PREPARATION OF 6-METHYLURIDINE, 6-ETHYLURIDINE, AND 2'-DEOXY-6-ETHYLURIDINE*

A. HOLÝ

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

Received March 15th, 1974

Benzoylation of 6-methyl-$O^{2,2'}$-anhydrouridine (*Ia*) and 6-ethyl-$O^{2,2'}$-anhydrouridine (*Ib*) afforded the 3',5'-di-O-benzoyl derivatives *II* which were converted by reaction with stannic chloride in methanol into the isomeric 3',5'- and 2',5'-dibenzoates of 6-methyluridine and 6-ethyluridine (*Va* and *Vb*, resp.). Alkali-catalysed methanolysis of compounds *V* afforded 6-methyluridine (*VIa*) and 6-ethyluridine (*VIb*). On treatment with hydrogen chloride in dimethylformamide, the dibenzoate *IIb* was converted into 3',5'-di-O-benzoyl-2'-chloro-2'-deoxy-6-ethyluridine (*VIIb*) which was reduced with tri-n-butyltin hydride to yield 3',5'-di-O-benzoyl-2'-deoxy-5-ethyluridine (*VIIIb*). Removal of benzoyl groups from compound *VIIIb* by methanolysis afforded 2'-deoxy-6-ethyluridine (*IXb*).

In an earlier[1] paper of this series, there has been reported a preparation of 6-alkyl-$O^{2,2'}$-anhydrouridines *I* starting from alkyl β-alkyl-β-chloroacrylates and 2-amino-β-D-arabinofuro-[1',2' : 4,5]oxazoline. Another preparative method consisting in addition of the latter oxazoline to esters of acetylenic acids[2,3] gives low yields in the case of esters of homologous acetylenecarboxylic acids. The cyclonucleosides *I* represent potential starting substances in the synthesis of 6-substituted uracil nucleosides. Thus, the corresponding arabinofuranosides are obtained from the cyclonucleosides *I* without any difficulty[3]. Conversion of compounds *I* to the appropriate ribonucleosides would be of an extraordinary interest. Some time ago, there has been in this Laboratory developed a stereospecific and quantitative method of a "reversed" opening of $O^{2,2'}$-anhydronucleosides in the uracil series[4]. The principle of this method consists in the use of 3',5'-di-O-benzoyl-$O^{2,2'}$-anhydronucleosides of type *II* which are accessible from compounds *I* by benzoylation with benzoyl cyanide[5,6]. Compounds *II* form in methanol in the presence of boron trifluoride etherate with participation of the vicinal benzoyl group at position 2' a cyclic acyloxonium derivative of type *III*. This unstable intermediate is decomposed in a protic solvent (obviously *via* the cyclic 2',3'-methoxybenzylidene derivative *IV*) to afford as the final product a mixture of 2',5'- and 3',5'-di-O-benzoyl derivatives of the corresponding ribo-

* Part CLXX in the series Nucleic Acid Components and Their Analogues; Part CLXIX: This Journal *39*, 3177 (1974).

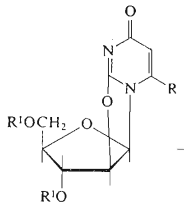
nucleoside *V*. The $O^{2,2'}$-anhydronucleosides *I* of the 6-alkyluracil series as well as the 6-methoxycarbonyl derivative (the orotidine derivative) are completely resistant towards the action of boron trifluoride etherate in methanol even for a considerably long periods of time. In the present paper, we wish to report another variant of the anomalous opening of the type *I* or *II* anhydronucleosides, which variant may also be applied in the above mentioned resistant cases.

Replacement of boron trifluoride etherate by stronger Lewis acid, namely, stannic chloride, proved to be sufficient for realisation of the reaction with 6-alkyl derivatives. The reaction sequence in the preparation of 6-methyluridine (*VIa*) and 6-ethyluridine (*VIb*) shown in Scheme 1 consists in conversion of the anhydronucleoside *I* to the 3',5'-dibenzoate *II* by reaction with benzoyl cyanide in the presence of triethylamine and the subsequent reflux of this dibenzoate *II* with stannic chloride in methanol. Since stannic chloride is a rather strong Lewis acid, prolonged reaction time results in decomposition of the nucleoside molecule. It is therefore advisable to interrupt the reaction prior to the complete conversion of compound *II* (refluxing for 3 h proved to be satisfactory) and isolate the mixture of isomeric 2'(3'),5'-dibenzoates *V* by chromatography. Both the isomeric dibenzoates *Va* and *Vb* were obtained in pure state and their structure was confirmed by analysis and NMR spectra. The unexpectedly easy separation of the dibenzoates *V* (in comparison to the earlier investigated analogous compounds) is probably due to interference of the two bulky groups, the 2'-O-benzoyl group and the 6-alkyl substituent of the heterocyclic nucleus.

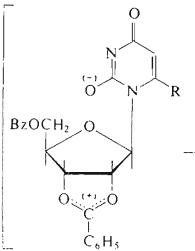
The alkali-catalysed methanolysis of dibenzoates *V* affords the free nucleosides *VIa* (6-methyluridine) and *VIb* (6-ethyluridine) in a high yield. The earlier preparation of 6-methyluridine by glycosylation of 6-methyluracil[7,8] was accompanied (because of the steric shielding by the 6-alkyl group) by the preferential ribosylation at position N^3 and by the formation of the diribosyl derivative. 6-Ethyluridine (*VIb*) has not been so far reported; the attempted preparation by a direct ribosylation of 6-ethyluracil would obviously meet with analogous difficulties as in the case of the lower homologue. The 6-alkylnucleosides are interesting from several standpoints. Their conformation is affected by the steric influence of the 6-alkyl group (6-methyluridine is of the *syn* conformation) and also some other properties might be ascribed to the presence of the 6-alkyl substituent such as failure of some enzymatic reactions[9,10] or appearence of novel reactions due to enzymes, *e.g.*, degradation of 6-methyl-2'-deoxyuridine *in vivo* by *E. coli*[11]. The present method is more advantageous than the classical ribosylation which requires a laborious separation of a small amount of the desired product from the by-products. Furthermore, the dibenzoates *V* are suitable intermediates in the preparation of 6-alkylcytosine derivatives *via* thiation and ammonolysis using the 2',3',5'-tribenzoate of the nucleoside *VI* as the starting substance.

The preparation of 6-methyl-2'-deoxyuridine (*IXa*) has been reported earlier[3]. In contrast to 6-methyluridine (*Va*), compound *IXa* does not appear to exist in the *syn* conformation. It was therefore of interest to examine also in the homologous

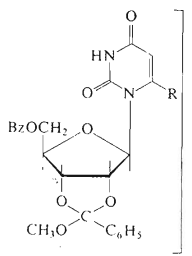
6-ethyl series the conformation and the mutual behaviour of the riboside *VIb* and the 2′-deoxyriboside *IXb*. The latter compound was prepared analogously to 6--methyl-2′-deoxyuridine[3] (*IXa*) as follows. On treatment with hydrogen chloride in dimethylformamide, the cyclonucleoside *IIb* was converted to the 2′-chloro-2′-deoxy-



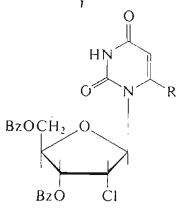
I, $R^1 = H$
II, $R^1 = C_6H_5CO$



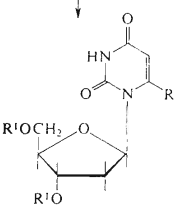
III, $Bz = C_6H_5CO$



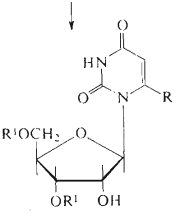
IV, $Bz = C_6H_5CO$



VII, $Bz = C_6H_5CO$



VIII, $R^1 = C_6H_5CO$
IX, $R^1 = H$



V, $R^1 = C_6H_5CO$ (+2′,5′-isomer)
VI, $R^1 = H$

In formulae *I*–*IX*,
a R = CH_3
b R = CH_2CH_3

nucleoside *VIIb* with the *ribo* configuration of the C—Cl bond. The structure was confirmed by analysis and NMR spectra. Reaction of compound *VIIb* with tri-n-butyltin hydride afforded 3',5'-di-O-benzoyl-2'-deoxy-6-ethyluridine (*VIIIb*), homogeneous according to NMR spectrum. Alkali-catalysed methanolysis of the latter dibenzoate led to the free 6-ethyl-2'-deoxyuridine (*IXb*). Analogously to the preparation of 6-methyl-2'-deoxyuridine[3], the synthesis of the nucleoside *IXb* is also stereospecific and affords exclusively the anomer of the β series.

The 6-substituted uracil nucleosides are attractive as models of nucleosides with a markedly affected conformation by virtue of the presence of a bulky substituent on the heterocyclic base interfering with the sugar moiety. It has been shown by means of CD spectra that in 6-methyluridine (*VIa*) there is preferred the *syn* conformation[12]. The CD spectrum of 6-ethyluridine (*VIb*) is almost identical with that of compound *VIa* with respect to extrema positions and molar ellipticity values. It is rather striking that the sign of the CD maximum of the low $\mathbf{B}_{2u}$ band is opposite to that of the corresponding transition of compound *VIa*. Consequently, the *syn* conformation appears to be preferred in aqueous solutions of both 6-methyluridine (*VIa*) and 6-ethyluridine (*VIb*), *cf.* Table I. A similar accordance has been found with CD spectra of 6-methyl-2'-deoxyuridine[3] and its 6-ethyl homologue *IXb*. With compound *IXb*, a bathochromic shift of extrema may be observed. The molar ellipticity sign of $\mathbf{B}_{2u}$, $\mathbf{B}_{1u}$, and $\mathbf{E}_{1u}$ transitions in CD spectrum of compound *IXb* corresponds to that of 2'-deoxyuridine and 2'-deoxythymidine[12] and does not differ in this respect from that of 6-

TABLE I

UV and CD Spectra in Aqueous Solutions (molar ellipticities in parentheses)

Compound	UV-Spectra		Circular dichroism spectra[a]			
	λ_{max}, nm	ε_{max}	$\mathbf{B}_{2u}$	$\mathbf{B}_{1u}$	$\mathbf{E}_{1u}$	$\lambda\Phi = 0$
Uridine[12]	262	10 000	267(8 500)	240(−3 700)	215(−4 400)	—
VIa	262	12 000	260−270(−300)	250(1 000)	214(−10 000)	
VIb	262	10 600	258(800)	245(1 100)	219·5(−9 600)	232
2'-Deoxyuridine[12]	262	10 000	267(6 000)	237(−3 600)	215(−5 800)	—
IXa	262	12 000	261·5(5 700)	246s(4 500)	(−1 600)[b]	229
IXb	262	10 700	269(3 750)	256·5(5 300)[c]	219(11 350)	—
$O^{2,2'}$-Anhydro-uridine[12]	250	11 000	270(−1 000)	242(15 000)	217(−8 500)	
Ia[3]	251	10 000	—	241·5(17 400)	215·5(−6 300)	224
Ib	252[d]	9 500	—	240·5(17 600)	214(−7 700)	223·5

[a] For symbols, *cf.*[12]; [b] 200; [c] λ_{min} 235 (3 300); [d] λ_{max} 222 (ε_{max} 7 800).

-methyl-2′-deoxyuridine (*IXa*); the $\mathbf{E}_{1u}$ transition of this compound lies out of the measurement region. The CD spectra cannot therefore supply an unequivocal information on the conformation of 2′-deoxyuridine 6-substituted derivatives or at least confirm the occurence of the *syn* conformation if any. The CD and UV spectra of $O^{2,2'}$-anhydronucleosides *I* and the unsubstituted $O^{2,2'}$-anhydrouridine are identical and in accordance with the conformation corresponding to annelation of an additional ring.

Compounds *VIb* and *IXb* did not exhibit any bacteriostatic activity on the growth of *E. coli* in a synthetic glucose-containing medium. In this connection, neither 6-methyluridine (*VIa*) nor 6-methyl-2′-deoxyuridine (*IXa*) have been found to exhibit any affinity towards the nucleoside-transporting system in *E. coli*[13]; both *VIa* and *IXa* are rapidly degraded on the surface of *E. coli* bacteria to 6-methyluracil[11]. These two effects might manifest themselves also with the 6-ethyl homologues and cause their inactivity *in vivo*.

EXPERIMENTAL

Unless stated otherwise, the solutions were taken down on a rotatory evaporator at 35°C/15 Torr and substances were dried over phosphorus pentoxide at 0·1 Torr. Melting points were taken on a heated microscope stage (Kofler block) and are uncorrected.

Descending paper chromatography was performed on paper Whatman No 1 in the solvent systems S_1, 2-propanol–conc. aqueous ammonia–water (7 : 1 : 2), and S_2, 1-butanol–acetic acid–water (5 : 2 : 3). Thin-layer chromatography was carried out on ready-for-use Silufol UV_{235} (Kavalier Glassworks, Votice, Czechoslovakia) silica gel foils in the solvent systems S_3, chloroform–ethanol (95 : 5); S_4, benzene–ethyl acetate (7 : 3); S_5, benzene–ethyl acetate (1 : 1); and S_6, ethyl acetate. For the R_F values see Table II. Preparative separations were performed on a column of silica gel (particle size, 30—60 micron) or loose layers (50 × 16 × 0·4 cm) of fluorescent-indicator-containing silica gel (both materials are produced in Service Laboratories of this Institute). Paper electrophoresis was performed on paper Whatman No 3 MM in 0·1M triethylammonium borate (pH 7·5) at 20 V/cm.

The NMR spectra were measured in deuteriochloroform (unless stated otherwise) on a Varian 100 apparatus (hexamethyldisiloxane as internal standard). The chemical shift values are given in p.p.m. and the coupling constant values are expressed in Hz. The CD spectra (Table I) were measured in water on a Jouan Dichrograph 185. The UV spectra were taken in water on a Zeiss Specord apparatus.

3′,5′-Di-O-benzoyl-$O^{2,2'}$-anhydro-6-methyluridine (*IIa*)

To a suspension of 6-methyl-$O^{2,2'}$-anhydrouridine[1] (*Ia*; 22 g; 92 mmol) and benzoyl cyanide (30 g; 0·23 mmol) in acetonitrile (200 ml) there was added dropwise with stirring triethylamine (10 ml), the whole stirred at room temperature for 1 h, and diluted with ether (500 ml). The crystals were collected with suction, washed with ether, and dried under diminished pressure to afford 28·2 g (69%) of the chromatographically (S_3) homogeneous dibenzoate *IIa*, m.p. 222 to 223°C, identical with an authentic specimen[2,3].

TABLE II
Chromatography and Electrophoresis

Compound	S_1	S_2	S_3	S_5	S_6	E^a_{Urd}
Uridine	0·42	0·21			—	1·00
Ia	0·65	0·48			—	−0·05
Ib	0·69	0·48			—	−0·05
IIa	—	—	0·40		0	—
IIb	—	—	0·45		0	—
Va	—	—	0·60	0·33[c]	0·70[c]	—
				0·15[a]	0·40[d]	—
Vb	—	—	0·70	0·42[d]	0·76[d]	—
				0·27[c]	0·62[c]	—
VIa	0·48	0·30				1·00
VIb	0·58	0·42				1·00
VII	—	—	0·75	0·46[b]		—
VIII	—	—		0·17[b]		—
IXa	0·60	0·48				−0·10
IXb	0·66	0·52				−0·10

[a] Mobility in E_1 referred to uridine; [b] in S_4; [c] 3′,5′-isomer; [d] 2′,5′-isomer.

3′,5′-Di-O-benzoyl-$O^{2,2'}$-anhydro-6-ethyluridine (*IIb*)

To a mixture of 6-ethyl-$O^{2,2'}$-anhydrouridine[1] (*Ib*; 6·4 g; 25 mmol), benzoyl cyanide (8·0 g; 61 mmol), and acetonitrile (100 ml) there was added with stirring triethylamine (5 ml), the whole stirred at room temperature for 1 h, evaporated under diminished pressure, and the residue chromatographed on a column of silica gel (150 g) in chloroform. The column was eluted with chloroform, the eluate evaporated, and the residue crystallised from a mixture of ether and light petroleum to afford 9·0 g (78%) of compound *IIb*, m.p. 166–167°C. For $C_{25}H_{22}N_2O_7$ (462·3) calculated: 64·91% C, 4·79% H, 6·06% N; found: 64·64% C, 4·94% H, 6·09% N. NMR spectrum: 1·11 (t, 3 H, $J = 7·0$) CH_2CH_3; 2·55 (br q, 2 H, $J = 7·0$) CH_2CH_3; 4·37 (d, 2 H) 2 $H_{5'}$; 4·65 (m, 1 H) $H_{4'}$; 5·60–5·75 (m, 3 H) $H_{2'}$, $H_{3'}$ and H_5.

2′,5′- and 3′,5′-Di-O-benzoyl-6-methyluridine (*Va*)

To a suspension of compound *IIa* (28 g; 62 mmol) in methanol (500 ml) there was added dropwise with stirring stannic chloride (25 ml; 55·5 g; 214 mmol), the whole refluxed for 8 h under exclusion of atmospheric moisture (calcium chloride tube), and evaporated under diminished pressure. The residue was diluted with chloroform (200 ml), washed with two 50 ml portions of 10% aqueous thiosulfate and water, dried over anhydrous magnesium sulfate, and evaporated. The residue in 50 ml of ethyl acetate was applied to a column of silica gel (100 g) in ethyl acetate. The isomeric mixture of compounds *Va* (R_F 0·40 and 0·70 in S_6) was eluted with ethyl acetate, the eluate evaporated, the residue dissolved in chloroform (50 ml), and the solution applied to a column of silica

gel (100 g) in chloroform. Elution with chloroform afforded the 3′,5′- and 2′,5′-isomer. Yield, 6·4 g (13·7 mmol) of the 3′,5′-isomer, R_F 0·70 in S_6. For $C_{24}H_{22}N_2O_8$ (466·4) calculated: 61·80% C, 4·75% H, 6·00% N; found: 61·55% C, 4·91% H, 5·23% N. NMR spectrum: 2·32 (s, 3 H) C_6–CH_3; 3·85 (br s, 1 H) 2′-OH; 4·45—4·75 (m, 3 H) H_4′ and 2 H_5′; 5·26 (dd, 1 H, $J_{1',2'} = 2·6$, $J_{2',3'} = 6·2$) H_2′; 5·54 (s, 1 H) H_5; 5·65 (m, 2 H) H_1′ and H_3′; 7·15—8·10 (m, 10 H) aromatic protons; 10·27 (br s, 1 H) NH. Further elution afforded 5·0 g (10·7 mmol) of the amorphous 2′,5′-isomer, R_F 0·40 in S_6. Found: 62·16% C, 4·61% H, 5·62% N. NMR spectrum: 2·25 (s, 3 H) 6-CH_3; 4·0 (br s, 1 H) 3′-OH; 4·35 (m, 1 H) H_4′; 4·49 (d, 1 H, $J_{5'',4'} = 1·0$, $J_{gem} = 12·0$) H_5″; 4·75 (dd, 1 H, $J_{5',4'} = 2·7$) H_5′; 5·16 (q, 1 H, $J_{3',2'} = 6·4$, $J_{3',4'} = 8·5$) H_3′; 5·54 (s, 1 H) H_5; 5·68 (d, 1 H, $J_{1',2'} = 1·6$) H_1′; 6·01 (dd, 1 H, $J_{1',2'} = 1·6$, $J_{2',3'} = 6·4$) H_2′; 7·25—8·15 (m, 10 H) aromatic protons; 10·03 (br s, 1 H) NH. Overall yield of the 3′,5′- and 2′,5′-isomers, 11·4 g (24·4 mmol; 39·5%).

6-Methyluridine (*VIa*)

The mixture of 3′,5′- and 2′,5′-isomers (*Va*; 5·0 g; 10·7 mmol) was kept at room temperature in 0·1M methanolic sodium methoxide (100 ml) overnight and neutralised with dry Dowex 50 (H^+) cation exchange resin. The resin was filtered off, washed with methanol (100 ml), the combined filtrate and washings evaporated under diminished pressure, the residue diluted with water (100 ml), washed with two 25 ml portions of ether, and the aqueous phase evaporated under diminished pressure. The residue was coevaporated with three 50 ml portions of ethanol and finally crystallised from ethanol to afford 2·0 g (72%) of compound *VIa*, m.p. 172—173°C (reported[7], m.p. 179°C), $[\alpha]_D^{25}$ −28·5° (*c* 0·5; water). On chromatography in S_1 and S_2, electrophoresis in E_1, and analysis, the product is identical with 6-methyluridine.

2′,5′- and 3′,5′-Di-O-benzoyl-6-ethyluridine (*Vb*)

To a mixture of compound *IIb* (7 g; 15 mmol) and methanol (150 ml) there was added with stirring stannic chloride (6·0 ml; 13·4 g; 51·5 mmol), the whole refluxed for 3 h under exclusion of atmospheric moisture (calcium chloride tube), and evaporated under diminished pressure. The residue was diluted with chloroform (100 ml), washed with two 50 ml portions of 10% aqueous sodium thiosulfate and water (50 ml), dried over anhydrous magnesium sulfate, and evaporated. The residue (in 50 ml of benzene) was chromatographed on a column of silica gel (50 g) in benzene. Elution with 1 : 3 ethyl acetate–benzene afforded the two isomers. Yield, 2·5 g (5·2 mmol) of the amorphous 2′,5′-isomer, R_F 0·42 in S_5 and 0·76 in S_6. For $C_{25}H_{24}N_2O_8$ (480·5) calculated: 62·48% C, 5·03% H, 5·83% N; found: 62·50% C, 5·18% H, 5·49% N. NMR spectrum: 1·15 (t, 3 H), CH_2CH_3; 2·52 (q, 2 H) CH_2CH_3; 4·17 (m, 1 H) H_4′; 4·39 (q, 1 H, $J_{5'',4'}$ 5·8, $J_{gem} = 12·0$) H_5″; 4·65 (dd, 1 H, $J_{5',4'} = 2·7$) H_5′; 4·87 (q, 1 H, $J_{3',2'} = 6·5$, $J_{3',4'} = 8·0$) H_3′; 5·43 (br s, 1 H, $J_{5,NH} = 1·0$) H_5; 5·66 (d, 1 H, $J_{1',2'} = 2·3$) H_1′; 5·90 (q, 1 H) H_2; 7·25 to 8.15 (m, 10 H) aromatic protons; 11·14 (br s, 1 H) NH. Further elution afforded 0·5 g (1·0 mmol) of the 3′,5′-isomer, R_F 0·27 in S_5 and 0·62 in S_6. Found: 63·06% C, 5·31% H, 5·60% N. NMR spectrum: 1·20 (t, 3 H) and 2·55 (q, 2 H) CH_2CH_3; 4·55 (m, 3 H) H_4′ and 2 H_5′; 4·25 (br s, 1 H) 2′-OH; 5·06 (q, 1 H, $J_{2',1'} = 2·5$; $J_{2',3'} = 6·5$) H_2′; 5·45 (br s, 1 H, $J_{5,NH} = 1·0$) H_5; 5·58 (d, 1 H, $J_{1',2'} = 2·5$) H_1′; 5·70 (m, 1 H) H_3′; 7·20—8·10 (10 H) aromatic protons; 10·53 (br s, 1 H) NH. Overall yield of the 2′,5′-and 3′,5′-isomers, 6·2 mmol (41·2%).

6-Ethyluridine (*VIb*)

The mixture (2·9 g; 6 mmol) of *Vb* 2′,5′- and 3′,5′-isomers was kept at room temperature in 0·1M methanolic sodium methoxide overnight and processed analogously to compound *VIa*. Crystalli-

sation from ethanol and ether (until the solution was turbid) yielded 1·2 g (73%) of compound *VIb*, m.p. 119–121°C. For $C_{11}H_{16}N_2O_6$ (272·3) calculated: 48·52% C, 5·92% H, 10·28% N; found: 47·90% C, 6·16% H, 10·41% N. NMR spectrum (hexadeuteriodimethyl sulfoxide): 1·17 (t, 3 H) and 2·54 (q, 2 H) CH_2CH_3; 3·30–3·60 (m, 2 H) 2 $H_{5'}$; 3·69 (m, 1 H) $H_{4'}$; 4·0 (br s) OH; 4·12 (t, 1 H, $J_{3',2'} = J_{3',4'} = 6·5$) $H_{3'}$; 4·56 (q, 1 H, $J_{2',1'} = 4·0$, $J_{2',3'} = 6·5$) $H_{2'}$; 5·39 (d, 1 H, $J_{1',2'} = 4·0$) $H_{1'}$; 5·44 (br s, 1 H, $J_{5,NH} = 1·0$) H_5; 11·14 (br s, 1 H) NH.

3′,5′-Di-O-benzoyl-2′-chloro-2′-deoxy-6-ethyluridine (*VIIb*)

A solution of compound *IIb* (4·0 g; 8·7 mmol) in 3M hydrogen chloride in dimethylformamide (60 ml) was heated at 100°C for 1 h under exclusion of atmospheric moisture (the reaction was complete, as shown by chromatography in S_3). The mixture was poured with stirring into water (500 ml), the solid collected with suction, washed with water, and dissolved in chloroform (100 ml). The solution was dried over anhydrous magnesium sulfate and evaporated under diminished pressure to afford 2·8 g (65%) of compound *VIIb*, amorphous foam, R_F 0·76 in S_3 and 0·46 in S_4. For $C_{25}H_{23}ClN_2O_7$ (498·9) calculated: 60·18% C, 4·64% H, 7·10% Cl, 5·63% N; found: 59·66% C, 4·85% H, 7·29% Cl, 5·47% N. NMR spectrum: 1·24 (t, 3 H, $J_{CH_3,CH_2} = 7·0$) CH_2CH_3; 2·55 (q, 2 H) CH_2CH_3; 4·45–4·75 (m, 3 H, $J_{3',4'} = 6·0$) $H_{4'}$ and 2 $H_{5'}$; 5·58 (s, 1 H) H_5; 5·46 (q, 1 H, $J_{1',2'} = 3·3$, $J_{2',3'} = 6·6$) $H_{2'}$; 5·89 (d, 1 H, $J_{1',2'} = 3·3$) $H_{1'}$; 5·90 (m, 1 H) $H_{3'}$; 7·25–8·10 (m, 10 H) aromatic protons; 9·48 (br s, 1 H) NH.

3′,5′-Di-O-benzoyl-2′-deoxy-6-ethyluridine (*VIIIb*)

A mixture of compound *VIIb* (2·6 g; 5·2 mmol), tri-n-butyltin hydride (6·0 g), benzene (40 ml), and 2,2′-azobis(2-methylpropionitrile) (20 mg) was refluxed for 1 h (the reaction was complete, as shown by thin-layer chromatography in the solvent system S_5), evaporated under diminished pressure, and the residue chromatographed on two silica gel layers in S_5 as above. Elution with methanol, evaporation of the eluate, and drying yielded 1·6 g (66%) of compound *VIIIb*, amorphous foam, R_F 0·17 in S_5. For $C_{25}H_{24}N_2O_7$ (463·5) calculated: 64·64% C, 5·20% H, 6·03% N; found: 63·83% C, 5·27% H, 6·06% N. NMR spectrum: 1·24 (t, 3 H, $J_{CH_3,CH_2} = 7·0$) 6-CH_3CH_2; 2·62 (q, 2 H, $J_{CH_2,CH_3} = 7·0$) 6-CH_3CH_2; 2·43 (m, 1 H, $J_{2'',1'} = 8·8$, $J_{gem} = 14·0$, $J_{2'',3'} = 5·4$) $H_{2''}$; 3·36 (m, 1 H, $J_{2',1'} = 4·8$, $J_{2',3'} = 8·3$) $H_{2'}$; 4·48 (q, 1 H, $J_{4',3'} = J_{4',5'} = J_{4',5''} = 5·4$) $H_{3'}$; 4·71 (m, 2 H) 2 $H_{5'}$; 5·60 (s, 1 H) H_5; 6·12 (q, 1 H, $J_{1',2'} = 4·8$, $J_{1',2''} = 8·8$) $H_{1'}$; 7·30 to 8·10 (m, 10 H) aromatic protons; 9·35 (br s, 1 H) NH.

2′-Deoxy-6-ethyluridine (*IXb*)

A solution of compound *VIIIb* (1·4 g; 3 mmol) in 0·1M methanolic sodium methoxide (50 ml) was kept at room temperature for 2 days and processed analogously to compound *VIa*. Crystallisation from ethanol and ether (until the solution was turbid) yielded 0·54 g (71%) of the chromatographically homogeneous (S_1 and S_2) compound *IXb*, m.p. 81–82°C. For $C_{11}H_{16}N_2O_5$ (256·3) calculated: 51·54% C, 6·29% H, 10·90% N; found: 51·41% C, 6·61% H, 10·24% N. NMR spectrum (hexadeuteriodimethyl sulfoxide): 1·15 (t, 3 H) and 2·55 (q, 2 H, $J = 7·0$) CH_2CH_3; 2·03 (dq, 1 H, $J_{2',1'} = 7·5$, $J_{2',3'} = 4·2$) $H_{2'}$; 2·84 (pent, 1 H, $J_{2'',1'} = 7·0$, $J_{2'',3'} = 8·0$, $J_{gem} = 12·5$) $H_{2''}$; 3·62 (m, 2 H), $J_{5',4'} = 3·0$, $J_{5'',4'} = 5·0$) 2 $H_{5'}$; 3·80 (m, 1 H) $H_{4'}$; 4·05 (br s, 1 H) OH; 4·42 (dt, 1 H, $J_{3',2'} = 4·2$, $J_{3',4'} = 4·2$, $J_{3',2''} = 8·1$) $H_{3'}$; 5·45 (br s, 1 H) H_5; 5·95 (br s, $J_{1',2'} = J_{1',2''} = 7·5$) $H_{1'}$; 11·06 (br s, 1 H) NH.

The author wishes to thank Dr M. Masojídková for measurement and interpretation of NMR spectra and Dr I. Frič for measurement of CD spectra. The excellent technical assistance of Mrs B. Kopecká is gratefully acknowledged.

REFERENCES

1. Holý A.: This Journal, in press.
2. Holý A.: Tetrahedron Letters *1973*, 1147.
3. Holý A.: This Journal *38*, 3912 (1973).
4. Holý A.: This Journal *38*, 423 (1973).
5. Holý A., Souček M.: Tetrahedron Letters *1971*, 185.
6. Holý A.: Nucl. Acid Res. *1*, 289 (1974).
7. Prystaš M., Šorm F.: This Journal *34*, 2316 (1969).
8. Winkley M. W., Robins R. K.: J. Org. Chem. *33*, 2822 (1968).
9. Holý A., Bald R. W.: This Journal *36*, 2809 (1971).
10. Holý A., Bald R. W., Šorm F.: This Journal *37*, 592 (1972).
11. Votruba I., Holý A., Pichat L.: Nucl. Acid Res. *1*, 689 (1974).
12. Miles D. W., Robins M. J., Robins R. K., Winkley M. W., Eyring H.: J. Am. Chem. Soc. *91*, 824 (1969).
13. Doskočil J., Holý A.: Nucl. Acid Res. *1*, 645 (1974).

Translated by J. Pliml.