SYNTHESIS OF 1-(3-DEOXY-3-HALO-β-D-ARABINOFURANOSYL)-6-AZAURACIL, 1-(3-DEOXY-β-D-THREO-PENTOFURANOSYL)-6-AZAURACIL, AND THEIR ACETYL DERIVATIVES* **

J. BROKEŠ and J. BERÁNEK

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6

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Reaction of the trityl epoxy derivative *Ia* with hydrogen chloride (8%) in dimethylformamide at room temperature affords in 70% yield the 3-chloro derivative *IIa* of the *arabino* series. By reaction with hydrogen bromide (hydrogen chloride) in dimethylformamide, the epoxy derivative *Ib* is converted to the 3'-bromo (3'-chloro) derivative *IIc* (*IIa*) in 87% (77%) yield. The acetyl derivative *IIb* (*IId*) prepared by acetylation with acetyl chloride in acetic acid, is reduced with tri-n-butyltin hydride to the 3'-deoxy derivative *IIe* in 62% (75%) yield. Methanolysis of compound *IIe* affords the 3'-deoxy derivative *IIf* whereas the partial methanolysis with methanolic ammonia results in the formation of the 5'-monoacetyl derivative *IIg*. By reaction with one equivalent of sodium methoxide, the 3'-bromo derivative *IIc* is converted to the epoxy derivative *Ib*. On comparison of $J_{1',2'}$ and $J_{2',3'}$ coupling constants in ^{1}H NMR spectra of compounds *IIa*—*IIi* with those of 6-azauracil ribofuranosyl and arabinofuranosyl derivatives, the *arabino* or *threo* configuration of these compounds has been established.

In the previous paper[2], the reaction of the 2',3'-epoxy derivatives *Ia* and *Ib* with ammonia has been examined. As a continuation of the study on the reactivity of epoxy derivatives in the nucleoside series towards nucleophilic agents, the reaction of derivatives *Ia* and *Ib* with hydrogen halides is reported in the present paper.

In the earlier work[2], the detritylation of the epoxy derivative *Ia* with ethereal hydrogen chloride has been observed to be accompanied even under very mild conditions, *i.e.*, at room temperature, by a cleavage of the epoxide ring with the formation of the 3'-chloro derivative *IIa*. The detritylated product *Ib* was almost insoluble in the reaction medium and only a partial opening of the epoxide ring took place in the heterogeneous phase[2]; at a higher concentration (3M) of ethereal hydrogen chloride there was obtained only 14% of the 3'-chloro derivative *IIa* while a lower concentration (0·6M) favoured a higher yield (61%) of compound *IIa*. When the reaction was performed in solution with hydrogen chloride (8%) in dimethylformamide

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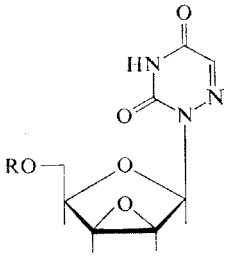
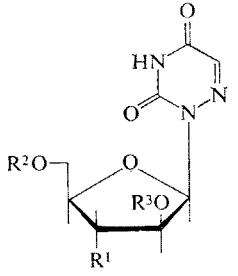
as solvent at room temperature, a single product was obtained from compound *Ia*, namely the 3′-chloro derivative *IIa*. The reaction rate increased with the increasing concentration of hydrogen chloride. As expected in accordance with the nucleophilicity of the two reagents, the reaction of compound *Ib* with hydrogen bromide was faster by one order of magnitude than the reaction with hydrogen chloride, under otherwise the same reaction conditions. Moreover, the yield of the 3′-bromo derivative *IIc* was by about 10% higher than that one of the 3′-chloro derivative *IIa*.



Ia, R = Tr
Ib, R = H



IIa, R^1 = Cl, R^2 = R^3 = H
IIb, R^1 = Cl, R^2 = R^3 = Ac
IIc, R^1 = Br, R^2 = R^3 = H
IId, R^1 = Br, R^2 = R^3 = Ac
IIe, R^1 = H, R^2 = R^3 = Ac
IIf, R^1 = R^2 = R^3 = H
IIg, R^1 = H, R^2 = Ac, R^3 = H
IIh, R^1 = NHAc, R^2 = R^3 = Ac
IIi, R^1 = NHAc, R^2 = R^3 = H
IIj, R^1 = OAc, R^2 = R^3 = Ac

In contrast to the reaction of sugar furanoside epoxy derivatives with hydrogen halides which affords a mixture of the two possible isomers, namely, the corresponding 2- and 3-halo derivatives[3–7], only the formation of the 3′-halo derivatives is observed in the nucleoside series[8,9]. In accordance with these[8,9] results, the 3′-halo derivative of the *arabino* configuration was the single product of the reaction of compound *Ia* with hydrogen halides. Compounds *IIa* and *IIc* were isolated in 77% and 87% yields, resp. In mother liquors remaining after crystallisation of compound *IIc* there was chromatographically detected the presence of a small amount of an additional substance (of a close R_F value and a different IR spectrum), probably 1-(2-bromo-2-deoxy-β-D-xylofuranosyl)-6-azauracil. The quantity of this by-product was not sufficient to allow an exact identification. By the action of one equivalent of sodium methoxide, the 3′-bromo derivative *IIc* was transformed into the epoxy derivative *Ib*, identical with an authentic specimen[2].

Acetylation with acetyl chloride and acetic anhydride in acetic acid[10] was used to convert the 3'-halo derivatives *IIa* and *IIc* to the corresponding diacetyl derivatives *IIb* and *IId* in 90% yield. These diacetyl derivatives were used in spectral measurements and in the preparation of the 3'-deoxy derivative *IIf*. The acetylated halo derivatives *IIb* and *IId* were reduced with tri-n-butyltin hydride[11–13] in refluxing benzene in the presence of 2,2'-azobis(2-methylpropionitrile)[12]. Concerning the course of the reduction, the reaction rate was considerably higher in the case of the 3'-bromo derivative *IId* (30 min) than with the 3'-chloro derivative *IIb* (3 h). Furthermore, the yield with compound *IId* was higher (75%) than that with compound *IIb* (62%). These results are in accordance with those reported[12]. Even the reduction of the more reactive 3'-bromo derivative *IId* did not take place without the addition of 2,2'-azobis(2-methylpropionitrile) in spite of the use of refluxing benzene as the reaction medium.

The sodium methoxide-catalysed methanolysis of the reduction product *IIe* yielded 81% of 1-(3-deoxy-β-D-*threo*-pentofuranosyl)-6-azauracil (*IIf*). By the action of methanolic ammonia (18%) at room temperature for 2 h, compound *IIe* afforded a mixture of the monoacetyl derivative *IIg*, the 3'-deoxy derivative *IIf*, and the starting diacetyl derivative *IIe*. From this mixture, the 5'-monoacetyl derivative *IIg* was isolated in 51% yield by thin-layer chromatography on silica gel. Position of the acetyl group was determined by means of ^{1}H-NMR spectra from comparison of chemical shifts of protons at positions 2' and 5'. With compounds *IIf* and *IIg*, the signal of the $H_{2'}$ proton occurs in the same region and differs from the $H_{2'}$ signal of the diacetyl derivative *IIe*; consequently, the acetyl group of compound *IIg* can not be placed at position 2'. In accordance with this finding, the chemical shifts of $H_{5'}$ protons are similar in the case of the diacetyl derivative *IIe* and the monoacetyl derivative *IIg* and differ from the chemical shifts of $H_{5'}$ protons of the deacetylated compound *IIf*. Both comparisons confirm the substitution at position 5' of compound *IIg*. This preferential methanolysis of the secondary acetyl group could be compared with the earlier observations on the methanolysis of 6-azauridine formyl derivatives[14] which results in a preferential selective solvolysis of secondary formyl groups at the expense of the primary formyl group.

The ^{1}H-NMR spectra of the present compounds are in accord with the assumed structures. The $J_{1',2'}$ and $J_{2',3'}$ coupling constants of the 3'-acetamido (*IIh* and *IIi*), 3'-halo (*IIa–d*), and 3'-deoxy (*IIe–g*) derivatives were compared with the known ^{1}H-NMR spectra of 6-azauracil ribofuranosyl and arabinofuranosyl derivatives. The $J_{1',2'}$ coupling constants of derivatives *IIa–e,g* (6·5–6·9 Hz), *IIf* (6·1 Hz), and *IIi* (6·0 Hz) were in full accordance with the $J_{1',2'}$ value (6·5 Hz) of compound *IIj*. Also some further 6-azauracil derivatives with a *cis* system of protons at positions 1' and 2' exhibit the $J_{1',2'}$ value higher than 5·0 Hz such as 1-β-D-arabinofuranosyl-6-azaisocytosine[15] (6·5 Hz), 1-(5-O-benzoyl-β-D-lyxofuranosyl)-6-azauracil[16] (7·0 Hz), 1-(2,3,5-tri-O-acetyl-β-D-lyxofuranosyl)-6-azauracil[16] (5·0 Hz). On the other hand,

the $J_{1',2'}$ coupling constant of compounds with a *trans* system of protons at positions 1′ and 2′ is appreciably lower, *e.g.* in the case of tri-O-acetyl-6-azauridine (3·5 Hz), 5′-O-benzoyl-6-azauridine[16] (2·0 Hz), 5′-O-acetyl-3′-O-tosyl-6-azauridine[17] (3·5Hz), 1-(5-O-acetyl-3-deoxy-3-iodo-β-D-xylofuranosyl)-6-azauracil[17] (1·5 Hz), and 1-(3-deoxy-β-D-*erythro*-pentofuranosyl)-6-azauraci[17] (1·5 Hz).

With compounds *IIa–d,h*, the $J_{2',3'}$ coupling constant was in the region of 8·7–9·5 Hz; in the case of the 3′-deoxy derivatives *IIe–g*, the $J_{2',3'}$ value was between 7·7 and 8·0 Hz and the $J_{2',2''}$ value was between 10·3 and 10·6 Hz. On the other hand in the series of 6-azauracil ribofuranosyl derivatives, the $J_{2',3'}$ coupling constant was 5·5 Hz (tri-O-acetyl-6-azauridine) and 5·0 Hz (5′-O-acetyl-3′-O-(p-toluenesulfonyl)-6-azauridine[17]). On comparison of $J_{1',2'}$ and $J_{2',3'}$ coupling constants, the *arabino* (or *threo*) configuration of compounds *IIa–i* has been unequivocally established. While the difference between coupling constants in the 6-aza series is great enough and unambiguously indicates the *arabino* or *ribo* configuration of the particular nucleosides, the uracil series exhibits only a small difference between the $J_{1',2'}$ coupling constants of uridine tri-O-acetyl derivative (4·6 Hz) and arabinofuranosyluracil tri-O-acetyl derivative (3·9 Hz) and it is therefore hardly possible in the uracil series to use these coupling constant values as the single criterion in configurational determinations.

Conformation of the sugar moiety of the present compounds can not be exactly determined from the above mentioned ^{1}H-NMR spectral values. Notwithstanding, the E_2 conformation might be ascribed to the 3′-halo derivatives *IIa–d* on the basis of calculations with the use of a simple Karplus equation which has also been used in conformational determinations of the 3′-halo derivatives in the uracil series[8]. The E_2 conformation has also been calculated[18] for methyl 1-β-D-arabinofuranosides. The difference between the 6-azauracil and uracil series (the T_1^0 conformation has been calculated[8] for the latter series) might be explained by the influence of the aglycon portion of the nucleoside on the steric arrangement of the sugar moiety.

EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block) and were not corrected. Analytical samples were dried at 50°C/0·1 Torr for 12 h. Thin-layer chromatography was performed on ready-for-use Silufol UV_{254} (Kavalier Glassworks, Votice, Czechoslovakia) silica gel foils in the solvent systems S_1, ethyl acetate; S_2, ethyl acetate–benzene (1 : 1); and S_3, ethyl acetate–methanol (9 : 1). Spots were detected by viewing under UV light. Column chromatography was carried out on Pitra silica gel (particle size 30–60 μ) and preparative thin-layer chromatography was performed on fluorescent silica gel; both materials are produced by Service Laboratories of this Institute. The UV spectra were taken on a single-beam Optica Milano CF-4 spectrophotometer. The IR spectra were recorded on a Zeiss Model UR-20 apparatus. The ^{1}H-NMR spectra were measured on a Varian HA-100 apparatus at 100 MHz. Optical rotations were determined on a Perkin-Elmer Model 141 MC polarimeter. Unless stated otherwise, the solutions were taken down on a rotatory evaporator at 20 Torr and temperatures

between 20°C and 50°C depending on the boiling point of the solvent. Pyridine was dried over potassium hydroxide at room temperature. Other solvents were dried as usual and stored over molecular sieves Potassit 3 (Research Institute for Petroleum and Hydrocarbons, Bratislava, Czechoslovakia).

1-(3-Chloro-3-deoxy-β-D-arabinofuranosyl)-6-azauracil (*IIa*)

A. A solution of the trityl derivative[2] *Ia* (469·5 mg; 1 mmol) in 8% hydrogen chloride in dimethylformamide (20 ml) was kept at room temperature overnight, evaporated, and the residue coevaporated with three 30 ml portions of toluene to remove excess hydrogen chloride. The final residue (60°C/0·5 Torr) was distributed between water (150 ml) and chloroform (three 50 ml portions). The aqueous phase was evaporated under diminished pressure, the residue coevaporated with three 20 ml portions of 1 : 1 ethanol–benzene, and finally chromatographed on a loose silica gel layer (40 × 18 × 0·1 cm) in ethyl acetate. The band corresponding by its mobility to the nucleoside *IIa* was eluted with methanol and the eluate evaporated. Crystallisation of the residue (262 mg) from ethyl acetate (5 ml) yielded 161 mg (61·1%) of compound *IIa*, m.p. 188–191°C. The mother liquors were evaporated and the residue (102 mg) crystallised from ethyl acetate (1 ml) to afford additional 24 mg (9·1%) of compound *IIa*, m.p. 182–186°C.

B. A solution of the epoxy derivative[2] *Ib* (227 mg; 1 mmol) in 8% hydrogen chloride in dimethylformamide (15 ml) was kept at room temperature overnight and processed analogously to paragraph *A*. Crystallisation of the residue (272 mg) from ethyl acetate (5 ml) yielded 171 mg of the chloro derivative *IIa*, m.p. 186–190°C. Work-up of mother liquors yielded additional 31 mg of the same product, m.p. 182–185°C; overall yield, 76·8%. Optical rotation: $[\alpha]_D^{25}$ −54·3° (*c* 0·55; methanol). UV spectrum (ethanol). λ_{max} 267 nm (log ε 3·73) and λ_{min} 233 nm (log ε 3·43). IR spectrum (nujol): 3445 and 3350 cm^{-1} (OH), 1725 and 1684 cm^{-1} (C=O). ^{1}H-NMR spectrum in a mixture of hexadeuteriodimethyl sulfoxide and deuteriochloroform (hexamethyldisiloxane as internal standard, recalculated to tetramethyl silane, chemical shifts in p.p.m., CF_3COOD exchange): 3·60 (m, 2 H, $J_{4',5'a}$ = 6 Hz, $J_{4',5'b}$ = 3·2 Hz, J_{gem} = 12·0 Hz, $H_{5'a}$, $H_{5'b}$), 3·92 (septet, 1 H, $J_{4',3'}$ = 8·7 Hz, $H_{4'}$), 4·24 (t, 1 H, $J_{3',2'}$ = 8·7 Hz, $H_{3'}$), 4·52 (q, 1 H, $J_{2',1'}$ = 6·8 Hz, $H_{2'}$), 6·20 (d, 1 H, $H_{1'}$); before the exchange: 4·70 (t, 1 H, $J_{OH,5'}$ = 6·0 Hz, $O^5'H$), 5·95 (d, 1 H, $J_{OH,2'}$ = 6·0 Hz, $O^2'H$). For $C_8H_{10}ClN_3O_5$ (263·6) calculated: 36·45% C, 3·82% H, 15·94% N, 13·45% Cl; found: 36·34% C, 3·87% H, 16·16% N, 13·58% Cl.

1-(2,5-Di-O-acetyl-3-chloro-3-deoxy-β-D-arabinofuranosyl)-6-azauracil (*IIb*)

A mixture of the chloro derivative *IIa* (211 mg; 0·8 mmol), acetic anhydride (5 ml), acetyl chloride (1 ml), and acetic acid (5 ml) was stirred until the solid dissolved, the solution kept at room temperature overnight, diluted with toluene (40 ml), and evaporated under diminished pressure. The residue was coevaporated with three 30 ml portions of toluene and with methanol (30 ml). Crystallisation of the final residue (281 mg) from benzene (4 ml) yielded 253 mg (91%) of the chromatographically homogeneous compound *IIb*, m.p. 141–144°C. Optical rotation: $[\alpha]_D^{25}$ −82·7° (*c* 0·54; methanol). UV spectrum (ethanol): λ_{max} 262 nm (log ε 3·76) and λ_{min} 223 nm (log ε 3·45). IR spectrum (chloroform): 3376 cm^{-1} (NH free), 3207 (NH bound), 1744 cm^{-1} (C=O acetate), 1722 and 1701 cm^{-1} (C=O azauracil), 1594 cm^{-1} (C=N). ^{1}H-NMR spectrum in a mixture of hexadeuteriodimethyl sulfoxide and deuteriochloroform (hexamethyldisiloxane as internal standard, recalculated to tetramethylsilane, chemical shifts in p.p.m.): 4·24 (m, 2 H, $J_{4',5'a}$ = 2·4 Hz, $J_{4',5'b}$ = 1·8 Hz, J_{gem} = 9·0 Hz, $H_{5'a}$, $H_{5'b}$), 4·47 (m, 1 H, $J_{4',3'}$ = 9·5 Hz, $H_{4'}$), 4·63 (t, 1 H, $J_{3',2'}$ = 9·5 Hz, $H_{3'}$), 5·53 (2 d, 1 H, $J_{2',1'}$ = 6·9 Hz, $H_{2'}$), 6·61 (d, 1 H, $H_{1'}$),

7·47 (s, 1 H, H_5), 9·76 (broad s, 1 H, NH), 2·07 (s, 3 H, CH_3CO), 2·09 (s, 3 H, CH_3CO). For $C_{12}H_{14}ClN_3O_7$ (347·7) calculated: 41·45% C, 4·06% H, 12·08% N, 10·20% Cl; found: 41·37% C, 4·06% H, 12·27% N, 10·34% Cl.

1-(3-Bromo-3-deoxy-β-D-arabinofuranosyl)-6-azauracil (*IIc*)

A solution of the epoxy derivative *Ib* (227 mg, 1 mmol) in 3% hydrogen bromide in dimethylformamide (15 ml) was kept at room temperature for 2 h, coevaporated with three 30 ml portions of toluene to remove excess hydrogen bromide, and finally evaporated at 60°C/0·5 Torr. The residue was chromatographed on a layer (40 × 18 × 0·1 cm) of loose silica gel in ethyl acetate. The band corresponding by its mobility to the bromo derivative *IIc*, was eluted with methanol, the eluate evaporated, and the residue crystallised from ethyl acetate (4 ml) to afford 203 mg (65·9%) of compound *IIc*, m.p. 175–177°C. The mother liquors were evaporated and the residue crystallised from ethyl acetate (1 ml) to yield additional 67 mg (21·4%) of the chromatographically homogeneous nucleoside *IIc*, m.p. 170–179°C (after repeated crystallisation from ethyl acetate). Optical rotation: $[\alpha]_D^{25}$ −50·4° (*c* 0·48; methanol). UV spectrum (ethanol): λ_{max} 267 nm (log ε 3·67) and λ_{min} 233 nm (log ε 3·33). IR spectrum (nujol): 1593 cm^{-1} (C=N), 1676, 1700 and 1714 cm^{-1} (C=O), 3190 and 3285 cm^{-1} (NH, OH), 3525 cm^{-1} (OH). ^{1}H-NMR spectrum in a mixture of deuteriochloroform and hexadeuteriodimethyl sulfoxide (hexamethyldisiloxane as internal standard, recalculated to tetramethylsilane, chemical shifts in p.p.m.): 3·95 (broad s, 2 H, O^2H, O^5H), 3·55 (2 d, 1 H, $J_{5'a,4'}$ = 5·8 Hz, J_{gem} = 12·0 Hz, $H_{5'a}$), 3·70 (2 d, 1 H, $J_{5'b,4'}$ = 3·0 Hz, $H_{5'b}$), 4·03 (septet, 1 H, $J_{4',3'}$ = 9·0 Hz, $H_{4'}$), 4·24 (t, 1 H, $J_{3',2'}$ = = 8·8 Hz, $H_{3'}$), 4·58 (q, 1 H, $J_{2',1'}$ = 6·8 Hz, $H_{2'}$), 6·18 (d, 1 H, $H_{1'}$), 7·40 (s, 1 H, H_5), 12·11 (broad s, 1 H, NH). For $C_8H_{10}BrN_3O_5$ (308·1) calculated: 31·19% C, 3·27% H, 13·64% N, 25·94% Br; found: 31·32% C, 3·39% H, 13·64% N, 26·12% Br.

1-(2,5-Di-O-acetyl-3-bromo-3-deoxy-β-D-arabinofuranosyl)-6-azauracil (*IId*)

A mixture of the bromo derivative *IIc* (200 mg, 0·65 mmol), acetic anhydride (5 ml), acetyl chloride (1 ml), and acetic acid (5 ml) was stirred until the solid dissolved, the solution kept at room temperature overnight, diluted with toluene (40 ml), and evaporated under diminished pressure. The residue was coevaporated with three 40 ml portions of toluene and with methanol (30 ml). Crystallisation of the final residue (259 mg) from benzene (4 ml) yielded 230 mg (90·2%) of the chromatographically homogeneous diacetyl derivative *IId*, m.p. 143–145°C. Optical rotation: $[\alpha]_D^{25}$ −83·4° (*c* 0·52; methanol). UV spectrum (ethanol): λ_{max} 263 nm (log ε 3·73) and λ_{min} 226 nm (log ε 3·41). IR spectrum (chloroform): 1591 cm^{-1} (C=N), 3205 cm^{-1} (NH bound) 3376 cm^{-1} (NH free). ^{1}H-NMR spectrum in a mixture of deuteriochloroform and hexadeuteriodimethyl sulfoxide (hexamethyldisiloxane as internal standard, recalculated to tetramethylsilane, chemical shifts in p.p.m.): 1·98 (s, 3 H, CH_3CO), 2·00 (s, 3 H, CH_3CO), 4·00–4·50 (m, 3 H, $H_{4'}$, $H_{5'a}$, $H_{5'b}$), 4·57 (broad t, 1 H, $J_{4',3'}$ = 9·0 Hz, $H_{3'}$), 5·55 (q, 1 H, $J_{3',2'}$ = 9·5 Hz, $H_{2'}$), 6·45 (d, 1 H, $J_{1',2'}$ = 7·0 Hz, $H_{1'}$), 7·39 (s, 1 H, H_5), 12·23 (broad s, 1 H, NH). For C_{12}. $H_{14}BrN_3O_7$ (392·2) calculated: 36·75% C, 3·60%H, 10·71% N, 20·38% Br; found: 36·44% C, 3·62% H, 10·52% N, 20·75% Br.

1-(2,3-Epoxy-β-D-lyxofuranosyl)-6-azauracil (*Ib*)

A mixture of the bromo derivative *IIc* (62 mg; 0·2 mmol) and 1M methanolic sodium methoxide (0·4 ml) was kept at room temperature for 4 h, diluted with methanol (10 ml), and neutralised by the addition of Dowex 50 (H^+) ion exchange resin previously washed with methanol. The resin

was filtered off and the filtrate passed through a column of Dowex 3 (OH^-) ion exchange resin previously washed with methanol. The residue (45 mg) of the efluent contained a single UV-absorbing compound *Ib*, m.p. 189—194°C (methanol), identical with an authentic specimen[2].

1-(2,5-Di-O-acetyl-3-deoxy-β-D-*threo*-pentofuranosyl)-6-azauracil (*IIe*)

A. *From* 1-(2,5-*di*-O-*acetyl*-3-*chloro*-3-*deoxy*-β-D-*arabinofuranosyl*)-6-*azauracil* (IIb). A refluxing solution of the chloro derivative *IIb* (139 mg; 0·4 mmol), tri-n-butyltin hydride (466 mg; 1·6 mmol), and benzene (10 ml) was treated with 2,2'-azobis(2-methylpropionitrile) (50 mg), the reflux continued for 3 h, and the reaction mixture evaporated under diminished pressure. The residue was chromatographed on a layer (40 × 18 × 0·1 cm) of loose silica gel in the solvent mixture 1 : 1 ethyl acetate–benzene. The band containing the diacetyl derivative *IIe* was eluted with ethyl acetate, the eluate evaporated, and the chromatographically homogeneous residue (91 mg) crystallised from 2-propanol (1 ml) to afford 77 mg (61·5%) of the diacetyl derivative *IIe*, m.p. 136—139°C. Optical rotation: $[\alpha]_D^{25}$ −41·2° (*c* 0·50; methanol). UV spectrum (ethanol): λ_{max} 266 nm (log ε 3·71) and λ_{min} 228 nm (log ε 3·38). IR spectrum (chloroform): 1589 cm^{-1} (C=N), 1711 sh cm^{-1} (C=O), 3200 cm^{-1} (NH bound), 3379 cm^{-1} (NH free). ^{1}H-NMR spectrum in deuteriochloroform (hexamethyldisiloxane as internal standard, recalculated to tetramethylsilane, chemical shifts in p.p.m.): 1·92 (s, 3 H, CH_3CO), 2·02 (s, 3 H, CH_3CO), 4·00—4·50 (m, 3 H, $H_{5'a}$, $H_{5'b}$, $H_{4'}$), 2·00—2·50 (m, 2 H, $J_{2',3'a}$ = 8·0 Hz, $J_{2',3'b}$ = 10·5 Hz, $H_{3'a}$, $H_{3'b}$), 5·41 (dq, 1 H, $J_{2',1'}$ = 6·8 Hz, $H_{2'}$), 6·43 (d, 1 H, $H_{1'}$), 7·34 (s, 1 H, H_5), 12·03 (broad s, 1 H, NH). For $C_{12}H_{15}N_3O_7$ (313·3) calculated: 46·01% C, 4·83% H, 13·41% N; found: 45·72% C, 4·96% H, 13·28% N.

B. *From* 1-(2,5-*di*-O-*acetyl*-3-*bromo*-3-*deoxy*-β-D-*arabinofuranosyl*)-6-*azauracil* (IId). A mixture of the bromo derivative *IId* (79 mg; 0·2 mmol), tri-n-butyltin hydride (233 mg, 0·8 mmol), and benzene (7 ml) was heated to the boiling point; 2,2'-azobis(2-methylpropionitrile) (30 mg) was then added, the whole refluxed for 30 min, and evaporated under diminished pressure. The residue was chromatographed on a layer (40 × 18 × 0·1 cm) of loose silica gel in the solvent system 1 : 1 ethyl acetate–benzene. The band corresponding to the diacetyl derivative *IIe* was eluted with ethyl acetate, the eluate evaporated, and the residue (52 mg) crystallised from 2-propanol (0·8 ml) to afford 47 mg (74·6%) of compound *IIe*, m.p. 137—141°C, identical in every respect with the substance obtained by reduction of the chloro derivative *IIb*.

1-(3-Deoxy-β-D-*threo*-pentofuranosyl)-6-azauracil (*IIf*)

A solution of the diacetyl derivative *IIe* (150 mg; 0·48 mmol) in 1M methanolic sodium methoxide (2 ml) was kept at room temperature for 3 h and then neutralised by the addition of Dowex 50 (H^+) ion exchange resin. The resin was filtered off, the filtrate evaporated under diminished pressure, and the residue (112 mg) crystallised from ethyl acetate (4 ml) to afford 70 mg (63·6%) of the nucleoside *IIf*, m.p. 133·0—135·5°C. The mother liquors were evaporated and the residue crystallised from ethyl acetate (1 ml) to yield additional 19 mg (17·3%) of the same product, m.p. 130—133°C. Overall yield, 81%. Optical rotation: $[\alpha]_D^{25}$ −29·3° (*c* 0·33; methanol). UV spectrum (ethanol): λ_{max} 269 nm (log ε 3·75) and λ_{min} 232 nm (log ε 3·35). IR spectrum (nujol): 1594 cm^{-1} (C=N), 1683, 1694 and 1715 cm^{-1} (C=O), 3155, 3235 and 3390 cm^{-1} (NH, OH), 3470 and 3508 cm^{-1} (OH). ^{1}H-NMR spectrum in deuteriochloroform with 5% of hexadeuteriodimethyl sulfoxide (hexamethyldisiloxane as internal standard, recalculated to tetramethylsilane, chemical shifts in p.p.m.): 1·75—2·30 (m, 2 H, $J_{3'a,2'}$ = 10·3 Hz, $J_{3'b,2'}$ = 7·9 Hz, $H_{3'a}$, $H_{3'b}$), 3·67 (d, 2 H, $J_{5'a,4'} = J_{5'b,4'}$ = 5·5 Hz, $H_{5'a}$, $H_{5'b}$), 4·08 (m, 1 H, $J_{4',3'a}$ = 6 Hz, $J_{4',3'b}$ =

= 7 Hz, $H_{4'}$), 4·60 (m, 1 H, $J_{2',1'}$ = 6·4 Hz, $H_{2'}$), 6·21 (d, 1 H, $H_{1'}$), 7·36 (s, 1 H, H_5), 11·96(broad s, 1 H, NH). For $C_8H_{11}N_3O_5$ (229·2) calculated: 41·92% C, 4·84% H, 18·33% N; found: 42·02% C, 4·85% H, 18·28% N.

TABLE I

Thin-Layer Chromatography of Compounds *Ia—IIg*: R_F Values in Solvent Systems S_1—S_3

Compound	*Ia*	*Ib*	*IIa*	*IIb*	*IIc*	*IId*	*IIe*	*IIf*	*IIg*
S_1	0·91	0·13	0·56	0·93	0·59	0·94	0·82	0·09	0·43
S_2	0·63	0·03	0·13	0·58	0·14	0·59	0·37	0·0	0·09
S_3	0·96	0·55	0·82	0·97	0·89	0·97	0·93	0·49	0·79

1-(5-O-Acetyl-3-deoxy-β-D-*threo*-pentofuranosyl)-6-azauracil (*IIg*)

A solution of the diacetyl derivative *IIe* (147 mg; 0·47 mmol) in 18% methanolic ammonia was kept at room temperature for 2 h and evaporated under diminished pressure. The residue was chromatographed on a layer (40 × 18 × 0·1 cm) of loose fluorescent silica gel in ethyl acetate. The R_F 0·4 band was eluted with methanol, the eluate evaporated, and the residue (72 mg) crystallised from 2-propanol (1·5 ml) to yield 65 mg (51%) of the nucleoside *IIg*, m.p. 137—139°C. UV spectrum (ethanol): λ_{max} 269 nm (log ε 3·73) and λ_{min} 233 nm (log ε 3·34). IR spectrum (nujol): 1 597 cm^{-1} (C=N), 1 681, 1 701 and 1 712 cm^{-1} (C=O azauracil), 1 745 cm^{-1} (C=O acetate), 3 205 and 3 350 cm^{-1} (NH, OH). ^{1}H-NMR spectrum in deuteriochloroform with 5% hexadeuteriodimethyl sulfoxide (hexamethyldisiloxane as internal standard, recalculated to tetramethylsilane, chemical shifts in p.p.m.): 2·05 (s, 3 H, CH_3CO), 1·80—2·40 (m, 2 H, $J_{3'a,2'}$ = 10·6 Hz, $J_{3'b,2'}$ = 7·7 Hz, $H_{3'a}$, $H_{3'b}$), 4·10—4·35 (m, 3 H, $H_{5'a}$, $H_{5'b}$, $H_{4'}$), 4·65 (m, 1 H, $J_{2',1'}$ = 6·5 Hz, $H_{2'}$), 6·28 (d, 1 H, $H_{1'}$), 11·85 (broad s, 1 H, NH). For $C_{10}H_{13}N_3O_6$ (271·2) calculated: 44·28% C, 4·83% H, 15·49% N; found: 43·99% C, 4·99% H, 15·40% N.

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