2-*C*-Nitromethyl and 2-*C*-Aminomethyl Derivatives of D-Ribose. Preparation of 2'-*C*-Nitromethyluridines.

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Syntheses of derivatives of 2-*C*-nitromethyl-D-ribofuranose from a 3-*C*-nitromethyl-D-allofuranose are reported. The use of two of these compounds in nucleoside syntheses and their catalytic reduction, which takes place with acetyl migration, are discussed.

REPORTS [1] that the modified nucleosides 2'- and 3'-*C*-methyladenosine and 3'-*C*-methylcytidine are effective antiviral agents in mice have led to the syntheses of a variety of other branched-chain nucleosides.[2] Although most of these were prepared [3,4] by attack of a suitable nucleophile on a glycos-3-ulose to obtain branched-chain sugars which were then used for nucleoside syntheses, some were also prepared by attack of nucleophiles on preformed 2'- or 3'-oxonucleosides.[5,6]

Few 2'-*C*-substituted branched-chain nucleosides have been described,[1,5,6] and the report [6] that two 2'-*C*-nitromethylhexopyranosylpurines were active against KB tumour cells has prompted us to investigate methods of synthesizing other 2'-*C*-nitromethyl nucleosides.

It was of interest that although both a protected 9-(β-D-xylofuranosulosyl)adenine [5] and a protected 7-(β-D-glucopyranosulosyl)theophylline [5] reacted readily with nitromethane and base to give 2'-*C*-substituted products, 1-(3,5-di-*O*-trityl-β-D-ribofuranosulosyl)uracil [7] was very labile towards alkali and readily lost the uracil moiety through β-elimination. Protected β-D-ribofuranosulosyluracils therefore seemed to be unsuitable starting materials for the syntheses of 2'-*C*-substituted uridines. Also, although nucleophilic attack on suitably protected D-*erythro*-pentofuranosulosides would probably result in branched-chain *ribo*- or *arabino*-derivatives which could be elaborated to nucleosides, these furanosulosides have not as yet been described and multi-step syntheses would be required to obtain them.

To circumvent these difficulties it was decided to adapt the method developed [8] for preparing 2-deoxy-2-fluoro-pentofuranoses from 3-deoxy-3-fluoro-hexofuranoses to the synthesis of a 2-deoxy-2-*C*-nitromethylribofuranose. It was considered that a ribofuranose containing a 2-*C*-nitromethyl substituent would be useful not only for nucleoside syntheses but also as a starting material for conversion into sugars bearing other 2-*C*-substituents such as aminomethyl,[2,4] or hydroxymethyl.[9]

The known [4] 3-deoxy-1,2-*O*-isopropylidene-3-*C*-nitromethyl-α-D-allofuranose was selectively monobenzoylated to give the benzoate (1). The 1,2-*O*-isopropylidene group was then removed by acidic hydrolysis to give the product (2), which was oxidized with sodium periodate to give the ribofuranose (3). The n.m.r. spectrum of compound (2) in [$^2H_6$]dimethyl sulphoxide was poorly resolved and could not be used to confirm that the compound had a furanose structure. It therefore had to be borne in mind that compound (2) could have rearranged [8] to a pyranose form which would be oxidized by periodate to 5-*O*-benzoyl-2-deoxy-4-*O*-formyl-2-*C*-nitromethyl-*aldehydo*-D-ribose. However,

[1] R. F. Nutt, M. J. Dickenson, F. W. Holly, and E. Walton, *J. Org. Chem.*, 1968, **33**, 1789; S. R. Jenkins, B. Arison, and E. Walton, *ibid.*, p. 2490; E. Walton, S. R. Jenkins, R. F. Nutt, F. W. Holly, and M. Nemes, *J. Medicin. Chem.*, 1969, **12**, 306.

[2] A. Rosenthal and C. M. Richards, *Carbohydrate Res.*, 1974, **32**, 53, 67; A. Rosenthal and D. A. Baker, *J. Org. Chem.*, 1973, **38**, 193, and references cited therein.

[3] A. J. Brink and A. Jordaan, *Carbohydrate Res.*, 1975, **41**, 355.

[4] H. P. Albrecht and J. G. Moffatt, *Tetrahedron Letters*, 1970, 1063.

[5] A. Rosenthal, M. Sprinzl, and D. A. Baker, *Tetrahedron Letters*, 1970, 4233.

[6] F. Leclercq, M. Bessodes, J. Jumelet, and K. Antonakis, *J. Carbohydrates Nucleosides Nucleotides*, 1974, **1**, 349.

[7] A. F. Cook and J. G. Moffatt, *J. Amer. Chem. Soc.*, 1967, **89**, 2697.

[8] U. Reichman, K. A. Watanabe, and J. J. Fox, *Carbohydrate Res.*, 1975, **42**, 233.

[9] W. P. Blackstock, C. C. Kuenzle, and C. H. Eugster, *Helv. Chim. Acta*, 1974, **57**, 1003.

only the furanose (3), for which the structure was unequivocally established by n.m.r. spectroscopy, was isolated (in high yield) from the reaction mixture, leaving no doubt that compound (2) was also a furanose.

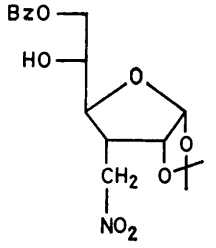
Attempts to acetylate compound (3) with acetic anhydride–pyridine were unsuccessful because of extensive decomposition of the starting material, and acetylation with acetic anhydride–toluene-*p*-sulphonic acid gave a mixture containing only *ca.* 50% of compound (4), probably because the *O*-formyl group was partially transesterified to an acetate. For these reasons the *O*-formyl group of compound (3) was selectively removed by brief treatment with methanolic sodium methoxide to give the anomeric mixture (5), which was acetylated with acetic anhydride–sodium acetate to give an anomeric mixture of the 1-*O*-acetyl compounds (6) and (7) in the ratio *ca.* 3 : 1. Chromatography afforded the crystalline β-compound (6) and the α-compound (7) as an oil. Montgomery's empirical rule [10] that, for an anomeric pair of carbohydrate derivatives, H-1 resonates at lower field when the substituents at C-1 and C-2 are *cis* than when they are *trans*, served to distinguish between the anomeric pair (6) and (7). These assignments of anomeric configurations were also supported by Hudson's isorotation rules.

Catalytic hydrogenation of the nitro-sugar (6) gave a product (8) containing an *N*-acetyl and a hydroxy-group. Clearly, after reduction of the nitro-group to a primary amino-group, an acetyl migration had taken place from the *cis* 3-*O*-position to the nearby amino-methyl group, probably through a six-membered transition state. A comparison of the n.m.r. spectra of compound (6) and its hydrogenation product (8) showed that their H-1 chemical shifts were very similar (τ 3.80 and 3.93, respectively), but that H-3 of compound (6), which was deshielded by the 3-*O*-acetyl group, resonated at much lower field than H-3 of compound (8) (τ 4.61 *vs.* 5.4—5.80, respectively).

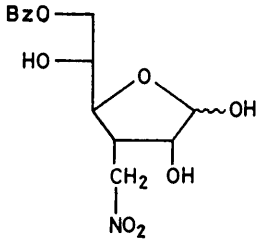
Acetylation of the *N*-acetyl compound (8) gave the di-*O*-acetyl compound (9), the n.m.r. spectrum of which showed marked deshielding of H-3 by the newly formed 3-*O*-acetyl group. [for compound (9), τ 4.48; for compound (8), τ 5.60].

As found during hydrogenation of compound (6), catalytic hydrogenation of the nitro-compound (7) also gave an *N*-acetyl product (10). In this case the n.m.r. spectrum of compound (10) showed that the acetyl group had not migrated from the *cis* 3-*O*-position but from the more reactive *cis* 1-*O*-position. The chemical shifts of H-3 in compounds (7) and (10) were similar (τ 4.56 and 4.70, respectively), but H-1 of compound (7), which was deshielded by the 1-*O*-acetyl group, resonated at much lower field than H-1 of compound (10) (τ 3.48 and 4.48, respectively).

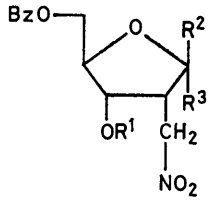
The $J_{1,2}$ value (4 Hz) for the amino-sugar (10) was such that the anomeric configuration could not be estab-



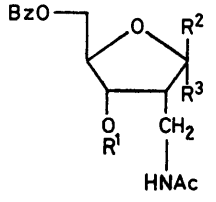
(1)



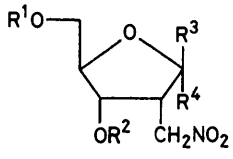
(2)



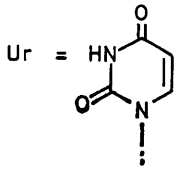
(3) R^1 = CHO, R^2R^3 = H, OH
(4) R^1 = CHO, R^2R^3 = H, OAc
(5) R^1 = H, R^2R^3 = H, OH
(6) R^1 = Ac, R^2 = OAc, R^3 = H
(7) R^1 = Ac, R^2 = H, R^3 = OAc



(8) $R^1 = R^3$ = H, R^2 = OAc
(9) R^1 = Ac, R^2 = OAc, R^3 = H
(10) R^1 = Ac, R^2R^3 = H, OH



(11) R^1 = Bz, R^2 = Ac, R^3 = H, R^4 = Ur
(12) R^1 = Bz, R^2 = Ac, R^3 = Ur, R^4 = H
(13) $R^1 = R^2 = R^3$ = H, R^4 = Ur
(14) $R^1 = R^3 = R^4$ = H, R^3 = Ur



[10] J. A. Montgomery, *Carbohydrate Res.*, 1974, **33**, 184, and references cited therein.

lished.[11] However, on acetylation of compound (10) only one product, the β-anomer (9), was formed, and it followed that during the reduction of the α-1-*O*-acetyl compound (7) and acetylation to the β-1-*O*-acetyl compound (9) an inversion of configuration at C-1 had taken place.

Protected pyrimidine nucleosides were prepared from each of the anomers (6) and (7) by treatment with bis-(trimethylsilyl)uracil using tin(IV) chloride as catalyst. The same anomeric pair of nucleoside derivatives (11) and (12) was formed in the ratio *ca.* 10 : 1. Again the rules of Montgomery[10] and the revised version of Hudson's rules for pyrimidine nucleosides[12] were invoked for the assignments of anomeric configuration. Although the β-anomer (6) is formed preferentially to the α-anomer (7) on acetylation of compound (5), this configurational preference was reversed when nucleosides were formed from compounds (6) and (7); mainly the α-anomer (11) was obtained.

Compound (11) was treated with sodium methoxide to give the deprotected crystalline nucleoside (13). Similarly, deblocking of compound (12) gave compound (14) as an oil, which was incompletely characterized.

EXPERIMENTAL

All solvent extracts were dried (Na_2SO_4), filtered, and evaporated below 50 °C *in vacuo*. T.l.c. [methanol–chloroform (1 : 19)] and column chromatography were performed on silica gel (Merck GF_{254}) [100 g of silica per g of residue for column separations]. M.p.s were determined with a hot-stage apparatus. Unless otherwise stated, i.r. spectra were measured for solutions in chloroform with a Perkin-Elmer 237 spectrophotometer, and n.m.r. spectra with a Varian HA-100 instrument (tetramethylsilane as internal standard; solutions in $CDCl_3$). Optical rotations were measured for solutions in chloroform with a Perkin-Elmer 241 automatic polarimeter (*c* 1.0 ± 0.3) and mass spectra with an A.E.I. MS9 spectrometer by direct insertion.

6-O-*Benzoyl*-3-*deoxy*-1,2-O-*isopropylidene*-3-C-*nitromethyl*-α-D-*allofuranose* (1).—To a solution of 3-deoxy-1,2-*O*-isopropylidene-3-*C*-nitromethyl-α-D-allofuranose[4] (4.24 g) in dry pyridine (40 ml), cooled to −20 °C in an ice-bath, a solution of benzoyl chloride (2.27 g, 1 equiv.) in dichloromethane (20 ml) was added. The flask was stoppered and the mixture was stirred at −20 °C for 3 min and then stored for 4 h at −20 °C in a refrigerator. The solvent was removed *in vacuo* and the residue was taken up in chloroform (200 ml). The chloroform solution was washed with ice-cold hydrochloric acid (100 ml; 0.1%), saturated aqueous sodium hydrogen carbonate (100 ml), and water (100 ml), and the solvent was removed to leave an oil which was purified by column chromatography [ethyl acetate–hexane (1 : 2) as eluant] to give *compound* (1) as an oil (3 g), $[\alpha]_D^{21}$ +62°, $\nu_{max.}$ 3 480 (OH), 1 720 (ester), and 1 550 cm^{-1} (NO_2), *m/e* 352 ($M^+ - CH_3$), τ 1.80—2.10 (2 H, m, arom. H), 2.20—2.80 (3 H, m, arom. H), 4.12 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 4.90—6.30 (7 H, m, H-2, -4, and -5, H_2-6, and C3-H_2), 6.76br (1 H, s, disappears on addition of D_2O, OH), *ca.* 7.0br (1 H, m, H-3), 8.48 (3 H, s, CH_3), and 8.66 (3 H, s, CH_3) (Found: C, 55.4; H, 5.6: N, 3.6. $C_{17}H_{21}NO_8$ requires C, 55.6; H, 5.8; N, 3.8%).

6-O-*Benzoyl*-3-*deoxy*-3-C-*nitromethyl*-α-D-*allofuranose* (2).—Compound (1) (1.9 g) was dissolved in dioxan (40 ml) and water (40 ml) was added with stirring. After addition of Amberlite IR-120 (H^+), the mixture was stirred for 20 h at 80 °C, filtered, and evaporated to leave an oil (1.57 g), which was purified by chromatography [ethyl acetate–hexane, (1 : 1) as eluant] to give pure *compound* (2) as an oil (1.01 g), $[\alpha]_D^{21}$ +22°, $\nu_{max.}$ 3 400br (OH), 1 715 (ester), and 1 550 cm^{-1} (NO_2), τ [$(CD_3)_2SO$] 1.90—2.20 (2 H, m, arom. H), 2.25—2.60 (3 H, m, arom. H), 3.62 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 4.96 (1 H, d, $J_{2,1}$ 4 Hz, H-2), *ca.* 7.05br (1 H, m, H-3), and 4.50—6.50 [*ca.* 9 H, m, H-4 and -5, H_2-6, 3-CH_2 and 3 × OH (changes on addition of D_2O)] (Found: C, 51.4; H, 5.3; N, 3.9. $C_{14}H_{17}NO_8$ requires C, 51.3; H, 5.2; N. 4.3%).

5-O-*Benzoyl*-2-*deoxy*-3-O-*formyl*-2-C-*nitromethyl*-D-*ribofuranose* (3).—Compound (2) (7.5 g) was dissolved in methanol (200 ml) and water (100 ml), and an aqueous solution (25 ml) of sodium periodate (5 g, 1 equiv.) was added with stirring. The mixture was stored in the dark at 25 °C for 2 h, the excess of oxidizing agent was destroyed with ethylene glycol (1 ml), the precipitate of sodium iodate was filtered off, and the filtrate was evaporated. The residue was extracted with chloroform (3 × 100 ml). Removal of the solvent afforded an oil (7 g) which was purified by chromatography (ethyl acetate as eluant) to give *compound* (3) as an oil (3 g), $[\alpha]_D^{21}$ +27°, $\nu_{max.}$ 3 590, 3 350 (OH), 1 725 (ester), and 1 550 cm^{-1} (NO_2), *m/e* 105 ($C_6H_5CO^+$), τ 1.86—2.10 (3 H, m, 2 arom. H, OCHO), 2.30—2.70 (3 H, m, 3 arom. H), 4.31 [1 H, d, $J_{1,2}$ 4 Hz, H-1 (α or β)], 4.51 (1 H, d, $J_{3,2}$ 7 Hz, H-3), 5.30 (2 H, d, *J* 7 Hz, 3-CH_2), 5.40—5.80 (3 H, m, H-4 and H_2-5), and 6.32br (1 H, m, H-2) [on irradiation at τ 6.32 (H-2) the doublets at τ 4.31, 4.51, and 5.30 (H-1 and -3, and 3-CH_2, respectively) collapse to singlets] (Found: C, 51.6; H, 4.6; N, 4.0. $C_{14}H_{15}NO_8$ requires C, 51.7; H, 4.7; N, 4.3%).

1-O-*Acetyl*-5-O-*benzoyl*-2-*deoxy*-3-O-*formyl*-2-C-*nitromethyl*-D-*ribofuranose* (4).—Compound (3) (200 mg) was dissolved in acetic anhydride (2 ml) and toluene-*p*-sulphonic acid (20 mg) was added. The mixture was stirred at 25 °C for 48 h, then poured into ice–water (100 ml) and stirred for 2 h before extraction with chloroform (2 × 100 ml). The combined extracts were washed with aqueous sodium hydrogen carbonate (100 ml) and water (100 ml), and the solvent was removed to leave an oily mixture containing mainly one component (t.l.c.). Chromatography [ethyl acetate–hexane (1 : 2)] gave pure *compound* (4) as an oil (100 mg), $\nu_{max.}$ 1 745 (ester) and 1 555 cm^{-1} (NO_2), τ 1.92 (1 H, s, CHO), 2.03 (2 H, m, 2 arom. H), 2.40—2.70 (3 H, m, 3 arom. H), 3.51 [1 H, d, $J_{1,2}$ 4 Hz, H-1, (α or β)], 4.46 (1 H, d, $J_{2,3}$ 7 Hz, H-3), 5.20—5.60 (5 H, m, H-4, H_2-5, and 3-CH_2), *ca.* 6.55br (1 H, m, H-2), and 7.90 (3 H, s, OAc) (Found: *m/e*, 324.072. $C_{14}H_{14}NO_8$ requires $M^+ - CH_3CO$, 324.072).

5-O-*Benzoyl*-2-*deoxy*-2-C-*nitromethyl*-D-*ribofuranose* (5).—A solution of compound (3) (5.5 g) in methanol (200 ml) was treated dropwise with methanolic sodium methoxide (1M) and the hydrolysis was followed by t.l.c. After the reaction was complete, the solution was neutralized by stirring with Amberlite IR-120 (H^+), filtered, and evaporated to give *compound* (5) (4.25 g, 85%) as an oil, $[\alpha]_D^{21}$ +21°, $\nu_{max.}$ 3 420 (OH), 1 720 (CO), and 1 550 cm^{-1} (NO_2), *m/e*

[11] D. R. Bundle and R. U. Lemieux, *Methods Carbohydrate Chem.*, 1976, **7**, 79.

[12] T. R. Emerson and T. L. V. Ulbricht, *Chem. and Ind.*, 1964, 2127.

297 (M^+), 279 ($M^+ - H_2O$), τ 1.86—2.84 (5 H, m, 5 arom. H), 4.47 (1 H, d, $J_{1,2}$ 5 Hz, H-1), 5.31 (1 H, q, $J_{2,3}$ 7, $J_{3,4}$ 4 Hz, H-3), 5.25—5.86 (7 H, m, 3-CH_2, H-4, H_2-5, and 2 × OH), and 7.13 (1 H, m, H-2) (Found: C, 52.4; H, 5.1; N, 4.4. $C_{13}H_{15}NO_7$ requires C, 52.5; H, 5.1; N, 4.7%).

1,3-*Di*-O-*acetyl*-5-O-*benzoyl*-2-*deoxy*-2-C-*nitromethyl*-β-D-*ribofuranose* (6) *and its* α-*Anomer* (7).—Compound (5) (6 g) was stirred at 25 °C for 18 h with acetic anhydride (200 ml) and sodium acetate (2 g). The solvent was removed and the residue was extracted with chloroform (4 × 100 ml). The chloroform was evaporated off to leave an oil (6 g), which was chromatographed [ethyl acetate–hexane (1 : 1)] to give the β-*anomer* (6) (1.8 g) as an oil which crystallized from ethyl acetate–hexane as needles, m.p. 79—80 °C, $[\alpha]_D^{20}$ −49°, $\nu_{max.}$ 1 740 (ester) and 1 550 cm^{-1} (NO_2), *m/e* 338 ($M^+ - CH_3CO$), 322 ($M^+ - CH_3CO_2$), τ 1.80—2.10 (2 H, m, 2 arom. H), 2.40—2.80 (3 H, m, 3 arom. H), 3.80 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 4.61 (1 H, $J_{3,2}$ 7, $J_{3,4}$ 2 Hz, H-3), 5.20—5.70 (5 H, m, 3-CH_2, H-4, and H_2-5), 6.4—6.70br (1 H, m, H-2), 7.93 (3 H, s, OAc), and 8.05 (3 H, s, OAc) (Found: C, 53.8; H, 5.3; N, 3.5. $C_{17}H_{19}NO_9$ requires C, 53.5; H, 5.0; N, 3.7%).

Mixed fractions (400 mg) were then eluted, followed by the pure α-*anomer* (7) as an oil (800 mg), $[\alpha]_D^{20}$ +43°, $\nu_{max.}$ 1 740 (ester) and 1 550 cm^{-1} (NO_2), *m/e* 338 ($M^+ - CH_3CO$) and 322 ($M^+ - CH_3CO_2$), τ 1.96 (2 H, q, J_o 8, J_m 2 Hz, 2 arom. H), 2.30—2.80 (3 H, m, 3 arom. H), 3.48 (1 H, d, $J_{1,2}$ 5 Hz, H-1), 4.56 (1 H, $J_{3,4}$ 2 Hz, H-3), 5.30—5.70 (5 H, m, 3-CH_2, H-4, and H_2-5), 6.40—6.70br (1 H, m, H-2), 7.88 (3 H, s, OAc), and 7.91 (3 H, s, OAc) (Found: *m/e*, 322.095. $C_{15}H_{16}NO_7$ requires $M^+ - CH_3CO_2$, 322.093).

2-C-*Acetamidomethyl*-1-O-*acetyl*-5-O-*benzoyl*-2-*deoxy*-β-D-*ribofuranose* (8).—Compound (6) (600 mg) in absolute ethanol (40 ml) was hydrogenated at 25 lb in^{-2} over Raney nickel. The mixture was filtered and evaporated to leave *compound* (8) as an oil (550 mg), which crystallized from acetone–hexane as needles, m.p. 127—129 °C, $[\alpha]_D^{20}$ −21°, $\nu_{max.}$ 3 450—3 300br (OH, NH), 1 715 (ester), and 1 650 cm^{-1} (amide), *m/e* 333 ($M^+ - H_2O$), 308 ($M^+ - CH_3CO$), and 291 ($M^+ - CH_3COOH$), τ 1.90—2.70 (5 H, m, 5 arom. H), 3.63br (1 H, m, disappears on addition of D_2O, NH), 3.93 (1 H, d, $J_{1,2}$ 4 Hz, H-1), *ca.* 5.10br (1 H, s, disappears on addition of D_2O, OH), 5.40—5.80 (4 H, m, H-3 and -4, and H_2-5), *ca.* 6.5 (2 H, *m*, simplifies on addition of D_2O, 3-CH_2), *ca.* 7.57br (1 H, m, H-2), and 8.02 and 8.07 (6 H, 2s, NAc and OAc) (Found: C, 58.2; H, 5.7; N, 3.7. $C_{17}H_{21}NO_7$ requires C, 58.1; H, 5.7; N, 3.7%).

2-C-*Acetamidomethyl*-3-O-*acetyl*-5-O-*benzoyl*-2-*deoxy*-α-*or* β-*ribofuranose* (10).—Catalytic reduction of compound (7) (750 mg) and work-up as described for the preparation of compound (8) gave an oil (730 mg) which was purified by chromatography [chloroform–methanol (9 : 1)] to give pure *compound* (10) as an oil which crystallized from ethyl acetate–hexane as needles, m.p. 140—142 °C, $[\alpha]_D^{20}$ −21°, $\nu_{max.}$ 3 400br (OH, NH), 1 730 (ester), and 1 670 cm^{-1} (amide), *m/e* 273 ($M^+ - H_2O - CH_3COOH$), τ 2.00 (2 H, m, 2 arom. H), 2.52 (3 H, m, 3 arom. H), *ca.* 3.87br (1 H, m, disappears on addition of D_2O, NH), 4.48 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 4.70 (1 H, m, H-3), 5.50—5.90 (3 H, m, H-4 and H_2-5), *ca.* 6.60 (2 H, m, simplifies on addition of D_2O, 3-CH_2), *ca.* 7.5br (1 H, m, H-2), and 7.91 and 8.07 (6 H, 2s, OAc and NAc) (Found: C, 57.7; H, 6.0; N, 3.8. $C_{17}H_{21}NO_7$ requires C, 58.1; H, 6.0; N, 4.0%).

2-C-*Acetamidomethyl*-1,3-*di*-O-*acetyl*-5-O-*benzoyl*-β-D-*ribofuranose* (9).—Compound (8) (150 mg) was dissolved in pyridine (2 ml) and acetic anhydride (0.5 ml) and the mixture was kept at 20 °C for 18 h. It was then poured into ice–water (100 ml) and the resulting mixture was extracted with chloroform (3 × 50 ml). The combined extracts were washed with cold hydrochloric acid (1N; 100 ml), saturated aqueous sodium hydrogen carbonate (50 ml), and water (100 ml) and evaporated to leave an *oil* (150 mg), which crystallized from ethyl acetate–hexane as needles, m.p. 111—113 °C, $[\alpha]_D^{20}$ −21°, $\nu_{max.}$ 3 450 (NH), 1 725 (ester), and 1 670 cm^{-1} (amide), *m/e* 273 ($M^+ - 2CH_3CO_2H$), τ 1.89 (2 H, m, 2 arom. H), 2.47 (3 H, m, 3 arom. H), 3.70 (1 H, d, $J_{1,2}$ 3 Hz, H-1), 4.02br (1 H, m, disappears on addition of D_2O, NH), 4.48 (1 H, q, $J_{3,2}$ 7, $J_{3,4}$ 2 Hz, H-3), *ca.* 5.45 (3 H, m, H-4 and H_2-5), 6.52 (2 H, m, simplifies on addition of D_2O, 3-CH_2), 7.08br (1 H, m, H-2), and 7.88 and 8.00 (9 H, 2s, NAc and 2 OAc) (Found: C, 57.9; H, 5.6; N, 3.8. $C_{19}H_{23}NO_8$ requires C, 58.0; H, 5.9; N, 3.6%).

Acetylation of compound (10) (320 mg) and work-up as described for acetylation of compound (8) gave crystals (347 mg) identical with compound (9) (m.p., mixed m.p., and spectra).

1-(3-O-*Acetyl*-5-O-*benzoyl*-2-*deoxy*-2-C-*nitromethyl*-β-D-*ribofuranosyl*)*uracil* (12) *and its* α-*Anomer* (11).—Compound (9) (381 mg, 1 mmol) in dry 1,2-dichloroethane (15 ml) was treated with bis(trimethylsilyl)uracil (350 mg, 1.35 mmol) and tin(IV) chloride. The mixture was stirred at 20 °C for 4 h, then poured into cold, saturated aqueous sodium hydrogen carbonate (50 ml); the resulting mixture was filtered through Celite. The filtrate was extracted with chloroform (4 × 50 ml), and the solvent was removed to give a mixture (300 mg) of two products. Column chromatography [chloroform–methanol (20 : 1)] gave the β-*anomer* (12) (10 mg) as an oil, $[\alpha]_D^{20}$ −29°, −18° (*c* 0.7 in MeOH), $\nu_{max.}$ 3 400 (NH) 1 720 (CO), 1 695 (amide), and 1 560 cm^{-1} (NO_2), log ε_{230} 4.11, log ε_{258} 3.76, *m/e* 322 (M^+ — base), τ [$(CD_3)_2SO$] *ca.* 1.84 (2 H, m, 2 arom. H), 2.20—2.70 (3 H, m, 3 arom. H), 2.31 (1 H, d, $J_{6,5}$ 8 Hz, H-6), 3.95 (1 H, d, $J_{1',2'}$ 9 Hz, H-1'), 4.35 (1 H, d, $J_{5,6}$ 8 Hz, H-5), 4.51 (1 H, q, $J_{3',2'}$ 7, $J_{3',4'}$ 2 Hz, H-3'), 5.0—5.5 (4 H, m, 5'-H_2 and 3'-CH_2), 5.62 (1 H, m, H-4'), *ca.* 6.5br (1 H, m, H-2'), and 7.92 (3 H, s, OAc) (Found: *m/e*, 322.092. $C_{15}H_{16}NO_7$ requires $M^+ - C_4H_3N_2O_2$, 322.093).

Compound (11) (104 mg) was then eluted as an oil which crystallized from methanol as needles, m.p. 200—202 °C, $[\alpha]_D^{20}$ −54°, −45° (*c* 0.35 in MeOH), $\nu_{max.}$ 3 400 (NH), 1 725 (ester), 1 670 (amide), and 1 560 cm^{-1} (NO_2), log ε_{228} 4.15, log ε_{262} 3.84, *m/e* 322 (M^+ —base), τ [$(CD_3)_2SO$] 1.93 (2 H, m, 2 arom. H), 2.20—2.60 (4 H, m, 3 arom. H and H-6) 3.56 (1 H, d, $J_{1',2'}$ 7 Hz, H-1'), 4.32 (1 H, q, $J_{3',2'}$, 8, $J_{3',4'}$ 3 Hz, H-3'), 4.42 (1 H, d, $J_{5,6}$ 8 Hz, H-5), 5.00—6.00 (6 H, m, 3'-CH_2, H-2' and -4', and H_2-5'), and 7.98 (3 H, s, OAc) (Found: C, 52.7; H, 4.4; N, 9.7. $C_{19}H_{19}N_3O_9$ requires C, 52.7; H, 4.3; N, 9.7%).

Compounds (11) (152 mg) and (12) (30 mg) were also obtained when the β-anomer (8) (381 mg) was treated with bis(trimethylsilyl)uracil and tin(IV) chloride exactly as for the preparation of compounds (11) and (12) from compound (9).

1-(2-*Deoxy*-2-C-*nitromethyl*-α-D-*ribofuranosyl*)*uracil* (13).—Compound (11) (500 mg) was dissolved in methanol (80 ml) and methanolic sodium methoxide (5 ml; 0.5M) was added with stirring. After 18 h at 20 °C the solution was neutralized with Amberlite IRC 50 (H^+), filtered, and evaporated. The residue was dissolved in water (50 ml)

and washed with chloroform (2 × 20 ml). Freeze-drying of the water fraction gave a foam which crystallized from water as fine *needles* (311 mg), m.p. 215—216 °C, $[\alpha]_D^{20}$ +2° (*c* 0.8, in H_2O), $\nu_{max.}$ (KBr) 3 350br (NH and OH), 1 650 (amide), and 1 550 cm^{-1} (NO_2), τ [$CCD_3)_2SO$] 2.59 (1 H, d, $J_{6.5}$ 8 Hz, H-6), 3.58 (1 H, d, $J_{1'.2'}$ 8 Hz, H-1'), 4.39 (1 H, d, $J_{5.6}$ 8 Hz, H-5), and 5.20—6.70 (m, other protons, changes on addition of D_2O) (Found: C, 42.0; H, 4.3; N, 14.6. $C_{10}H_{13}N_3O_7$ requires C, 41.8; H, 4.6; N, 14.6%).

1-(2-*Deoxy*-2-C-*nitromethyl*-β-D-*ribofuranosyl*)*uracil* (14). —Compound (12) (50 mg) was treated as for the preparation of compound (13) to give a yellowish oil (30 mg), which was chromatographed [methanol–chloroform (1 : 4)] to give a colourless foam (7 mg). This appeared to be homogeneous (t.l.c. and n.m.r.) but did not give correct analytical figures; $[\alpha]_D^{20}$ +27° (*c* 0.7 in H_2O), ν_{max} (KBr) 3 300br (NH and OH), 1 660 (amide), and 1 550 cm^{-1} (NO_2), τ [$(CD_3)_2SO$] 2.15 (1 H, d, $J_{6.5}$ 8 Hz, H-6), 4.03 (1 H, d, $J_{1'.2'}$ 8.5 Hz, H-1'), 4.35 (1 H, d, $J_{5.6}$ 8 Hz, H-5), and 5.20—6.70 (m, other protons, changes on addition of D_2O) (Found: C, 40.9; H, 4.5; N, 14.3. $C_{10}H_{13}N_3O_7$ requires C, 41.8; H, 4.6; N, 14.6%).

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