_{11}N_3O_4 . 1/2\ H_2O$ (234·2) calculated: 46·15% C, 5·17% H, 17·94% N; found: 45·90% C, 5·17% H, 18·01% N.

B) The same procedure starting from [2*R*-(2α,3β,3aβ,9aβ]-2-chloromethyl-2,3,3a,9a-tetrahydro-3-hydroxy-6-imino-6*H*-furo[2′,3′:4,5]oxazolo[3,2-a]pyrimidine hydrochloride[3] (560 mg; 2 mmol) afforded 344 mg (73%) of *Ia*.

4-Acetamido-1-(3-O-acetyl-2,5-anhydro-β-D-arabinofuranosyl)pyrimidin-2(1*H*)-one (*Ib*)

A mixture of *Ia* (hemihydrate; 117 mg; 0·5 mmol), pyridine (2 ml), and acetanhydride (1·5 ml) was stirred until it dissolved. The mixture was left to stand at room temperature for 12 h, then methanol (2 ml) was added and after 10 min, the solvents were evaporated under diminished pressure. Crystallization of the residue from 2-propanol–methanol afforded 134 mg (87%) of *Ib*, m.p. 242—245°C. ^{1}H NMR spectrum (60 MHz, C^2HCl_3): 2·16 (s, 3 H, $OCOCH_3$), 2·30 (s, 3 H, $NHCOCH_3$), 4·04 (s, 2 H, $H_{5'}$), 4·80 (s, 1 H, $H_{4'}$), 4·83 (d, 1 H, $H_{3'}$, $J_{3',2'} = 1·5$), 5·30 (dd, 1 H, $H_{2'}$, $J_{2',3'} = 1·5$, $J_{2',1'} = 3$), 6·20 (d, 1 H, $H_{1'}$, $J_{1',2'} = 3$), 7·52 (d, 1 H, H_5, $J_{5,6} = 7·5$), 8·12 (d, 1 H, H_6, $J_{6,5} = 7·5$), 10·35 (broad s, 1 H, $NHCOCH_3$). For $C_{13}H_{15}N_3O_6$ (309·3) calculated: 50·48% C, 4·89% H, 13·59% N; found: 50·24% C, 4·87% H, 13·75% N.

4-Amino-1-(5-bromo-5-deoxy-β-D-arabinofuranosyl)pyrimidin-2(1*H*)-one (*IIIa*)

Anhydronucleoside *Ia* (hemihydrate; 2·34 g; 10 mmol) was heated in a 2·2M solution of hydrogen bromide in dimethylformamide (25 ml) at 120°C for 25 min. Dimethylformamide was evaporated under diminished pressure, the residue was coevaporated with dimethylformamide (3 × 30 ml) and dissolved in water (50 ml). The solution was decolourized with charcoal and submitted onto a column of Dowex 3 (CH_3COO^-; 20—50 mesh; 200 ml). The column was eluted with water. The UV-absorbing fraction was evaporated and the residue was crystallized from water to afford 1·38 g (45%) of the bromo derivative *IIIa*, m.p. 191—192°C, $[\alpha]_D^{25}$ +140° (*c* 0·44; water). For $C_9H_{12}BrN_3O_4$ (306·1) calculated: 35·31% C, 3·95% H, 13·75% N, 26·11% Br; found: 35·19% C, 3·92% H, 13·64% N, 26·00% Br.

The mother liquors residue was acetylated with the mixture of acetic anhydride (2 ml) and pyridine (2 ml). After a 12 h standing at room temperature, methanol (3 ml) was added and after 15 min, the solvents were evaporated under diminished pressure. The residue was triturated with methanol (10 ml) and the undissolved N^4-acetylcytosine was collected by filtration and washed with methanol (4 ml). Yield, 313 mg (20%) of N^4-acetylcytosine. Combined filtrates were evaporated *in vacuo* and the residue was chromatographed on a silica gel column (50 g) in the system ethyl acetate–acetone–ethanol–water (20 : 3 : 1 :1). Crystallization of the residue of the first fraction from 2-propanol–methanol afforded 145 mg (3%) of *IIIb*, identical with an authentic specimen prepared by acetylation of *IIIa*. Crystallization of the second fraction residue from 2-propanol–methanol yielded 101 mg (3%) of *Ib*.

4-Acetamido-1-(2,3-di-O-acetyl-5-bromo-5-deoxy-β-D-arabinofuranosyl)pyrimidin-2(1*H*)-one (*IIIb*)

Compound *IIIb* was prepared on acetylation of *IIIa* with pyridine–acetic anhydride. After crystallization from mixture 2-propanol–methanol, melting point was 224–225·5°C, $[\alpha]_D^{25}$ +94° (*c* 0·48; ethyl acetate). ^{1}H NMR spectrum (60 MHz, C^2HCl_3): 1·96 (s, 3 H, 2'-OCOCH$_3$), 2·13 (s, 3 H, 3'-OCOCH$_3$), 2·29 (s, 3 H, NHCOCH$_3$), 3·72 (d, 2 H, $H_{5'}$, $J_{5',4'}$ = 5), 4·25 (m, 1 H, $H_{4'}$, $J_{4',3'}$ = 3, $J_{4',5'}$ = 5), 5·13 (dd, 1 H, $H_{3'}$, $J_{3',2'}$ = 1, $J_{3',4'}$ = 3), 5·50 (dd, 1 H, $H_{2'}$, $J_{2',1'}$ = 3·5, $J_{2',3'}$ = 1), 6·37 (d, 1 H, $H_{1'}$, $J_{1',2'}$ = 3·5), 7·52 (d, 1 H, H_5, $J_{5,6}$ = 7), 8·02 (d, 1 H, H_6, $J_{6,5}$ = 7), 10·28 (broad s, 1 H, NHCOCH$_3$). For $C_{15}H_{18}BrN_3O_7$ (432·2) calculated: 41·68% C, 4·20% H, 9·72% N, 18·49% Br; found: 41·79% C, 4·25% H, 9·46% N, 18·48% Br.

4-Acetamido-1-(2,3-di-O-acetyl-5-chloro-5-deoxy-β-D-arabinofuranosyl)pyrimidin-2(1*H*)-one (*IIId*)

Compound *IIIc* was prepared on acetylation of 4-amino-1-(5-chloro-5-deoxy-β-D-arabinofuranosyl)pyrimidin-2(1*H*)-one[3] with a pyridine–acetic anhydride mixture. M.p., 198–200°C after crystallization from 2-propanol–methanol. ^{1}H NMR spectrum (60 MHz, C^2HCl_3): 1·97 (s, 3 H, 2'-OCOCH$_3$), 2·13 (s, 3 H, 3'-OCOCH$_3$), 2·30 (s, 3 H, NHCOCH$_3$), 3·87 (d, 2 H, $H_{5'}$, $J_{5',4'}$ = 5), 4·23 (m, 1 H, $H_{4'}$, $J_{4',5'}$ = 5, $J_{4',3'}$ = 3), 5·17 (dd, 1 H, $H_{3'}$, $J_{3',4'}$ = 3, $J_{3',2'}$ = 1), 5·51 (dd, 1 H, $H_{2'}$, $J_{2',3'}$ = 1, $J_{2',1'}$ = 3·5), 6·38 (d, 1 H, $H_{1'}$, $J_{1',2'}$ = 3·5), 7·51 (d, 1 H, H_5, $J_{5,6}$ = 7), 8·01 (d, 1 H, H_6, $J_{6,5}$ = 7), 10·05 (broad s, 1 H, NHCOCH$_3$). For $C_{15}H_{18}ClN_3O_7$ (387·8) calculated: 46·46% C, 4·68% H, 10·84% N, 9·14% Cl; found: 46·70% C, 4·59% H, 10·67% N, 9·15% Cl.

1-(2,5-Anhydro-β-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)-dione (*IIa*)

A) A solution of 2,2'-anhydro-1-(5-chloro-5-deoxy-β-D-arabinofuranosyl)uracil[4] (2·45 g; 10 mmol) in 0·2M aqueous solution of sodium hydroxide (140 ml) was, after 30 h, neutralized with Dowex 50 (H^+). The resin was filtered off, washed with water (60 ml), and the combined filtrates were evaporated *in vacuo*. Crystallization of the residue from water afforded 1·75 g (71%) of *IIa*, m.p. 260–263°C. $[\alpha]_D^{25}$ +207° (*c* 0·43; water). Reported[1], m.p. 249–256°C (dec.) and $[\alpha]_D^{25}$ +193°.

B) A solution of *IVb* (27 mg) in 0·2M aqueous solution of sodium hydroxide (2·5 ml) was left to stand at room temperature for 6 h and then neutralized with Dowex 50 (H^+). The resin was filtered off, washed with water (5 ml), and the combined filtrates were evaporated *in vacuo*. Crystallization of the residue from water afforded 14 mg (89%) of *IIa*, identical with the product prepared according to procedure *A*.

1-(3-O-Acetyl-2,5-anhydro-β-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)-dione (*IIb*)

Compound *IIb* was prepared on acetylation of *IIa* in pyridine–acetic anhydride. M.p., 225—226°C (from 2-propanol). ^{1}H NMR spectrum (100 MHz; C^2HCl_3 with 5% hexadeuteriodimethylsulfoxide): 2·16 (s, 3 H, $OCOCH_3$), 4·09 (s, 2 H, $H_{5'}$), 4·59 (dd, 1 H, $H_{3'}$, $J_{3',2'} = 3$, $J_{3',4'} < 1$), 4·74 (s, 1 H, $H_{4'}$), 5·27 (d, 1 H, $H_{2'}$, $J_{2',3'} = 3$), 5·66 (d, 1 H, H_5, $J_{5,6} = 8$), 6·05 (s, 1 H, $H_{1'}$), 7·74 (d, 1 H, H_6, $J_{6,5} = 8$), 10·28 (broad s, 1 H, $NHCOCH_3$). For $C_{11}H_{12}N_2O_6$ (286·2) calculated: 49·25% C, 4·51% H, 10·45% N; found: 48·98% C, 4·50% H, 10·25% N.

Cleavage of *IIa* with Hydrogen Bromide in Dimethylformamide

A solution of the anhydro derivative *IIa* (2·26 g; 10 mmol) in a 2·2M solution of hydrogen bromide in dimethylformamide (25 ml) was heated at 120°C for 5 min and then evaporated *in vacuo*. The residue was coevaporated with dimethylformamide (2 × 15 ml) disolved in water (40 ml), and the solution was submitted onto a column of Dowex 3 (CH_3COO^-; 200 ml). The column was eluted with water and the UV-absorbing fractions were evaporated *in vacuo*. The residue was dissolved in 2-propanol (50 ml). Deposited uracil was filtered off (620 mg; 55%) and washed with 2-propanol. The combined filtrates were evaporated under diminished pressure and the residue was acetylated in pyridine (5 ml)–acetic anhydride (5 ml). After 12 h, methanol (5 ml) was added and after standing for additional 15 min the solvents were evaporated *in vacuo*. The residue was chromatographed on a column of silica gel (100 g) in the system toluene–ethyl acetate (2 : 3). Crystallization of the first fraction from 2-propanol yielded 191 mg (5%) of *IVb*, m.p. 133—135°C. $[\alpha]_D^{25}$ +71·4° (*c* 0·45; ethyl acetate). ^{1}H NMR spectrum (100 MHz; C^2HCl_3): 2·03 (s, 3 H, 2'-$OCOCH_3$), 2·17 (s, 3 H, 3'-$OCOCH_3$), 3·75 (d, 2 H, $H_{5'}$, $J_{5',4'} = 4$), 4·21 (q, 1 H, $H_{4'}$, $J_{4',5'} = 4$, $J_{4',3'} = 4$), 5·18 (dd, 1 H, $H_{3'}$, $J_{3',2'} = 1·5$, $J_{3',4'} = 4$), 5·42 (dd, 1 H, $H_{2'}$, $J_{2',1'} = 4$, $J_{2',3'} = 1·5$), 5·77 (d, 1 H, H_5, $J_{5,6} = 8$), 6·31 (d, 1 H, $H_{1'}$, $J_{1',2'} = 4$), 7·60 (d, 1 H, H_6, $J_{6,5} = 8$), 9·30 (broad s, 1 H, NH). For $C_{13}H_{15}BrN_2O_7$ (391·2) calculated: 39·91% C, 3·87% H, 7·16% N, 20·43% Br; found: 40·01% C, 3·84% H, 7·04% N, 20·56% Br.

Crystallization of the second fraction afforded 397 mg (10%) of *V* in the form of a solid foam. The IR and ^{1}H NMR spectra were identical with those of the compound prepared by unambiguous synthesis from 1-(α-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)-dione.

1-(2,3-Di-O-acetyl-5-chloro-5-deoxy-β-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)-dione (*IVc*)

Compound *IVc* was prepared on acetylation of 1-(5-chloro-5-deoxy-β-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)-dione[4] in pyridine–acetic anhydride. M.p. after crystallization from 2-propanol–methanol 146—147°C. ^{1}H NMR spectrum (60 MHz; C^2HCl_3): 2·03 (s, 3 H, 2'-$OCOCH_3$), 2·15 (s, 3 H, 3'-$OCOCH_3$), 3·90 (d, 2 H, $H_{5'}$, $J_{5',4'} = 4$), 4·20 (q, 1 H, $H_{4'}$, $J_{4',3'} = 4$, $J_{4',5'} = 4$), 5·21 (dd, 1 H, $H_{3'}$, $J_{3',2'} = 1·5$, $J_{3',4'} = 4$), 5·40 (dd, 1 H, $H_{2'}$, $J_{2',1'} = 4$, $J_{2',3'} = 1·5$), 5·80 (d, 1 H, H_5, $J_{5,6} = 8$), 6·33 (d, 1 H, $H_{1'}$, $J_{1',2'} = 4$), 7·60 (d, 1 H, H_6, $J_{6,5} = 8$), 9·86 (broad s, 1 H, NH). For $C_{13}H_{15}ClN_2O_7$ (346·7) calculated: 45·03% C, 4·36% H, 8·08% N, 10·23% Cl; found: 45·05% C, 4·26% H, 8·16% N, 10·15% Cl.

1-(5-O-Triphenylmethyl-α-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)-dione (*VI*)

A solution of 1-(α-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)-dione[8] (2·45 g; 10 mmol) and triphenylmethyl chloride (3·50 g) in pyridine (50 ml) was allowed to stand for 4 days at room temperature and then evaporated *in vacuo*. The residue was triturated with chloroform (500 ml), the chloroform solution was washed with water (3 × 200 ml), dried with magnesium sulfate,

and evaporated *in vacuo*. The residue was chromatographed on a silica gel column (500 g) in the system ethyl acetate–acetone–ethanol–water (21 : 2 : 1 : 0·5). Yield, 3·32 g (68%) of amorphous product. IR spectrum ($CHCl_3$, *c* 0·003 mol l^{-1}): 3 617 cm^{-1} (OH), 3 397 cm^{-1} (NH); *c* 2%: 1 695 cm^{-1} (C=O), 1 599, 1 493, and 1 450 cm^{-1} (triphenyl ring). For $C_{28}H_{26}N_2O_6$ (486·5) calculated: 69·12% C, 5·39% H, 5·76% N; found: 68·98% C, 5·38% H, 5·49% N.

1-(2, 3-Di-O-acetyl-5-O-triphenylmethyl-α-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)-dione (*VII*)

Compound *VII* was prepared on acetylation of the trityl derivative *VI* (2·43 g; 5 mmol) in pyridine–acetic anhydride. Chromatography on a column of silica gel (250 g) afforded 2·42 g (85%) of *VII* in the form of a solid foam. IR spectrum ($CHCl_3$, *c* 0·003 mol l^{-1}): 3 395 cm^{-1} (NH); *c* 2%: 1 752 cm^{-1} (C=O acetate), sh 1 716 and 1 695 cm^{-1} (C=O uracil), 1 634 cm^{-1} (C=C), 1 601, 1 495, and 1 451 cm^{-1} (triphenylmethyl ring). ^1H NMR spectrum (60 MHz, C^2HCl_3): 1·97 (s, 3 H, $OCOCH_3$), 2·05 (s, 3 H, $OCOCH_3$), 3·36 (d, 2 H, $H_{5'}$, $J_{5',4'} = 5$), 4·50 (m, 1 H, $H_{4'}$), 5·38 (m, 2 H, $H_{2'}$, $H_{3'}$), 5·81 (d, 1 H, H_5, $J_{5,6} = 8$), 6·11 (d, 1 H, $H_{1'}$, $J_{1',2'} = 3$), 7·18 to 7·70 (m, 16 H, arom. protons, H_6), 9·30 (broad s, 1 H, NH). For $C_{32}H_{30}N_2O_8$ (570·6) calculated: 67·36% C, 5·30% H, 4·91% N; found: 67·16% C, 5·26% H, 4·70% N.

1-(2,3-Di-O-acetyl-α-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)-dione (*VIII*)

A solution of *VII* (1·14 g; 2 mmol) in 85% acetic acid (10 ml) was left to stand at room temperature for 4 days. Deposited triphenylmethanol was filtered off and washed with 85% acetic acid (1 ml). The combined filtrates were evaporated *in vacuo*. The residue was chromatographed on a silica gel column (50 g) in the system ethyl acetate–acetone–ethanol–water (20 : 3 : 1 : 0·5). Yield, 581 mg (88%) of the chromatographically pure acetyl derivative *VIII* in the form of a solid foam. ^1H NMR spectrum (60 MHz; C^2HCl_3): 2·10 (s, 6 H, 2 × $OCOCH_3$), 3·83 (d, 2 H, $H_{5'}$, $J_{5',4'} = 4$), 4·44 (q, 1 H, $H_{4'}$, $J_{4',3'} = 4$, $J_{4',5'} = 4$), 5·31 (t, 1 H, $H_{3'}$, $J_{3',2'} = 4$, $J_{3',4'} = 4$), 5·54 (t, 1 H, $H_{2'}$, $J_{2',1'} = 4$, $J_{2',3'} = 4$), 5·81 (d, 1 H, H_5, $J_{5,6} = 8$), 6·01 (d, 1 H, $H_{1'}$, $J_{1',2'} = 4$), 7·39 (d, 1 H, H_6, $J_{6,5} = 8$), 9·56 (broad s, 1 H, NH). For $C_{13}H_{16}N_2O_8$ (328·3) calculated: 47·56% C, 4·91% H, 8·54% N; found: 47·61% C, 5·01% H, 8·49% N.

1-(2,3-Di-O-acetyl-5-O-methanesulfonyl-α-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)-dione (*IX*)

A solution of the diacetate *VIII* (656 mg; 2 mmol) in the mixture of pyridine (4 ml) and methanesulfonyl chloride (1 ml) was left to stand for 2 h at room temperature, then for 12 h at 4°C, and eventually evaporated *in vacuo*. Ethyl acetate (50 ml) and water (15 ml) were added to the residue, the whole was shaken, the aqueous layer was separated and extracted with ethyl acetate (50 ml). The combined ethyl acetate extracts were washed with water (2 × 20 ml) and saturated solution of sodium chloride (15 ml), dried with magnesium sulfate, and evaporated *in vacuo*. The residue was chromatographed on a column of silica gel (75 g) in the system ethyl acetate–acetone–ethanol–water (40 : 6 : 1 : 0·5). Yield, 649 mg (80%) of *IX* in the form of a solid foam. ^1H NMR spectrum (60 MHz; C^2HCl_3): 2·10 (s, 3 H, $OCOCH_3$), 2·12 (s, 3 H, $OCOCH_3$), 3·09 (s, 3 H, $CH_3—SO_2$), 4·35–4·79 (m, 3 H, $H_{4'}$, $H_{5'}$), 5·30 (t, 1 H, $H_{3'}$, $J_{3',2'} = 4$, $J_{3',4'} = 4$), 5·60 (t, 1 H, $H_{2'}$, $J_{2',1'} = 4$, $J_{2',3'} = 4$), 5·67–5·96 (m, 2 H, $H_{1'}$, H_5), 7·50 (d, 1 H, H_6, $J_{6,5} = 8$), 9·70 (broad s, 1 H, NH). For $C_{14}H_{18}N_2O_{10}S$ (406·4) calculated: 41·38% C, 4·46% H, 6·90% N, 7·89% S; found: 41·26% C, 4·40% H, 6·78% N, 7·95% S.

1-(2,3-Di-O-acetyl-5-bromo-5-deoxy-α-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)-dione (*V*)

A solution of the mesyl derivative *IX* (406 mg; 1 mmol) and tetrabutylammonium bromide (1·8 g) in acetonitrile (15 ml) was heated at 90°C for 2·5 h and then evaporated *in vacuo*. The residue was dissolved in the mixture (2·5 ml) of ethyl acetate and toluene (4 : 1). The deposited compound was filtered off and washed with the mixture ethyl acetate–toluene (2 × 0·5 ml). The combined filtrates were submitted onto a column of silica gel (60 g). The column was eluted with ethyl acetate–toluene (4 : 1) to afford 344 mg (88%) of the bromo derivative *V* in the form of a solid foam. $[\alpha]_D^{25}$ −0·3 (*c* 0·45; ethyl acetate). IR spectrum ($CHCl_3$): 3 395 and 3 195 cm^{-1} (NH), 1 751 cm^{-1} (C=O acetate), sh 1 718 and 1 696 cm^{-1} (C=O uracil), 1 635 cm^{-1} (C=C). ^1H NMR spectrum (100 MHz; C^2HCl_3): 2·10 (s, 3 H, $OCOCH_3$), 2·13 (s, 3 H, $OCOCH_3$), 3·58 (d, 2 H, $H_{5'}$, $J_{5',4'}$ = 5·5), 4·63 (m, 1 H, $H_{4'}$), 5·34 (t, 1 H, $H_{3'}$, $J_{3',2'}$ = 3·5, $J_{3',4'}$ = 3·5), 5·54 (t, 1 H, $H_{2'}$, $J_{2',1'}$ = 3·5, $J_{2',3'}$ = 3·5), 5·77 (d, 1 H, H_5, $J_{5,6}$ = 8), 5·93 (d, 1 H, $H_{1'}$, $J_{1',2'}$ = 3·5), 7·31 (d, 1 H, H_6, $J_{6,5}$ = 8), 9·45 (broad s, 1 H, NH). For $C_{13}H_{15}BrN_2O_7$ (391·2) calculated: 39·91% C, 3·87% H, 7·16% N, 20·43% Br; found: 40·18% C, 3·82% H, 7·28% N, 20·53% Br.

1-(2,5-Anhydro-α-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)dione (*Xa*)

A solution of compound *V* (351 mg; 1 mmol) in 0·5M-NaOH (8 ml) was allowed to stand at room temperature for 5 h and then neutralized with Dowex 50 (H^+). The resin was filtered off, washed with water (20 ml), and the combined filtrates were neutralized with Dowex 3 (OH^-). The resin was filtered off, washed with water (20 ml), and the combined filtrates were evaporated *in vacuo*. Crystallization of the residue from 2-propanol–methanol afforded 203 mg (90%) of *Xa*, m.p. 219—224°C (decomp.) $[\alpha]_D^{25}$ −39·4° (*c* 0·51; water). UV spectrum (pH 2): λ_{max} 264 nm (log ε 4·04), λ_{min} 231 nm (log ε 3·29); pH 12: λ_{max} 262 nm (log ε 3·91), λ_{min} 242 nm (log ε 3·68). For $C_9H_{10}N_2O_5$ (226·2) calculated: 47·79% C, 4·46% H, 12·39% N; found: 47·54% C, 4·39% H, 12·19% N.

1-(3-O-Acetyl-2,5-anhydro-α-D-arabinofuranosyl)pyrimidin-2,4(1*H*,3*H*)-dione (*Xb*)

The acetyl derivative *Xb* was prepared on acetylation of *Xa* with pyridine–acetic anhydride. The product obtained on crystallization from 2-propanol–methanol melted at 225—230°C. ^1H NMR spectrum (60 MHz; C^2HCl_3 + 5% hexadeuteriodimethylsulfoxide): 2·00 (s, 3 H, $OCOCH_3$), 4·01 (q, 2 H, $H_{5'}$, $H_{5''}$, $J_{5',5''}$ = 9), 4·68 (d, 1 H, $H_{3'}$, $J_{3',2'}$ = 2), 4·87 (s, 1 H, $H_{4'}$), 5·10 (d, 1 H, $H_{2'}$, $J_{2',3'}$ = 2), 5·62 (s, 1 H, $H_{1'}$), 5·63 (d, 1 H, H_5, $J_{5,6}$ = 8), 7·68 (d, 1 H, H_6, $J_{6,5}$ = 8) 11·16 (broad s, 1 H, NH). For $C_{11}H_{12}N_2O_6$ (286·2) calculated: 49·25% C, 4·51% H, 10·45% N. found: 49·31% C, 4·62% H, 10·34% N.

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