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BRANCHED-CHAIN SUGAR NUCLEOSIDES. SYNTHESIS OF 3′-*C*-ETHYL (AND 3′-*C*-BUTYL)URIDINE

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ABSTRACT

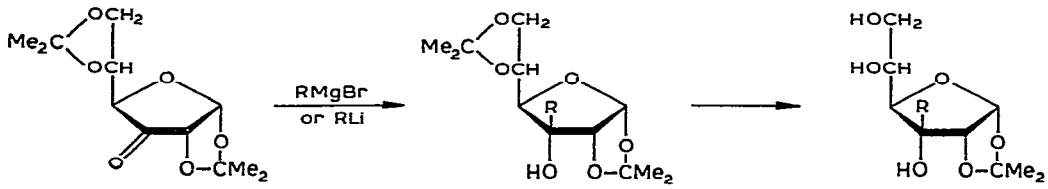
Syntheses of 3′-*C*-ethyl(and 3′-*C*-butyl)uridine (**13** and **15**) are described. Addition of ethyl (and butyl)magnesium bromide or the corresponding alkyllithiums to 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose (**1**) gave 3-*C*-ethyl (and 3-*C*-butyl)-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**2** and **3**). Selective hydrolysis of **2** and **3**, followed by periodate cleavage of the 5,6-diol and subsequent reduction, yielded the diols **6** and **7**. Selective benzoylation of the latter compounds afforded 5-*O*-benzoyl-3-*C*-ethyl(and 3-*C*-butyl)-1,2-*O*-isopropylidene-α-D-ribofuranose (**8** and **9**). Hydrolysis of the latter compounds, followed by acetylation, yielded anomeric mixtures of branched-chain sugar triacetates **10** and **11**. These were condensed with bis(trimethylsilyl)uracil and the products deacylated with methanolic ammonia to afford in high yield the title nucleosides **13** and **15**.

INTRODUCTION

3′-*C*-Methyladenosine and 3′-*C*-methylcytidine, the first synthetic 3′-*C*-alkyl, branched-chain sugar nucleoside analogues of the naturally occurring ribonucleosides, were reported[1,2] a decade ago. Because these branched-chain sugar nucleosides[3–8], containing a tertiary hydroxyl group at C-3′, exhibit interesting activity against Vaccinia virus infection in mice, we were led to undertake the synthesis of additional C-3′ branched-chain nucleosides having various alkyl chain-branches. Support for this undertaking was provided by a recent report[9] that enhanced growth-inhibiting activity was observed against CCRF-CEM human lymphoblastic leukemia cells in culture as the length of the alkyl side-chain in the sugar and the resultant lipophilic character of the nucleoside were increased. In this paper, we report the synthesis of 3′-*C*-branched alkyl analogues of uridine.

RESULTS AND DISCUSSION

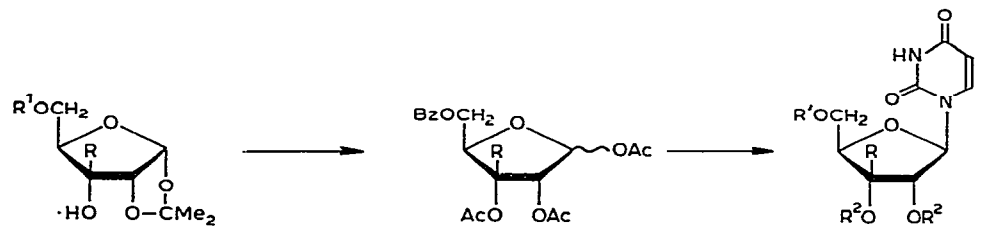
For the synthesis of 3′-*C*-ethyl(and 3′-*C*-butyl)uridine, the readily available 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose[10,11] (**1**) was chosen as the starting ketose. Treatment of **1** with ethylmagnesium bromide in the presence of



1

2 R = Et
3 R = Bu

4 R = Et
5 R = Bu



6 R = Et, R¹ = H
7 R = Bu, R¹ = H
8 R = Et, R¹ = Bz
9 R = Bu, R¹ = Bz

10 R = Et
11 R = Bu

12 R = Et, R¹ = Bz, R² = Ac
13 R = Et, R¹ = R² = H
14 R = Bu, R¹ = Bz, R² = Ac
15 R = Bu, R¹ = R² = H

magnesium bromide at −30° was stereospecific and afforded crystalline 3-*C*-ethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**2**) in 68% yield. Similar addition of butylmagnesium bromide to ketose **1** yielded the 3-*C*-butyl homologue **3** in only 42% yield. Use of butyllithium rather than the Grignard reagent gave a 57% yield of the branched-chain sugar **3**. The factors controlling the yield of various C-3-alkyl branched-chain *allo* sugars, as well as proof of their structure, have been described previously[12]. Ethynylation of ketose **1** afforded the *allo* product exclusively[13].

Selective hydrolysis of **2** and **3** with 80% acetic acid removed the 5,6-*O*-isopropylidene group to afford the branched-chain triols **4** and **5** in almost quantitative yield. Treatment of these with sodium metaperiodate, followed by reduction of the resulting aldehydes with sodium borohydride, yielded the branched-chain D-*ribo* diols **6** and **7** crystalline in 90 and 85% yields, respectively. Selective benzoylation of **6** and **7** with one equivalent of benzoyl chloride in pyridine yielded 5-*O*-benzoyl-3-*C*-ethyl(and 3-*C*-butyl)-1,2-*O*-isopropylidene-α-D-ribofuranose (**8** and **9**) in 73 and 91% yields, respectively. Hydrolysis of the latter compounds with 90% aqueous trifluoroacetic acid by an established procedure[4] afforded branched-chain triols that were immediately acetylated with acetic anhydride and pyridine, followed by acetic anhydride and *p*-toluenesulfonic acid, to afford the fully acetylated, branched-chain anomeric acetates **10** and **11** in >90% yield. The latter compounds were condensed with bis(trimethylsilyl)uracil in anhydrous acetonitrile in the presence of tin tetrachloride, according to a known procedure[15], for 40 h at room temperature to afford 1-[2,3-di-*O*-acetyl-5-*O*-benzoyl-3-*C*-ethyl(and 3-*C*-butyl)-β-D-ribofuranosyl]uracil **12**

and **14**, respectively, in 75% yield. The latter, protected compounds were deacylated with methanolic ammonia for 16 h at 20° to give crystalline 1-(3-*C*-ethyl-β-D-ribofuranosyl)uracil (**13**) and the 3′-*C*-butyl analogue **15** in 83 and 70% yield, respectively. The site of glycosylation[15,16] in nucleosides **13** and **15** was established as N-1, as both nucleosides exhibited u.v. maxima at 260 nm. The assignment of anomeric configuration of **13** and **15** was based on their c.d. spectra. Both nucleosides exhibited strongly positive c.d. curves at λ_{max} 268 nm. A positive Cotton-effect has been found[17–19] characteristic of the β-D configuration in furanoid pyrimidine nucleosides. The ^{1}H-n.m.r. spectra of **14** and **15** clearly showed doublets for H-1′ at δ 5.99 and 5.95, having $J_{1',2'}$ = 8.0 Hz. The large values of $J_{1',2'}$ for compounds **13** and **15** are in accord with the unexpectedly high value (8.2 Hz) of $J_{1',2'}$ of 3′-*C*-methyladenosine[2].

Preliminary, *in vitro* bioassay of 3′-*C*-ethyluridine (**13**) and 3′-*C*-butyluridine (**15**) with cultured L-1210 cells showed inhibitions of 20 and 21%, respectively, at a concentration of 1×10^{-4} M.

EXPERIMENTAL

General methods. — Solutions were dried with anhydrous sodium sulfate and evaporated under diminished pressure. Column chromatography was performed on t.l.c.-grade Silica Gel H without binder (Merck) under a pressure of 4–8 lb.in.$^{-2}$ with flow rates of 70–140 mL/h. ^{1}H-N.m.r. spectra were determined in chloroform-*d* (unless otherwise specified) solution with tetramethylsilane as the internal standard (set at δ = 0) by using a Varian XL-100 spectrometer. I.r. spectra were recorded with a Perkin–Elmer 337 spectrometer. Optical rotations were measured with a Perkin–Elmer Model 141 automatic polarimeter. C.d. spectra were determined with a Jasco-20 spectrometer. All melting points are uncorrected. Elemental analyses were performed by Mr. P. Borda, Microanalytical Laboratory, University of British Columbia, Vancouver.

Preparation of 3-C-ethyl-1,2:5,6-di-O-isopropylidene-α-D-allofuranose (**2**). — *Procedure A.* To a mixture of magnesium powder (0.84 g, 35 mmol) in anhydrous ether (20 mL) was added dropwise with stirring 1,2-dibromoethane (0.86 mL, 10 mmol) under nitrogen. After the reaction had reached completion, ethyl bromide (25 mmol) in anhydrous ether (5 mL) was added dropwise. The solution was cooled to −30°, and then a solution of the ketose **1** (1.29 g, 5 mmol) in anhydrous ether (15 mL) was added dropwise. The mixture was kept with stirring for 2 h at −30°. The complex was decomposed with 30 mL of wet ether, with subsequent addition of M hydrochloric acid to pH 8–9. The ether layer was decanted and the residue washed with ether (2 × 50 mL), and the combined ether extracts were dried, evaporated, and the residue dried under diminished pressure for 20 h. Based on analysis of the ^{1}H-n.m.r. spectrum of the mixture of products, the ratio of compound **2** to 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose was 14:3. No *gluco* isomer was present in the mixture, as evidenced by the n.m.r. spectrum of the product (H-1 of

the *gluco* isomer resonates at δ 5.91, whereas H-1 of the *allo* isomer resonates at δ 5.77). Compound **2** was purified by column chromatography on silica gel with 19:1 dichloromethane–ethyl acetate as developer. Recrystallization of the product from ether–hexane gave pure compound **2**; yield 0.98 g (68%), m.p. 93–94°, $[\alpha]_D$ 20.5° (*c* 1, chloroform); n.m.r.: δ 5.66 (d, $J_{1,2}$ 3.9 Hz, H-1), 4.13 (d, H-2), 1.55, 1.41, and 1.31 (3 s, Me).

Anal. Calc. for $C_{14}H_{24}O_6$: C, 58.32; H, 8.39. Found: C, 58.42; H, 8.60.

Procedure B. The reaction was performed as in Procedure *A*, except for the temperature. The reactants were kept for 0.5 h at 20°. The ratio of compound **2**: *allo*:*gluco* reduction-products was 15:4:1 (determined by analysis of the n.m.r. spectrum of the product).

Procedure C. The reaction was performed as in Procedure *B*, except that the magnesium bromide was omitted. The ratio of products (see Procedure *B*) was 13:5:2.

Reaction of ketose **1** *with butyllithium to yield* **3**. — To a stirred solution of butyllithium (16 mmol) in anhydrous hexane (10 mL) kept at −30° was added dropwise ketose **1** (7.29 g, 5 mmol) in anhydrous ethyl ether (30 mL). The mixture was stirred for 1 h at 30°, and the temperature of the mixture was then allowed to rise to 0°. Wet ether, followed by M hydrochloric acid, was then added dropwise to neutrality. The ether layer was separated and the aqueous solution was extracted with ether (2 × 50 mL). The combined ether extracts were then washed with water, dried, and evaporated. The residue was recrystallized from hexane to afford 3-*C*-butyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**3**); yield 0.9 g (57%). No reduction products were obtained during the reaction of ketose **1** with butyllithium. Compound **3** had m.p. 98–99°, $[\alpha]_D^{25}$ +12.1° (*c* 1, chloroform); n.m.r.: δ 5.66 (d, $J_{1,2}$ 3.9 Hz, H-1), 4.33 (d, H-2), 1.57, 1.43, and 1.33 (3 s, 12, Me).

Anal. Calc. for $C_{16}H_{28}O_6$: C, 60.74; H, 8.92. Found: C, 60.85; H, 9.00. Application of the Grignard synthesis to ketose **1** gave **3** in 42% yield.

3-C-Ethyl-1,2-O-isopropylidene-α-D-allofuranose (**4**) *and the 3-C-butyl homologue* (**5**). — A solution of compound **2** (5.76 g, 20 mmol) in 80% acetic acid (80 mL) was selectively hydrolyzed for 40 h at room temperature. The solvent was removed and the residue azeotropically dried with ethanol (5 × 20 mL). The product **4** (4.96 g), which could not be crystallized, was obtained in quantitative yield (R_F 0.22 in 9:1 chloroform–methanol).

Similar hydrolysis of **3** afforded the 3-*C*-butyl analogue **5**. Crystallization of **5** from chloroform–hexane afforded crystalline **5** in 88% yield; m.p. 132–133°, $[\alpha]_D^{25}$ +23.9° (*c* 1, methanol); R_F 0.80 (9:1 chloroform–methanol); n.m.r.: δ 5.75 (d, 1, $J_{1,2}$ 4.0 Hz, H-1), 4.39 (d, 1, H-2), 3.80–4.00 (m, 4, H-4,5,6,6'), 2.0–2.60 (broad, OH), 1.60 (s, 3, CH_3), 1.38 (s, 3, CH_3), and 0.80–1.80 (m, 9, Bu).

Anal. Calc. for $C_{13}H_{24}O_6$: C, 56.51; H, 8.75. Found: C, 56.31; H, 8.81.

3-C-Ethyl-1,2-O-isopropylidene-α-D-ribofuranose (**6**) *and its 3-C-butyl homologue* (**7**). — To a solution of compound **4** (4.96 g, 20 mmol) in water (30 mL) was added sodium metaperiodate (20 mmol), and the solution was stirred for 1 h at 20°. Ethanol

(15.0 mL) was added, and the solid was removed by filtration and washed with one portion of ethanol (30 mL). To the combined ethanol filtrates was added sodium borohydride (2.3 g, 60 mmol), and the resulting solution was stirred for 16 h at room temperature. The solution was made neutral with acetic acid, and water (40 mL) and chloroform (150 mL) were added. The organic layer was separated from the water layer and the latter was further extracted with chloroform (100 mL). The combined organic extracts were evaporated, and to the residue was added methanol (3 × 30 mL), and the methanol was then evaporated off to yield **6** (3.9 g, 90%). An analytical sample was obtained by sublimation; m.p. 94–96°, $[\alpha]_D^{25}$ +31.3° (*c* 1, methanol); n.m.r.: δ 5.80 (d, 1, $J_{1,2}$ 4.0 Hz, H-1), 4.22 (d, 1, H-2), 3.80–4.10 (m, 3, H-4,5,5′), 1.60 and 1.38 (2 s, 6, CH_3), 1.40–1.70 (m, 2, CH_2), and 1.00 (t, 3, CH_3).

Anal. Calc. for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 55.07; H, 8.17.

Degradation and reduction of the 3-*C*-butyl derivative **5** by a similar procedure yielded 3-*C*-butyl-1,2-*O*-isopropylidene-α-D-ribofuranose (**7**) in 85% yield. Compound **7** was recrystallized from hexane–chloroform; m.p. 108–109°, $[\alpha]_D^{25}$ +28.5° (*c* 1, methanol); n.m.r.: δ 5.82 (d, 1, $J_{1,2}$ 4.0 Hz, H-1), 4.35 (d, 1, H-2), 3.70–4.0 (m, 3, H-4,5,5′), 1.60 and 1.39 (2 s, 6, CH_3), and 0.80–1.80 (m, 9, Bu).

Anal. Calc. for $C_{12}H_{22}O_5$: C, 58.52; H, 9.0. Found: C, 58.71; H, 8.90.

5-O-Benzoyl-3-C-ethyl-1,2-O-isopropylidene-α-D-ribofuranose (**8**) *and its 3-C-butyl homologue* (**9**). — Compound **6** (3.27 g, 15 mmol) in anhydrous pyridine (20 mL) was selectively benzoylated with benzoyl chloride (2.1 mL, 18 mmol) for 16 h at 0°. Water (3 mL) was added and the mixture was stirred for 0.5 h at 20°. Additional water (30 mL) was added and the mixture was extracted with chloroform (100 mL), with a subsequent, second extraction of the water layer with chloroform (50 mL). The combined chloroform extracts were washed with aqueous sodium hydrogencarbonate and water, dried, and evaporated. The residue was azeotropically dried with toluene (3 × 10 mL). Column chromatography of the residue on silica gel (200 g) with 97:3 chloroform–methanol as developer gave compound **8**, which was recrystallized from hexane; yield 3.53 g (75%); m.p. 84–85°, $[\alpha]_D^{25}$ +7.9° (*c* 1, chloroform); $\nu_{max}^{CCl_4}$ 3580 (OH) and 1720 cm^{-1} (C=O); n.m.r.: δ 7.30–8.15 (m, 5, Bz), 5.89 (d, 1, $J_{1,2}$ 3.8 Hz, H-1), 4.30 (d, 1, H-2), 4.05–4.60 (m, 3, H-4,5,5′), 2.64 (s, 1, OH), 1.36 and 1.57 (2 s, 6, CH_3), 1.50–1.70 (m, 2, CH_2), and 1.02 (t, 3, CH_3).

Anal. Calc. for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 63.53; H, 7.04.

Benzoylation of compound **7** by a similar procedure afforded 5-*O*-benzoyl-3-*C*-butyl-1,2-*O*-isopropylidene-α-D-ribofuranose (**9**) in 91% yield; it was recrystallized from hexane; m.p. 91–92°, $[\alpha]_D^{25}$ +3.6° (*c* 0.5, chloroform); $\nu_{max}^{CCl_4}$ 3580 (OH) and 1720 cm^{-1} (C=O); n.m.r.: δ 7.40–8.20 (m, 5, Bz), 5.84 (d, 1, $J_{1,2}$ 3.8 Hz, H-1), 4.37 (d, 1, H-2), 4.10–4.70 (m, 3, H-4,5,5′), 2.66 (s, 1, OH), 1.39 and 1.61 (2 s, 6, CH_3), and 0.80–1.70 (m, 9, Bu).

Anal. Calc. for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 65.09; H, 7.43.

1,2,3-Tri-O-acetyl-5-O-benzoyl-3-C-ethyl-α,β-D-ribofuranose (**10**) *and the 3-C-butyl homologue* (**11**). — A solution of compound **8** (3.22 g, 10 mmol) in 90% aqueous

trifluoroacetic acid (20 mL) was stirred for 0.5 h at room temperature. The solution was evaporated and toluene (1 × 30 mL and 3 × 10 mL) was evaporated from the residue to remove the last traces of acid. The resulting syrup was acetylated with acetic anhydride (15 mL) and anhydrous pyridine (20 mL). After 16 h at room temperature, the solution was poured into ice–water (10 mL) and stirred for 0.5 h. The mixture was extracted with chloroform (100 mL) and the extract washed successively with aqueous sodium hydrogencarbonate and water, dried, and evaporated. The residue was dried by evaporation of toluene (3 × 30 mL) from it, and the tertiary hydroxyl group of the residue was then acetylated with acetic anhydride (15 mL) and *p*-toluenesulfonic acid monohydrate (0.76 g, 4 mmol). The mixture was kept for 3 days at ~25° and chloroform (100 mL) was then added. The resulting solution was washed consecutively with water, aqueous sodium hydrogencarbonate and water, dried, and evaporated. The residue was azeotropically dried with toluene (3 × 10 mL). Column chromatography of the product on silica gel (100 g) with 49:1 chloroform–methanol as developer gave compound **10** as a syrup (3.96 g, 97%). The ratio of α,β anomers (determined by n.m.r.) was 1:4; R_F 0.54 with 19:1 chloroform–methanol; n.m.r.: δ 7.40–8.75 (m, 5, Bz), 6.38 (d, $J_{1\alpha,2}$ 4.5 Hz, H-1α), 6.10 (d, $J_{1\beta,2}$ 2.5 Hz, H-1β), 5.54 (d, H-2), 5.36 (d, H-2), 4.30–4.90 (m, 3, H-4,5,5'), 1.98 and 2.34 (m, CH_2), 2.06, 2.05 and 1.92 (3 s, 9, Ac), 0.87 and 0.89 (t, *J* 6.7 Hz, CH_3).

Acetylation of the 3-*C*-butyl triol **9** according to a similar procedure afforded 1,2,3-tri-*O*-acetyl-5-*O*-benzoyl-3-*C*-butyl-α,β-D-ribofuranose (**11**) as a syrup in 90% yield. The ratio of α,β anomers (determined by n.m.r.) was 1:4; R_F 0.56 with 19:1 chloroform–methanol; n.m.r.: δ 7.40–8.20 (m, 5, Bz), 6.40 (d, $J_{1\alpha,2}$ 4.5 Hz, H-1α), 6.11 (d, $J_{1\beta,2}$ 2.5 Hz, H-1β), 5.56 (d, H-2), 5.37 (d, H-2), 4.30–4.90 (m, 3, H-4,5,5'), 1.95–2.30 (m, CH_2), 1.92, 2.04, and 2.08 (3 s, Ac), and 0.70–1.50 (m, $CH_2CH_2CH_3$).

1-(3-C-Ethyl-β-D-ribofuranosyl)uracil (*3'-C-ethyluridine*) (**13**) *and 3'-C-butyluridine* (**15**). — A mixture of compound **10** (1.63 g, 4 mmol), bis(trimethylsilyl)uracil (from 0.56 of g uracil, 5 mmol), and tin tetrachloride (0.45 mL, 4 mmol) in anhydrous acetonitrile (20 mL) was allowed to react for 4 h at room temperature according to a known procedure[13]. Chloroform (100 mL) and saturated aqueous sodium hydrogencarbonate (20 mL) were added, the mixture was stirred for 0.5 h at room temperature, and then filtered through Celite. The chloroform layer was washed with aqueous sodium hydrogencarbonate and water, dried, and evaporated. Chromatography of the residue on silica gel (60 g) with 97:5 chloroform–methanol as developer afforded 1-(2,3-di-*O*-acetyl-5-*O*-benzoyl-3-*C*-ethyl-β-D-ribofuranosyl)uracil (**12**) as a foam (1.38 g, 75% yield); R_F 0.19 on silica gel with 19:1 chloroform–methanol as developer; n.m.r.: δ 8.86 (s, 1, NH), 7.45–8.10 (m, 5, Bz), 7.45 (d, 1, $J_{5,6}$ 8.0 Hz, H-6), 6.21 (d, 1, $J_{1',2'}$ 8.0 Hz, H-1'), 5.50 (d, 1, H-2'), 5.40 (dd, 1, $J_{5,NH}$ 2.0 Hz, H-5), 4.95 (t, 1, H-4'), 4.40–4.85 (m, 2, H-5',5''), 2.61 and 1.90 (m, 2, CH_2), 2.10 and 2.18 (2 s, 6, Ac), and 0.90 (t, 3, *J* 7.0 Hz, CH_3).

Condensation of the 3-*C*-butyl analogue **11** with bis(trimethylsilyl)uracil by a similar procedure yielded the protected nucleoside **14** as a foam in 75% yield; R_F 0.25 on silica gel with 19:1 chloroform–methanol as developer; n.m.r.: δ 9.14 (s, 1,

NH), 7.45–8.10 (m, 5, Bz), 7.42 (d, 1, $J_{5,6}$ 8.0 Hz, H-6), 6.10 (d, 1, $J_{1',2'}$ 8.0 Hz, H-1′), 5.46 (d, 1, H-2′), 5.40 (d, 1, H-5), 4.90 (t, 1, H-4′), 4.40–4.85 (m, 2, H-5′,5″), 1.90 and 2.50 (2 m, 2, CH_2), 2.08 and 2.14 (2 s, 6, Ac), and 0.70–1.40 (m, 7, $CH_2CH_2CH_3$).

The protected 3′-*C*-ethyl nucleoside **12** (1.15 g, 2.5 mmol) was deacylated with methanolic ammonia (30 mL) (to a saturated methanol–ammonia solution at 0° was added an equal volume of methanol) for 16 h at room temperature. The mixture was evaporated to dryness and the residue crystallized from acetone to afford 3′-*C*-ethyluridine (**13**); yield 0.565 g (83%); m.p. 217–218°, $[\alpha]_D^{25}$ −7.9° (*c* 0.7, Me_2SO-d_6); $\lambda_{max}^{H_2O}$ 260 nm (ε 10,800), λ_{max}^{pH13} 260 nm (ε 8000); c.d. $\Delta\varepsilon$ +0.95 (λ_{max} 269 nm), $\Delta\varepsilon$ −1.1 (trough, 240 nm); n.m.r. (D_2O): δ 7.93 (d, 1, $J_{5,6}$ 8.0 Hz, H-6), 5.99 (d, 1, $J_{1',2'}$ 8.0 Hz, H-1′), 5.90 (d, 1, H-5), 4.22 (d, 1, H-2′), 4.08 (t, 1, H-4′), 3.77 (m, 2, H-5′,5″), 7.69 (m, 2, CH_2), and 0.96 (t, 3, CH_3).

Anal. Calc. for $C_{11}H_{16}N_2O_6$: C, 48.52; H, 5.92; N, 10.29. Found: C, 48.89; H, 5.92; N, 10.16.

Compound **14** was deprotected as just described for **13**, to afford 3′-*C*-butyluridine (**15**) crystalline in 70% yield; m.p. 221–223°, $[\alpha]_D$ −1.1° (*c* 0.44, dimethylsulfoxide); λ_{max} 260 nm (ε 10,500), λ_{max}^{pH13} 260 nm (ε 7600); c.d. $\Delta\varepsilon$ +1.0 (λ_{max} 268 nm), $\Delta\varepsilon$ −1.1 (trough, 258 nm); n.m.r. (Me_2SO-d_6): δ 11.30 (s, 1, NH, exchanged with D_2O), 8.15 (d, 1, $J_{5,6}$ 8.0 Hz, H-6), 5.95 (d, 1, $J_{1',2'}$ 8.0 Hz, H-1′), 5.71 (d, 1, H-5), 5.35 (d, 1, *J* 6.5 Hz, 2′-OH, exchanged with D_2O), 5.19 (t, 1, *J* 4.0 Hz, 5′-OH, exchanged with D_2O), 4.53 (s, 1, 3′-OH, exchanged with D_2O), 4.00 (d, 1, H-2′), 3.50–3.90 (m, 3, H-4′,5′,5″), and 0.80–1.70 (m, 9, Bu).

Anal. Calc. for $C_{13}H_{20}N_2O_6$: C, 51.99; H, 6.71; N, 9.33. Found: C, 52.17; H, 6.74; N, 9.16.

Biological studies. — 3′-*C*-Ethyluridine (**13**) exhibited 20% inhibition when tested on cell line L-1210 in culture at a concentration of 1×10^{-4}M. At the same concentration, 3′-*C*-butyluridine (**15**) exhibited 21% inhibition.

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