# SYNTHESIS OF 1-(3-AMINO-3-DEOXY-β-D-ARABINOFURANOSYL)-6-AZAURACIL AND ITS ACETYL DERIVATIVES* **

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The dimesyl derivative *I* affords the anhydro derivative *II* by heating in aqueous pyridine. By reaction with methanolic sodium methoxide at room temperature, compound *II* is converted to the epoxy derivative *IIIa*. By reaction with methanolic ammonia under pressure at 160°C, compound *IIIa* affords the amino derivative *IVa* which is transformed to the triacetyl derivative *IVc* by detritylation and the subsequent acetylation. The base-catalysed methanolysis of the triacetyl derivative *IVc* affords the N-acetyl derivative *IVd*. Detritylation of compound *IIIa* with ethereal hydrogen chloride leads to a mixture of the epoxy derivative *IIIb* and 3'-chloro derivative *Vc*. The ratio of *IIIb* to *Vc* depends on the concentration of hydrogen chloride in ether. On treatment with methanolic ammonia under the above conditions, compound *IIIb* affords the amino derivative *IVb* which is converted to the hydrochloride of the diacetyl derivative *IVc* by reaction with acetyl chloride. The tritylarabinosyl derivative *Va* is obtained by the alkali-induced ring opening of the known 2,2'-anhydro-1-(5-O-trityl-β-D-arabinofuranosyl)-6-azauracil. By reaction with ethereal hydrogen chloride, compound *Va* affords the arabinosyl derivative *Vb*.

In connection with the earlier synthetic works[2-4] from the field of 6-azauridine analogues as potential biologically active substances, our attention has been now directed to novel, chemically and biologically no less interesting nucleoside derivatives, namely, the 2',3'-epoxy derivatives. The reactions have been first investigated in the 6-azauridine series. The present paper relates to the preparation of the 2',3'-epoxy derivative *III* and its utilisation in the synthesis of 1-(3-amino-3-deoxy-β-D-arabinofuranosyl)-6-azauracil (*IVb*) and its acetyl derivatives *IVc*–*IVe*. The $^1$H-NMR spectra of these compounds and the synthesis of 3'-halo and 3'-deoxy derivatives are discussed in the next communication[5].

In the preparation of the epoxy derivative *IIIa*, use was made of the earlier examined high reactivity of 6-azauridine 2,2'-anhydro derivatives[3,4]. The starting derivative *I* (readily accessible from 5'-O-trityl-6-azauridine by mesylation[2]) was

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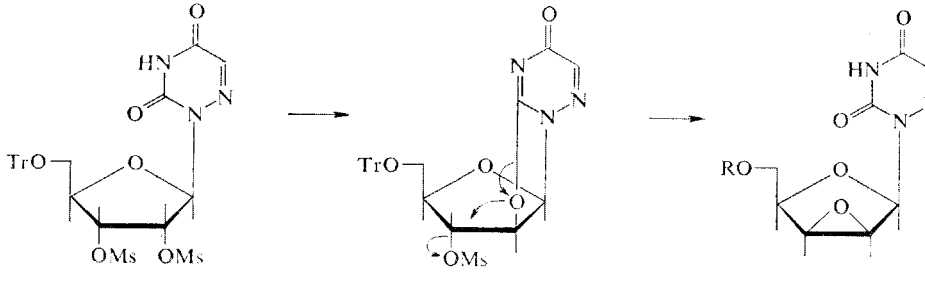
converted in 50% yield to the anhydro derivative *II* on heating in 60% aqueous pyridine[6]. The thus-obtained derivative *II* was identical with the substance obtained earlier either by mesylation of 2,2'-anhydro-1-(5-O-trityl-β-D-arabinofuranosyl)-6-azauracil[3] or by reaction of the derivative *I* with one equivalent of sodium ethoxide at an elevated temperature[2]. On the other hand, the attempted hydrolysis of the anhydro derivative *II* to 1-(5-O-trityl-β-D-lyxofuranosyl)-6-azauracil by the action of aqueous pyridine (analogously to the preparation of lyxofuranosylcytosine[6]) failed. When compared with the cytosine derivative, the hydrolysis is very slow and leads to a complex mixture which does not contain the expected *lyxo* isomer. By chromatography on silica gel, there were isolated three crystalline substances from which none was oxidised with periodic acid in contrast to the easy oxidation of 6-azauracil lyxofuranosyl and ribofuranosyl derivatives[2]. One of the isolated substances was identified as triphenylmethanol. None of the hydrolytical products was identical with derivatives *IIIa* or *Va*. For the purpose of comparison, the arabinosyl derivative *Va* was prepared by alkaline hydrolysis of 2,2'-anhydro-1-(5-O-trityl-β-D-arabinofuranosyl)-6-azauracil[7]. The subsequent removal of the trityl group by the action of ethereal hydrogen chloride furnished the arabinosyl-6-azauracil *Vb* identical with an authentic specimen[7].

In contrast to the 2',3'-epoxy derivative of the uracil series[8], the treatment of the 2',3'-dimesyl derivative *I* with excess sodium methoxide at room temperature does not bring about a direct conversion to the corresponding 2',3'-epoxy derivative *IIIa*. In the 6-aza series, a previous preparation of the 2,2'-anhydro compound *II* is necessary to obtain the epoxy derivative *IIIa*. It was thus unequivocally established in the 6-aza series that the formation of epoxy derivative *IIIa* from *I* (*cf.*[3]) proceeds *via* the 2,2'-anhydro derivative, in accordance with the earlier proposal for the uracil series[8]. The difference between reactivities of the two series (the uracil and 6-azauracil ones) is due to the more difficult formation of the 2,2'-anhydro bond in the 6-aza series in accord with the earlier observations[2,4,7]. From the anhydro compound

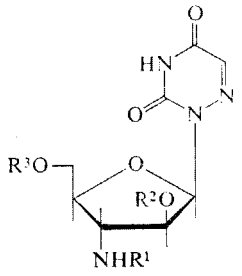



*I* *II* *IIIa*, R = Tr
*IIIb*, R = H

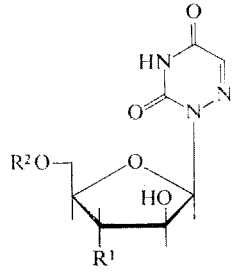
*II*, the epoxy derivative *IIIa* is formed very readily by the action of two equivalents of sodium ethoxide at room temperature in 89% yield. On treatment with methanolic sodium methoxide at the reflux temperature[2], the dimesyl derivative *I* fursnished the anhydro derivative *II* which was directly *in situ* converted to the epoxy derivative *IIIa* by the action of an additional equivalent of the base. Compound *IIIa* was isolated by chromatography on silica gel in 65·6% yield (referred to compound *I*).

As indicated by the literature, the treatment of 2,3-epoxypentofuranosides with nucleophilic agents may result in the formation of the corresponding 3- or 2-substituted derivatives depending on both the steric and polar effects or their combination[9]. In the field of sugar chemistry, 2,3--epoxy-*lyxo*-pentofuranoses afford exclusively the 3-amino derivatives of the *arabino* series by the action of ammonia[10–13]. In the field of nucleosides it also has been observed in the course of the synthesis of the antibiotic puromycin that the ammonolysis of the 2,3-epoxylyxofuranosyl derivative of the purine nucleoside affords the corresponding 3-amino derivative of the *arabino* series[14]. Similarly, 1-(3-amino-3-deoxy-β-D-arabinofuranosyl)uracil has been obtained by reaction of 1-(2,3-epoxy-β-D-lyxofuranosyl)uracil with ammonia[8].

On the basis of the above observations[8–14], the 2',3'-epoxy derivative *IIIb* might be expected to afford 1-(3-amino-3-deoxy-β-D-arabinofuranosyl)-6-azauracil (*IVb*) by reaction with ammonia. With the use of the trityl epoxy derivative *IIIa* as the starting compound, two routes are available, *1*) opening of the epoxy derivative *IIIa* by the action of ammonia with the formation of the trityl amino derivative *IVa* and the subsequent detritylation on treatment with hydrogen chloride to the hydrochloride of the amino derivative *IVb* and *2*) detritylation by hydrogen chloride to the epoxy derivative *IIIb* and the subsequent ammonolysis with the formation of the amino derivative *IVb*. Thus, the trityl epoxy derivative *IIIa* was opened to the trityl amino derivative *IVa* by heating with methanolic ammonia (18%) at 160°C for 7 h. When compared with the analogous reaction in the uracil series[8], a higher temperature




*IVa*, $R^1 = R^2 = H$, $R^3 = Tr$
*IVb*, $R^1 = R^2 = R^3 = H$
*IVc*, $R^1 = R^2 = R^3 = Ac$
*IVd*, $R^1 = Ac$, $R^2 = R^3 = H$
*IVe*, $R^1 = H$, $R^2 = R^3 = Ac$




*Va*, $R^1 = OH$, $R^2 = Tr$
*Vb*, $R^1 = OH$, $R^2 = H$
*Vc*, $R^1 = Cl$, $R^2 = H$

was required in the present treatment. The reaction product was directly detritylated by the action of ethereal hydrogen chloride (0·7M). The thus-obtained hydrochloride of the amino derivative *IVb* was acetylated with acetic anhydride in pyridine to afford the triacetyl derivative *IVc* in 48% yield (referred to the starting trityl epoxy derivative *IIIa*). Concerning the other route, the trityl epoxy derivative *IIIa* was detritylated by the action of ethereal hydrogen chloride at room temperature. Even under these mild conditions, the resulting epoxy derivative *IIIb* was accompanied by a by-product which was identified as the 3'-chloro derivative *Vc*. The epoxy derivative *IIIb* was obtained in solid state directly from the reaction mixture. The pure 3'-chloro derivative *Vc* resulted by column chromatography on silica gel.

The ratio of products *IIIb* and *Vc* depends on concentration of hydrogen chloride in ether. A higher concentration of hydrogen chloride (3·0M) brings about a higher yield of the epoxy derivative *IIIb* (77% of *IIIb* along with 14% of the 3'-chloro derivative *Vc*) whereas at a lower concentration of hydrogen chloride (0·6M) there is formed the 3'-chloro derivative *Vc* in a higher yield (61% of *Vc* along with 28% of the epoxy derivative *IIIb*). This behaviour might be explained by a different solubility of the starting compound *IIIa* and reaction products in the reaction mixture as well as by comparison of reaction rates of the detritylation and the cleavage. At a lower concentration of hydrogen chloride the detritylation of compound *IIIa* is slow and the trityl epoxy derivative *IIIa* (which is considerably more soluble in the reaction mixture than the epoxy derivative *IIIb*) is simultaneously cleaved with the formation of the 3'-chloro derivative *Vc*. At a higher concentration of hydrogen

TABLE I
Thin-Layer Chromatography

| Compound | $S_1$ | $S_2$ | $S_3$ | $S_4$ | $S_5$ |
|---|---|---|---|---|---|
| *I* | 0·95 | — | — | — | — |
| *II* | 0·67 | 0·17 | — | — | — |
| *IIIa* | 0·90 | 0·63 | 0·96 | — | — |
| *IIIb* | 0·12 | 0·03 | 0·55 | 0·76 | 0·70 |
| *IVb* | — | — | — | 0·11 | 0·10 |
| *IVc* | 0·20 | — | — | 0·85 | 0·86 |
| *IVd* | — | — | — | 0·39 | 0·40 |
| *IVe* | — | — | — | 0·48 | 0·66 |
| *Va* | 0·72 | 0·14 | — | — | — |
| 2,2'-Anhydro-1-(5-O-trityl-β-D-arabino-furanosyl)-6-azauracil | 0·56 | 0·11 | — | — | — |
| *Vc* | 0·55 | 0·13 | 0·82 | — | — |

chloride, the detritylation is considerably faster. The resulting epoxy derivative *IIIb* is almost insoluble in the reaction mixture and its cleavage to the 3'-chloro derivative *Vc* is strongly suppressed in the heterogeneous phase. The epoxy derivative *IIIb* was then converted to the amino derivative *IVb* by reaction with ammonia at a higher pressure and elevated temperature. By purification on a column of Dowex 50 ($H^+$) ion exchange resin, the free amino derivative was obtained as a chromatographically homogeneous solvate of compound *IVb* with one molecule of methanol. For purposes of identification, compound *IVb* was transformed to the crystalline acetyl derivatives *IVc–IVe*. Thus, acetylation with acetic anhydride in pyridine afforded the triacetyl derivative *IVc* identical with the above compound prepared by the process stated. The O-deacetylation of the triacetyl derivative *IVc* to the 3'-acetamido derivative *IVd* was performed in 77% yield by the sodium methoxide-catalysed methanolysis. Acetylation[15,16] with acetyl chloride in acetic acid of the amino derivative *IVb* afforded a 66% yield of the hydrochloride of the di-O-acetyl derivative *IVe*, the elemental analysis of which corresponded to a monohydrate. Analyses, spectra (NMR, IR, UV), chromatographical behaviour, and electrophoretical data of these acetates were in accordance with the structures proposed.

## EXPERIMENTAL

Melting points were taken on a heated microscope stage 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 sheets in the following solvent systems: $S_1$, ethyl acetate; $S_2$, ethyl acetate–benzene (1 : 1); $S_3$, ethyl acetate–methanol (9 : 1); $S_4$, ethyl acetate–methanol (4 : 1), and $S_5$, ethyl acetate–acetone–ethanol–water (6 : 1 : 1 : 1) Spots were detected by viewing under UV light. The trityl group-containing substances were detected by a spray with 50% aqueous sulfuric acid and the subsequent heating. Column chromatography was carried out on the Pitra silica gel (particle size 20–60 micron; produced by Service Laboratories of this Institute). The UV spectra were taken on a single-beam Optica Milano CF-4 apparatus, the IR spectra were recorded on a Model UR-20 Zeiss spectrophotometer, and the $^1H$ NMR spectra were measured on a Varian HA-100 apparatus at 100 MHz. Optical rotations were measured on a Model 141 MC Perkin-Elmer polarimeter. Solvents were taken off on a rotatory evaporator at 20 Torr and bath temperatures between 20 and 50°C according to the particular solvent. Pyridine was dried over potassium hydroxide. Other solvents were dried as usual and stored over molecular sieves Potassit 3 (Research Institute for Petroleum and Hydrocarbons, Bratislava, Czechoslovakia).

2,2'-Anhydro-1-(3-O-methanesulfonyl-5-O-trityl-β-D-arabinofuranosyl)-6-azauracil (*II*)

A solution of compound *I* (9·655 g; 15 mmol) in 66% aqueous pyridine (810 ml) was heated in a bath at 85°C for 90 min and evaporated under diminished pressure. The residue was co-evaporated with five 100 ml portions of 1 : 1 ethanol–toluene and finally with methanol (50 ml). The residue was extracted at room temperature with five 100 ml portions of ethyl acetate, the extracts combined, and evaporated under diminished pressure. The residue was refluxed in methanol (100 ml) for 10 min and the mixture kept at +3°C overnight. Yield, 4·095 g (49·8%) of the

chromatographically homogeneous compound *II*, m.p. 205–208°C, identical with an authentic specimen[2,3]. IR spectrum (nujol): 1180 $cm^{-1}$ ($SO_2$ sym.), 1372 $cm^{-1}$ ($SO_2$ asym.), 1541 and 1597 $cm^{-1}$ (C=N), 1680 $cm^{-1}$ (C=O).

1-(2,3-Epoxy-5-O-trityl-β-D-lyxofuranosyl)-6-azauracil (*IIIa*)

A. *From the anhydro derivative* II. A mixture of compound *II* (3·56 g; 6·5 mmol), 80% aqueous ethanol (20 ml), and 1M methanolic sodium methoxide (15 ml) was stirred at room temperature until the solid dissolved. The solution was kept at +3°C overnight, diluted with ethanol (150ml) and excess (15 ml) 2·5M acetic acid, and the whole evaporated under diminished pressure. The residue was coevaporated with five 50 ml portions of 1 : 1 ethanol–benzene and the final residue extracted with two 180 ml portions of refluxing benzene. The extracts were combined, evaporated, the residue coevaporated with two 25 ml portions of ethanol, and the final residue (3·23 g) crystallised from ethanol (65 ml) to afford 2·45 g (80·4%) of the chromatographically homogeneous compound *IIIa*, m.p. 198–202·5°C. The mother liquors were chromatographed on a column of silica gel in 1 : 1 ethyl acetate–benzene to yield additional 265 mg (8·7%) of compound *IIIa*, m.p. 192–198°C. Optical rotation: $[\alpha]_D^{25}$ −65·3° (*c* 0·52; ethyl acetate). UV spectrum (ethanol): $\lambda_{max}$ 213 and 260 nm (log ε 4·44 and 3·90), $\lambda_{min}$ 246 nm (log ε 3·80). IR spectrum (nujol): 1590 $cm^{-1}$ (C=N), 1693 and 1732 $cm^{-1}$ (C=O), 3225 $cm^{-1}$ (NH). For $C_{27}H_{23}N_3O_5$ (469·5) calculated: 69·07% C, 4·94% H, 8·95% N; found: 69·17% C, 4·97% H, 9·01% N.

B. *From the dimesyl derivative* I. To a suspension of the trityl dimesyl derivative[2] *I* (644 mg; 1 mmol) in 80% aqueous ethanol (10 ml) there was added 1M methanolic sodium methoxide (1 ml), and the whole refluxed for 10 min. After cooling to 40°C, the solution began to deposit substance *II* which was redissolved over 10 min by the addition of a further portion (2·4 ml) of 1M methanolic sodium methoxide with stirring. The solution was then kept at room temperature for 3 h, acidified with 2·5M acetic acid (1·6 ml), and evaporated under diminished pressure. The residue was coevaporated with three 20 ml portions of 1 : 1 ethanol–benzene and benzene alone (30 ml). The final residue was extracted with four 30 ml portions of benzene, the combined extracts evaporated under diminished pressure, and the residue (558 mg) chromatographed on a column of silica gel (50 g) in ethyl acetate as eluant. The first fractions containing the epoxy derivative *IIIa* were combined, evaporated under diminished pressure, and the residue (407 mg) crystallised from ethanol (7 ml) to afford 253 mg of compound *IIIa*, m.p. 200–203°C, identical with the substance prepared by procedure *A*. Work-up of mother liquors yielded additional 50 mg of the same substance. Overall yield, 65·6% of compound *IIIa*.

Reaction of Compound *IIIa* with Ethereal Hydrogen Chloride; Preparation of *IIIb* and *Vc*

*A*. A mixture of the trityl derivative *IIIa* (0·235 g; 0·5 mmol) and 3M ethereal hydrogen chloride (60 ml) was stirred at room temperature for 1 h and kept at +3°C overnight. The solid was collected with suction, washed with two 5 ml portions of ether, and dried under diminished pressure at 50°C to afford 88 mg (77%) of the chromatographically homogeneous compound *IIIb*, m.p. 191–193°C (after two crystallisations from methanol). Optical rotation: $[\alpha]_D^{25}$ −98·0° (*c* 0·51; ethanol). UV spectrum (ethanol): $\lambda_{max}$ 263 nm (log ε 3·46) and $\lambda_{min}$ 223 nm (log ε 3·16). IR spectrum (nujol): 1592 $cm^{-1}$ (C=N); 1692, 1725 and 1737 $cm^{-1}$ (C=O); 3210 $cm^{-1}$ (NH); 3480 $cm^{-1}$ (OH). NMR spectrum in a mixture of deuteriochloroform and hexadeuteriodimethyl sulfoxide (tetramethylsilane as internal standard; chemical shifts in p.p.m.); 3·60–3·80 (m, 3 H, $H_{5'a}$, $H_{5'b}$, OH); 3·85–4·15 (m, 3 H, $H_{2'}$, $H_{3'}$, $H_{4'}$); 6·03 (s, 1 H, $H_{1'}$); 7·41 (s, 1 H, $H_5$). For $C_8H_9N_3O_5$ (227·2) calculated: 42·30% C, 3·99% H, 18·50% N; found: 42·48% C, 4·01% H,

18·38% N. The etheral filtrate was processed analogously to the preparation of compound *Vc*, under *B*. Yield, 19 mg (14%) of the chromatographically homogeneous 3'-chloro derivative *Vc*.

*B*. A mixture of the trityl derivative *IIIa* (752 mg; 1·6 mmol) and 0·6M ethereal hydrogen chloride (200 ml) was stirred at room temperature for 1 h and then kept at +3° overnight. Compound *IIIb* was collected with suction and dried under diminished pressure (yield, 120 mg; 28·4%). The ethereal filtrate was evaporated under diminished pressure, the residue coevaporated with three 50 ml portions of methanol, and finally distributed between chloroform (500 ml) and water (three 100 ml portions). The aqueous solutions were combined, evaporated under diminished pressure, the residue coevaporated with three 50 ml portions of 1 : 1 ethanol–benzene and with methanol (20 ml). The final residue (290 mg) was chromatographed on a column of silica gel (100 g) with the use of ethyl acetate as eluant (300 ml; fractions 1—20). Work-up of fractions 13—19 afforded 258 mg (61·1%) of the chromatographically homogeneous compound *Vc*, identical with a specimen obtained by another route[5].

1-(3-Amino-3-deoxy-β-D-arabinofuranosyl)-6-azauracil (*IVb*)

A mixture of the epoxy derivative *IIIb* (455 mg; 2 mmol) and 18% methanolic ammonia (40 ml) was heated in a pressure vessel at 160°C for 6 h and then evaporated under diminished pressure. The residue (526 mg) was dissolved in methanol (50 ml) and the solution applied to a column of Dowex 50 ($H^+$) ion exchange resin (40 ml) previously washed with methanol. The column was washed with methanol (200 ml) and compound *IVb* eluted with 2·5% methanolic ammonia (250 ml). The eluate was evaporated under diminished pressure, the residue (464 mg) dissolved in methanol (100 ml), the solution filtered with active charcoal, and the filtrate evaporated under diminished pressure. The residue (447 mg) was dissolved in a minimum amount of boiling methanol, the solution diluted with hot ethanol (20 ml), and filtered. The filtrate was cooled down to deposit 177 mg of the amorphous compound *IVb*. In a similar manner, the filtrate yielded additional 76 mg of the chromatographically homogeneous compound *IVb*; overall yield, 52%. UV spectrum (ethanol); $\lambda_{max}$ 268 nm (log ε 3·62) and $\lambda_{min}$ 232 nm (log ε 3·33). For $C_8H_{12}N_4O_5 + CH_4O$ (276·3) calculated: 39·13% C, 5·84% H, 20·28% N; found: 38·78% C, 5·48% H, 20·74% N.

1-(2,5-Di-O-acetyl-3-amino-3-deoxy-β-D-arabinofuranosyl)-6-azauracil Hydrochloride (*IVe*)

A mixture of the amino derivative *IVb* (48 mg), acetic acid (2 ml), and acetyl chloride (1 ml) was stirred at room temperature for 1 h, kept overnight, and evaporated under diminished pressure. The residue was coevaporated with four 30 ml portions of 1 : 1 ethanol–toluene and finally crystallised (72 mg) from 96% ethanol to afford 36 mg of compound *IVe*, m.p. 211°C (decomp.). Work-up of mother liquors yielded additional 8 mg of the chromatographically homogeneous acetyl derivative *IVe*; overall yield, 67%. UV spectrum (ethanol): $\lambda_{max}$ 263 nm (log ε 3·77) and a plateau at 220—235 nm (log ε 3·57). IR spectrum (nujol): 1515 $cm^{-1}$ ($NH_3^+$ II), 1582 $cm^{-1}$ ($NH_3^+$ I), 1657, 1700, 1726, and 1745 $cm^{-1}$ (C=O), a band series at 2000 $cm^{-1}$ ($NH_3^+$), a band series at 2880 $cm^{-1}$ ($NH_3^+$), 3425 and 3530 $cm^{-1}$ (crystal $H_2O$). For $C_{12}H_{17}ClN_4O_7.H_2O$ (382·8) calculated: 37·66% C, 5·00% H, 14·64% N, 9·26% Cl; found: 37·96% C, 4·86% H, 14·55% N, 9·30% Cl.

1-(3-Acetamido-2,5-di-O-acetyl-3-deoxy-β-D-arabinofuranosyl)-6-azauracil (*IVc*)

*A*. A mixture of the trityl derivative *IIIa* (705 mg; 1·5 mmol) and 18% methanolic ammonia (50 ml) was heated in a pressure vessel at 160°C for 7 h, the resulting cold solution filtered, and the filtrate evaporated under diminished pressure. The residue was coevaporated with three 50 ml

portions of methanol, the final residue (750 mg) treated with 0·7M ethereal hydrogen chloride (65 ml), the mixture stirred at room temperature for 1 h, and kept at +3°C overnight. The hydrochloride *IVb* was collected with suction, washed with two 10 ml portions of ether, and dissolved in methanol (50 ml). The solution was filtered and the filtrate evaporated under diminished pressure. The residual hydrochloride of amine *IVb* (462 mg) was treated with pyridine (10 ml) and acetic anhydride (4 ml), the mixture kept at room temperature overnight, diluted with methanol (10 ml), kept for additional 30 min, and evaporated under diminished pressure. The residue was coevaporated with five 50 ml portions of 1 : 1 ethanol–toluene, methanol alone (50 ml), and triturated with ethyl acetate (300 ml). The insoluble solid was collected with suction, washed with four 5 ml portions of methanol, and dried. Crystallisation of the solid (210 mg) from methanol (15 ml) yielded 170 mg of compound *IVc*, m.p. 248–253°C. The remaining ethyl acetate solution was washed with three 10 ml portions of water and evaporated under diminished pressure. Crystallisation of the residue (148 mg) from ethanol (2 ml) afforded additional 53 mg of compound *IVc*, m.p. 249–254°C. Another crop of the acetyl derivative *IVc* was obtained (45 mg) from the mother liquors; overall yield, 268 mg (48·3%) of the chromatographically homogeneous compound *IVc*. Optical rotation: $[\alpha]_D^{25}$ −74·6° (*c* 0·33; pyridine). UV spectrum (ethanol): $\lambda_{max}$ 264 nm (log $\varepsilon$ 3·76) and $\lambda_{min}$ 233 nm (log $\varepsilon$ 3·46). IR spectrum (nujol): 1 552 $cm^{-1}$ (amide II), 1 597 $cm^{-1}$ (C=N), 1 650 $cm^{-1}$ (amide I), 1 694 and 1 715 $cm^{-1}$ (C=O azauracil), 1 747 $cm^{-1}$ (C=O acetate), 3 160 $cm^{-1}$ (NH azauracil), 3 300 $cm^{-1}$ (NH amide). NMR spectrum in hexadeuteriodimethyl sulfoxide (hexamethyldisiloxane as internal standard, recalculated to tetramethylsilane, chemical shifts in p.p.m.): 1·91 (s, 3 H, $C\underline{H}_3CONH$); 1·96 (s, 3 H, $C\underline{H}_3CO$); 2·01 (s, 3 H, $C\underline{H}_3CO$); 4·04 (m, 1 H, $J_{4',3'}$ = 8·5 Hz, $H_{4'}$); 4·24 (m, 2 H, $J_{5'a,4'}$ = 2·4 Hz, $J_{5'a,5'b}$ = = 9·0 Hz, $H_{5'a}$, $H_{5'b}$); 4·81 (m, 1 H, $J_{3',2'}$ = 9·1 Hz, $J_{3'NH}$ = 9·0 Hz, $H_{3'}$); 5·53 (2d, 1 H, $J_{2',1'}$ = 6·9 Hz, $H_{2'}$); 6·51 (d, 1 H, $H_{1'}$); 7·48 (s, 1 H, $H_5$); 7·83 (d, 1 H, $CH_3CONH$); 12·20 (broad s, 1 H, N$\underline{H}$ arom.). For $C_{14}H_{18}N_4O_8$ (370·3) calculated: 45·41% C, 4·90% H, 15·13% N; found: 45·71% C, 5·02% H, 14·76% N.

*B.* A mixture of the epoxy derivative *IIIb* (58 mg, 0·25 mmol) and 18% methanolic ammonia (30 ml) was heated in a pressure vessel at 160°C for 7 h, cooled down, evaporated under diminished pressure, and the residue coevaporated with three 25 ml portions of methanol. The final residue (62 mg) was dissolved in ethanol (15 ml), the solution filtered, and the filtrate evaporated under diminished pressure. A mixture of the residue (45 mg), pyridine (5 ml), and acetic anhydride (2 ml) was kept at room temperature overnight, diluted with methanol (5 ml), kept for additional 30 min, and evaporated. The residue was coevaporated with five 25 ml portions of 1 : 1 ethanol–toluene and with methanol (25 ml). The residue (70 mg) was dissolved in ethyl acetate (200 ml), the solution filtered, the filtrate washed with two 15 ml portions of water, and evaporated under diminished pressure. Crystallisation of the residue (68 mg) from ethanol (2 ml) yielded 32 mg (34·6%) of the chromatographically homogeneous compound *IVc*, identical with the substance obtained by procedure *A*.

1-(3-Acetamido-3-deoxy-β-D-arabinofuranosyl)-6-azauracil (*IVd*)

A solution of the triacetyl derivative *IVc* (178 mg; 0·48 mmol) in 0·1M methanolic sodium methoxide (10 ml) was kept at room temperature for 3 h, diluted with methanol (40 ml), and neutralised by the addition of Dowex 50 ($H^+$) ion exchange resin. The resin was then filtered off and washed with methanol. The filtrate and washings were combined and evaporated. Crystallisation of the residue (145 mg) from ethanol (2 ml) yielded 87 mg (63·5%) of compound *IVd*, m.p. 202–204°C. Work-up of mother liquors afforded additional 19 mg (13·9%) of the chromatographically homogeneous compound *IVd*. Optical rotation: $[\alpha]_D^{25}$ −48·7° (*c* 0·26; water). UV spectrum (ethanol): $\lambda_{max}$ 268 nm (log $\varepsilon$ 3·70) and $\lambda_{min}$ 234 nm (log $\varepsilon$ 3·37). IR spectrum (nujol): 1 578 $cm^{-1}$ (amide II),

1 680 $cm^{-1}$ (amide I), 1 694 and 1 715 $cm^{-1}$ (C=O azauracil), 3 060–3 270 $cm^{-1}$ (NH bound). NMR spectrum in hexadeuteriodimethyl sulfoxide (hexamethyldisiloxane as internal standard, recalculated to tetramethylsilane, chemical shifts in p.p.m.): 1·80 (s, 3 H, $C\underline{H}_3CONH$); 3·40 to 4·50 (m, 7 H, $H_{2'}$, $H_{3'}$, $H_{4'}$, $H_{5'a}$, $H_{5'b}$, $O^2\underline{H}$, $O^5\underline{H}$); 6·17 (d, 1 H, $J_{1',2'} = 6{\cdot}0$ Hz, $H_{1'}$); 7·47 (s, 1 H, $H_5$); 8·00 (broad s, 1 H, $J_{3',N\underline{H}} = 7{\cdot}0$ Hz, $N^3\underline{H}$); 12·01 (broad s, 1 H, $N\underline{H}$ arom.). For $C_{10}H_{14}N_4O_6$ (286·2) calculated: 41·96% C, 4·93% H, 19·57% N; found: 41·98% C, 5·06% H, 19·52% N.

1-(5-O-Trityl-β-D-arabinofuranosyl)-6-azauracil (*Va*)

To a suspension of 2,2'-anhydro-1-(5-O-trityl-β-D-arabinofuranosyl)-6-azauracil[7] (413 mg; 0·8 mmol) in 80% aqueous ethanol (10 ml) there was added 1M methanolic sodium methoxide (0·9 ml), the mixture stirred until the solid dissolved (about 30 min), the solution kept at room temperature for 4 h, acidified with 2M acetic acid (1 ml), and precipitated with stirring by the dropwise addition of water (40 ml). The precipitate was collected with suction, dissolved in the solvent mixture methanol–ethyl acetate, and dried by coevaporation with toluene. The residue was dissolved in 2-propanol (12 ml), the solution kept at +3°C overnight, and filtered to remove a small amount of a solid. The filtrate was evaporated under diminished pressure, the residue dissolved in methanol (2 ml), the solution diluted with benzene (10 ml), and evaporated under diminished pressure to afford 381 mg (97%) of compound *Va*; m.p. 140–142°C. Optical rotation: $[\alpha]_D^{25}$ −16·8° (*c* 0·39; methanol). UV spectrum (ethanol): $\lambda_{max}$ 212 and 263 nm (log ε 4·38 and 3·63, resp.) and $\lambda_{min}$ 248 nm (log ε 3·48). IR spectrum (chloroform): 1 061 $cm^{-1}$ (C=C), 1 588 $cm^{-1}$ (C=N), 1 693 sh, 1 713, 1 728 sh $cm^{-1}$ (C=O), 3 379 $cm^{-1}$ (NH), 3 612 $cm^{-1}$ (OH). For $C_{27}H_{25}N_3O_6$ (487·5) calculated: 66·52% C, 5·17% H, 8·62% N; found: 66·16% C, 5·37% H, 8·33% N.

1-β-D-Arabinofuranosyl-6-azauracil (*Vb*)

A suspension of the tritylarabinoside *Va* (60 mg; 0·123 mmol), ether (20 ml), and saturated ethereal hydrogen chloride (2 ml) was shaken at room temperature for 3 h, kept at +3°C overnight, and evaporated under diminished pressure. The residue was coevaporated with three 20 ml portions of 1 : 1 methanol–benzene and with methanol (20 ml). The final residue was purified by extraction with four 20 ml portions of boiling chloroform. The insoluble portion was dissolved in water (30 ml) and the aqueous solution purified by extraction with two 10 ml portions of chloroform. The remaining aqueous solution was filtered, the filtrate evaporated under diminished pressure, and the residue dried by coevaporation with benzene and with methanol. Yield, 26 mg (86%) of compound *Vb*, homogeneous on chromatography and identical with an authentic specimen[7].

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