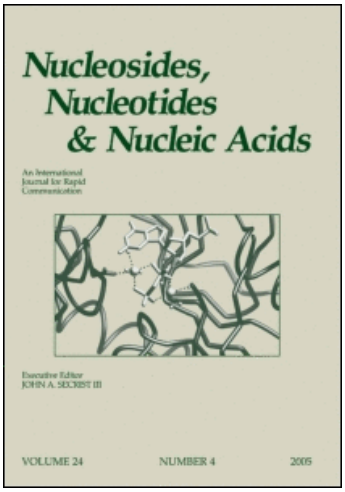

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SYNTHESIS OF 5'-C-CHAIN-EXTENDED URIDINES BY REACTION OF 5'-HALONUCLEOSIDES WITH MALONIC ACID TYPE DERIVATIVES.

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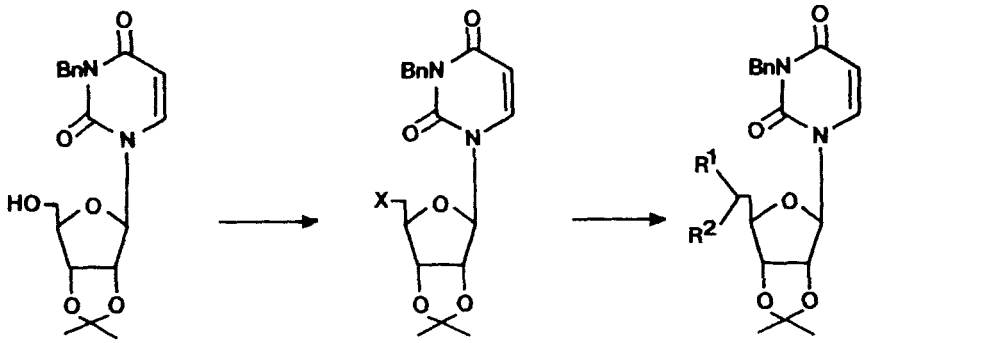
ABSTRACT. Reaction of 3-N-benzyl-5'-deoxy-5'-haloderivatives of uridine with the carbanions derived from diethyl malonate, ethyl acetoacetate, ethyl cyanoacetate and malondinitrile afforded the corresponding highly functionalized 5'-C-chain-extended uridines.

A number of naturally occurring nucleosides having a higher carbon sugar moiety, such as, polyoxins,[1-4] neopolyoxins,[1,2,4] nikkomycins,[1,2,4] Sinefungin,[1-3] Griseolic acid,[5,6] octosyl acids,[1,2] ezomycins,[1,2] and Tunicamycin[1,2,4] show antifungal, antiviral, antibacterial and enzyme inhibiting activity.[1-6] One of the key steps in the total synthesis of these compounds is the formation of a new C-C bond at 5'-position.[7] The methods used for the formation of such C-C bond usually involve the reaction of a nucleoside 5'-carboxaldehyde with organometallic reagents,[8] nitroalkanes,[9] cyanide ion,[10] phosphoranes,[11] dienes[12] or dimethyloxosulfonium methylide.[13] Other methods involve the substitution of a leaving group at C-5' by cyanide ion[14] or the reaction of a 5-deoxy-5-nitroribose derivative with a chiral aldehyde, followed by glycosylation.[15] The malonic synthesis, in spite of its well known utility for the formation of new C-C bonds, has never been applied to the preparation of 5'-C-chain-extended nucleosides. It has been used, however, to alkylate position 4 and 5 of the uracil residue of uridine nucleosides.[16,17]

In this paper we report the reaction of 5'-haloderivatives of uridine with active methylene compounds, such as, diethyl malonate, ethyl acetoacetate, ethyl cyanoacetate and malondinitrile, to afford highly functionalized 5'-C-extended-chain nucleosides, which can be versatile synthetic intermediates.

Reaction of 3-benzyl-2',3'-O-isopropylideneuridine (1)[18-20] with carbon tetrachloride or carbon tetrabromide and triphenylphosphine[21] in pyridine afforded the 5'-chloro-5'-deoxy and 5'-bromo-5'-deoxy derivatives of uridine 2 and 3 in 89 and 88% yield, respectively. A similar reaction of 1 with iodine and triphenylphosphite[22] in N,N-dimethylformamide gave a low yield (28%) of the 5'-deoxy-5'-iodo-uridine derivative 4. The latter was obtained in 99% yield by trans-halogenation reaction of 3 with sodium iodide in acetone.[23]



1

2, X = Cl

3, X = Br

4, X = I

5, $R^1 = R^2 = CO_2Et$

6, $R^1 = CH_3CO$; $R^2 = CO_2Et$

7, $R^1 = CN$; $R^2 = CO_2Et$

8, $R^1 = R^2 = CN$

9, $R^1 = CONH_2$; $R^2 = CO_2Et$

10, $R^1 = CONH_2$; $R^2 = CO_2Me$

Reaction of the 5'-chloro, 5'-bromo and 5'-iododerivatives 2, 3 and 4 with diethyl malonate and 1 equiv of sodium ethoxide in ethanol afforded the 5'-C-substituted-5'-deoxyuridine 5 in 25, 35 and 45% yield, respectively. A good yield (80%) of 5 was obtained by reaction of the iododerivative 4 with diethyl malonate and 2 equiv of sodium ethoxide in 1,2-dimethoxyethane. Similarly, reaction of 4, under the

latter experimental conditions, with ethyl acetoacetate, ethyl cyanoacetate and malondinitrile gave the 5'-C-substituted-5'-deoxyuridines **6**, **7**, and **8** in 87, 63 and 91% yield, respectively.

The attachment of the malonic acid type residues to C-5' was demonstrated by the chemical shift of the H-5' protons (δ 2.29-2.59 ppm), which appeared at higher field (1-1.5 ppm) than the H-5' protons of the starting materials **2-4**. The H-6' proton appeared at 3.48-3.73 ppm, as a triplet or a doublet of doublets by coupling with H-5'. The ^{1}H NMR spectra of **6** and **7** showed two sets of signals, in (1:1) approximate ratio, corresponding to the two possible diastereoisomers obtained by formation of a new chiral center at C-6'.

Reaction of the diethyl malonate derivative **5** with one equiv of methanolic ammonia in order to obtain the monoamide, afforded a 3:1 mixture of the carboxamide-ethyl ester **9** and the carboxamide-methyl ester **10**. The presence of two very close sets of signals in the ^{1}H NMR spectra of **9** and **10** suggested the formation of the two possible diastereoisomers by generation of the new chiral center at C-6'. The formation of the methyl ester **10**, which should be produced by transesterification reaction of the ethyl ester derivative **9** in the presence of methanol, was avoided by performing the ammonolysis of **5** with ethanolic ammonia. This allowed the formation of **9** in 68% yield.

Several attempts carried out to remove the benzyl group were unsuccessful. These attempts included the treatment of **5** or **8** with hydrogen and 10% palladium on charcoal in ethanol, with sodium and naphthalene,[19] and with 10% palladium on charcoal in the presence of ammonium formate in methanol.[24]

In conclusion, we describe a facile procedure for the formation of new C-C bonds at C-5' of nucleosides to afford highly functionalized C-5'-chain-extended nucleosides in good yields.

EXPERIMENTAL

^{1}H NMR spectra were recorded with a Varian XL-300 (300 MHz) and a Varian EM-390 (90 MHz) spectrometers using Me_4Si as the internal standard. IR spectra were recorded with a Shimadzu IR-435 spectrometer. UV absorption spectra were taken with a Perkin-Elmer 550 SE spectrophotometer. Analytical TLC was performed on aluminium sheets

coated with a 0.2 mm layer of silica gel 60 F_{254} purchased from Merck and preparative TLC on glass plates coated with a 2 mm layer of silica gel PF_{254} (Merck). Flash column chromatography was performed with silica gel 60 230-400 mesh (Merck). Compounds were detected by UV light (254 nm) or by spraying the plates with 30% H_2SO_4 in ethanol and heating.

3-Benzyl-2',3'-O-isopropylideneuridine (1).[18] To a solution of 2',3'-O-isopropylideneuridine (2 g, 7 mmol) in N,N-dimethylformamide (20 mL), sodium hydride (0.17 g, 7 mmol) was added at room temperature. After the sodium hydride reacted, benzyl bromide (0.85 mL, 7.2 mmol) was slowly added, and the mixture was stirred for 1 h. Methanol (5 mL) was added and the reaction mixture was evaporated to dryness. The residue was dissolved in chloroform (30 mL) and washed with water (2 x 50 mL). The organic phase was dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The residue was purified by flash column chromatography using ethyl acetate/hexane (2:1) as the eluent to afford **1** (2.35 g, 90%) as a syrup: UV λ_{max} (EtOH) 256 nm (ϵ 9,930); IR (Nujol) 3440 cm^{-1} (OH); ^1H NMR ($CDCl_3$, 90 MHz) δ 1.31, 1.55 (2s, 6H, isopropylidene), 3.35 (bs, 1H, 5'-OH), 3.75 (t, 2H, $J_{4',5'}$ = 6 Hz, H-5'), 4.22 (m, 1H, H-4'), 4.88 (m, 2H, H-2', H-3'), 5.05 (s, 2H, $CH_2C_6H_5$), 5.66 (d, 1H, $J_{1',2'}$ = 1.5 Hz, H-1'), 5.69 (d, 1H, $J_{5,6}$ = 8 Hz, H-5), 7.15-7.43 (m, 6H, C_6H_5, H-6).

Anal. Calcd. for $C_{19}H_{22}N_2O_6$: C, 60.96; H, 5.88; N, 7.49. Found: C, 60.88; H, 5.87; N, 7.39.

3-Benzyl-5'-chloro-5'-deoxy-2',3'-O-isopropylideneuridine (2). To a cold (0°C) solution of **1** (2 g, 5.35 mmol), pyridine (15 mL) and triphenylphosphine (2.8 g, 10.7 mmol), carbon tetrachloride (0.6 mL, 6.2 mmol) was added, and the mixture was stirred at room temperature for 24 h. Methanol (10 mL) was added and the resulting mixture was evaporated to dryness. The residue was purified by column chromatography with ethyl acetate/hexane (1:1) to give **2** (1.87 g, 89%) as a foam: UV λ_{max} (EtOH) 255 nm (ϵ 9,300); ^1H NMR ($CDCl_3$, 90 MHz) δ 1.35, 1.56 (2s, 6H, isopropylidene), 3.70 (m, 2H, H-5'), 4.32 (m, 1H, H-4'), 4.88 (m, 2H, H-2', H-3'), 5.08 (s, 2H, $CH_2C_6H_5$), 5.67 (d, 1H, $J_{1',2'}$ = 2 Hz, H-1'), 5.75 (d, 1H, $J_{5,6}$ = 8 Hz, H-5), 7.20-7.46 (m, 6H, C_6H_5, H-6).

Anal. Calcd. for $C_{19}H_{21}ClN_2O_5$: C, 58.09; H, 5.35; N, 7.13; Cl, 9.04. Found: C, 58.18; H, 5.39; N, 7.00; Cl, 9.32.

3-Benzyl-5'-bromo-5'-deoxy-2',3'-O-isopropylideneuridine (3). To a cold (0°C), stirred solution of **1** (2 g, 5.35 mmol) and triphenylphosphine (2.8 g, 10.7 mmol) in pyridine (15 mL), carbon tetrabromide (1.8 g, 5.42 mmol) was added, and the mixture was stirred at 0°C for 1 h. Methanol (10 mL) was added and the resulting mixture was evaporated to dryness. The residue was chromatographed (column) with ethyl acetate/hexane (1:2) as the eluent to yield **3** (2.06 g, 88%) as a white foam: UV λ_{max} (EtOH) 255 nm (ϵ 9,150); ^{1}H NMR ($CDCl_3$, 90 MHz) δ 1.37, 1.58 (2s, 6H, isopropylidene), 3.52 (m, 2H, H-5'), 4.32 (m, 1H, H-4'), 4.83 (m, 2H, H-2', H-3'), 5.07 (s, 2H, $\underline{CH_2}C_6H_5$), 5.68 (d, 1H, $J_{1',2'}$ = 1.5 Hz, H-1'), 5.77 (d, 1H, $J_{5,6}$ = 8 Hz, H-5), 7.13-7.46 (m, 6H, C_6H_5, H-6).

Anal. Calcd. for $C_{19}H_{21}BrN_2O_5$: C, 52.17; H, 4.81; N, 6.40; Br, 18.30. Found: C, 52.18; H, 4.88; N, 6.21; Br, 17.99.

3-Benzyl-5'-deoxy-5'-iodo-2',3'-O-isopropylideneuridine (4). From 3. A mixture of **3** (2 g, 4.58 mmol), acetone (25 mL) and sodium iodide (1.4 g, 9.3 mmol) was stirred at room temperature for 24 h, filtered and the filtrate evaporated to dryness. The residue was dissolved in chloroform (20 mL) and treated with a saturated solution of sodium thiosulfate (15 mL). The organic layer was extracted, washed with water (10 mL), dried over anhydrous sodium sulfate and evaporated to dryness to yield **4** (2.2 g, 99%) as a chromatographically homogeneous syrup: UV λ_{max} (EtOH) 255 nm (ϵ 9,370); ^{1}H NMR ($CDCl_3$, 90 MHz) δ 1.33, 1.51 (2s, 6H, isopropylidene), 3.31 (m, 2H, H-5'), 4.18 (m, 1H, H-4'), 4.68 (dd, 1H, $J_{2',3'}$ = 7 Hz, $J_{3',4'}$ = 4 Hz, H-3'), 4.98 (dd, 1H, $J_{1',2'}$ = 1.5 Hz, H-2'), 5.08 (s, 2H, $\underline{CH_2}C_6H_5$), 5.61 (d, 1H, H-1'), 5.77 (d, 1H, $J_{5,6}$ = 8 Hz, H-5), 7.20-7.42 (m, 6H, C_6H_5, H-6).

Anal. Calcd. for $C_{19}H_{21}IN_2O_5$: C, 47.11; H, 4.34; N, 5.79; I, 26.24. Found: C, 47.00; H, 4.39; N, 5.88; I, 25.97.

From 1. To a cold (0°C) solution of **1** (2 g, 5.35 mmol) in N,N-dimethylformamide (10 mL), triphenylphosphite (2.8 mL, 10.7 mmol) was added. The mixture was stirred at 0°C for 20 min, iodine (2.8 g, 11 mmol) was added, and the stirring was continued at room temperature for 2 h. Chloroform (50 mL) was added and the resulting mixture was

washed with a saturated solution of sodium thiosulfate (15 mL). The organic layer was worked up as before to give **4** (0.72 g, 28%), identical to that obtained before.

1,4-Anhydro-1-[3-benzyl(2,4 (1H, 3H)-pyrimidinedione-1-yl)]-1,5,6-trideoxy-6-C-ethoxy-carbonyl-2,3-O-isopropylidene- β -D-ribohepturonic acid ethyl ester (5). Method A. A mixture of sodium ethoxide (0.27 g, 4 mmol), 1,2-dimethoxyethane (20 mL), diethyl malonate (1.92 g, 12 mmol) and **4** (1 g, 2 mmol) was refluxed for 24 h and evaporated to dryness. The residue was stirred with ethyl ether (50 mL), filtered, and the filtrate concentrated under reduced pressure. The syrupy residue was purified by preparative TLC using ethyl acetate/hexane (1:2) as the eluent to afford **5** (0.82 g, 80%) as a syrup: UV λ_{max} (EtOH) 254 nm (ϵ 9,850); IR (Nujol) 1740 cm^{-1} (CO_2Et); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.21, 1.25 (2t, 6H, J = 7 Hz, $CO_2CH_2\underline{CH_3}$), 1.33, 1.54 (2s, 6H, isopropylidene), 2.36 (m, 2H, H-5'), 3.84 (t, 1H, $J_{5',6'}$ = 7.2 Hz, H-6'), 4.06-4.25 (m, 5H, $CO_2\underline{CH_2}CH_3$, H-4'), 4.65 (dd, 1H, $J_{2',3'}$ = 6.6, $J_{3',4'}$ = 4.8 Hz, H-3'), 4.92 (dd, 1H, $J_{1',2'}$ = 2.2 Hz, H-2'), 5.04, 5.15 (AB system, 2H, J = 13.7 Hz, $\underline{CH_2}$-C_6H_5), 5.62 (d, 1H, H-1'), 5.79 (d, 1H, $J_{5,6}$ = 8.1 Hz, H-5), 7.17 (d, 1H, $J_{5,6}$ = 8.5 Hz, H-6), 7.18-7.46 (m, 5H, C_6H_5).

Anal. Calcd. for $C_{26}H_{32}N_2O_9$: C, 60.47; H, 6.20; N, 5.43. Found: C, 60.49; H, 6.25; N, 5.61.

Method B. A solution of ethanol (10 mL), sodium (0.06 g, 2.6 mmol), and diethyl malonate (1.22 g, 7.62 mmol) was stirred at room temperature for 10 min, and **2** (1 g, 2.55 mmol) was added. The mixture was refluxed for 24 h and the solvent was evaporated under reduced pressure. The residue was stirred with ethyl ether (50 mL) and worked up as before to yield **5** (0.39 g, 30%).

Following this procedure, compound **5** was also obtained in 35 and 45% yield from the 5'-bromo and 5'-iododerivatives **3** and **4**, respectively.

6-C-[(R and S)-Acetyl]-1,4-anhydro-1-[3-benzyl (2,4 (1H, 3H)-pyrimidinedione-1-yl)] -1,5,6-trideoxy-2',3'-O-isopropylidene- β -D-ribohepturonic acid ethyl ester (6). A mixture of sodium ethoxide (0.27 g, 4 mmol), 1,2-dimethoxyethane (20 mL), ethyl acetoacetate (0.78 g, 6 mmol) and **4** (1 g, 2 mmol) reacted and were worked up as

indicate before for **5** (Method A) to afford **6** (0.8 g, 87%) as a syrup (1:1) mixture of two diastereoisomers : UV λ_{max} (EtOH) 255 nm (ϵ 12,220) IR (Nujol) 1720 (CO), 1740 cm^{-1} (CO_2Et); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.22, 1.26 (2t, 3H, J = 7 Hz, $CO_2CH_2\underline{CH_3}$), 1.33, 1.53 (2s, 6H, isopropylidene), 2.15, 2.22 (2s, 3H, CH_3CO), 2.29 (m, 2H, H-5'), 3.60 (t, 1H, $J_{5',6'}$= 7.3 Hz, H-6'), 3.99-4.23 (m, 3H, H-4', $CO_2\underline{CH_2}CH_3$), 4.62, 4.64 (2dd, 1H, $J_{2',3'}$ = 6.4 Hz, $J_{3',4'}$ = 4.8 Hz, H-3'), 4.91, 4.93 (2 dd, 1H, $J_{1',2'}$ = 2.2 Hz, H-2'), 5.09 (m, 2H, $\underline{CH_2}$-C_6H_5), 5.56, 5.59 (2d, 1H, H-1'), 5.80 (d, 1H, $J_{5,6}$ = 8 Hz, H-5), 7.13, 7.15 (2d, 1H, $J_{5,6}$ = 8 Hz, H-6), 7.16-7.46 (m, 5H, C_6H_5).

Anal. Calcd. for $C_{25}H_{30}N_2O_8$: C, 61.73; H, 6.17; N, 5.76. Found: C, 61.78; H, 6.01; N, 5.59.

1,4-Anhydro-1-[3-Benzyl(2,4 (1H, 3H)-pyrimidinedione-1-yl)]-6-C-[(R and S)-cyano]-1,5,6-trideoxy-2,3-O-isopropylidene-β-D-ribo-hepturonic acid ethyl ester (7). A mixture of sodium ethoxide (0.27 g, 4 mmol), 1,2-dimethoxyethane (30 mL), ethyl cyanoacetate (0.85 g, 6 mmol), and **4** (1 g, 2 mmol) reacted and were worked up as indicated before for **5** (Method A) to afford **7** (0.6 g, 63%) as a syrup [(1:1) mixture of two diastereoisomers]: UV λ_{max} (EtOH) 255 nm (ϵ 7,580); IR (Nujol) 2230 (CN), 1740 cm^{-1} (CO_2Et); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.26, 1.30 (2t, 3H, J = 7 Hz, $CO_2CH_2\underline{CH_3}$), 1.34, 1.56 (2s, 6H, isopropylidene), 2.22-2.55 (m, 2H, H-5'), 3.61 (m, 1H, H-6'), 4.14-4.28 (m, 3H, H-4', $CO_2\underline{CH_2}CH_3$), 4.80 (dd, 1H, $J_{2',3'}$ = 6.4, $J_{3',4'}$ = 4.3 Hz, H-3'), 5.09 (m, 3H, H-2', $\underline{CH_2}$-C_6H_5), 5.46 (d, 1H, $J_{1',2'}$ = 1.5 Hz, H-1'), 5.79 (d, 1H, $J_{5,6}$ = 7.8 Hz, H-5), 7.15 (d, 1H, $J_{5,6}$ = 7 Hz, H-6), 7.30-7.50 (m, 5H, C_6H_5).

Anal. Calcd. for $C_{24}H_{27}N_3O_7$: C, 61.40; H, 5.75; N, 8.96. Found: C, 61.48; H, 5.85; N, 8.59.

1,4-Anhydro-1-[3-benzyl(2,4 (1H, 3H)-pyrimidinedione-1-yl)]-6-C-cyano-1,5,6-trideoxy-2,3-O-isopropylidene-β-D-ribohepturononitrile (8) A mixture of sodium ethoxide (0.27 g, 4 mmol), 1,2-dimethoxyethane (20 mL), malondinitrile (1 g, 2 mmol), and **4** (1 g, 2 mmol) reacted and were worked up as indicated before for **5** (Method A) to afford **8** (0.77 g, 91%) as a syrup: UV λ_{max} (EtOH) 254 nm (ϵ 9,430); IR (Nujol) 2235 cm^{-1} (CN); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.35, 1.56 (2s, 6H, isopropylidene), 2.35 (ddd, 1H, $J_{5'a,6'}$ = 9.8, $J_{5'a,5'b}$ = 13.4,

$J_{4',5'a}$ = 3.5 Hz, H-5'a), 2.59 (ddd, 1H, $J_{5'b,6'}$ = 5.3, $J_{4',5'b}$ = 10.7 Hz, H-5'b), 3.73 (dd, 1H, H-6'), 4.31 (dt, 1H, $J_{3',4'}$ = 3.5 Hz, H-4'), 4.88 (dd, 1H, $J_{2',3'}$ = 6.4 Hz, H-3'), 4.99, 5.15 (AB system, 2H, J = 14.0 Hz, $C\underline{H}_2$-C_6H_5), 5.17 (dd, 1H, $J_{1',2'}$ = 1.3 Hz, H-2'), 5.38 (d, 1H, H-1'), 5.80 (d, 1H, $J_{5,6}$ = 7.9 Hz, H-5), 7.12 (d, 1H, $J_{5,6}$ = 9 Hz, H-6,), 7.25-7.48 (m, 5H, C_6H_5).

Anal. Calcd. for $C_{22}H_{22}N_4O_5$: C, 62,56; H, 5.21; N, 13.27. Found: C, 62.48; H, 5.21; N, 13.20.

1,4-Anhydro-1-[3-benzyl(2,4 (1H, 3H)-pyrimidinedione-1-yl)]-6-C-[(R and S)-carbamoyl]-1,5,6-trideoxy-2,3-O-isopropylidene-β-D-ribo-hepturonic acid ethyl ester (9). Through a cold (ice bath) solution of **5** (0.5 g, 1 mmol) in ethanol (15 mL), ammonia gas was bubbled for 10 min. The mixture was stirred at 0°C for 4 h and the solvent was evaporated under reduced pressure. The residue was purified by preparative TLC with ethyl acetate/n-hexane (2:1) as the eluent to give **9** (0.29 g, 62%) as a foam: UV λ_{max} (EtOH) 255 nm (ε 6,820): IR (Nujol) 3315, 3180 ($CONH_2$), 1735 cm^{-1} (CO_2Et); ^1H NMR ($CDCl_3$, 300 MHz) δ1.23, 1.26 (2t, 3H, J = 7 Hz, $CO_2CH_2C\underline{H}_3$), 1.33, 1.54 (2s, 6H, isopropylidene), 2.35 (m, 2H, H-5'), 3.34, 3.39 (2t, 1H, $J_{5',6'}$ = 7 Hz, H-6'), 4.07-4.22 (m, 3H, H-4', $CO_2C\underline{H}_2CH_3$), 4.65, 4.67 (2t, 1H, $J_{2',3'}$ = $J_{3',4'}$ = 4.5 Hz, H-3'), 4.94, 4.96 (2dd, 1H, $J_{1',2'}$ = 2.2 Hz, H-2'), 5.09 (s, 2H, $C\underline{H}_2$-C_6H_5), 5.57, 5.58 (2d, 1H, H-1'), 5.64, 6.15 (2bs, 2H, $CONH_2$), 5.80 (d, 1H, $J_{5,6}$ = 8 Hz, H-5), 7.16, 7.20 (2d, 1H, $J_{5,6}$ = 8 Hz, H-6), 7.23-7.44 (m, 5H, C_6H_5).

Anal. Calcd. for $C_{24}H_{29}N_3O_8$: C, 58.35; H, 5.95; N, 8.62. Found: C, 58.28; H, 6.11; N, 8.65.

1,4-Anhydro-1-[3-benzyl(2,4 (1H, 3H)-pyrimidinedione-1-yl)]-6-C-[(R and S)-carbamoyl]-1,5,6-trideoxy-2,3-O-isopropylidene-β-D-ribo-hepturonic acid methyl ester (10). A solution of compound **5** (0.5 g, 1 mmol) in methanol (15 mL) was treated with ammonia and worked up as indicated before for **9**. Under UV light the preparative plates showed two major bands which were isolated and extracted with ethyl acetate/methanol (5:1).

The faster band gave compound **9** (0.26 g, 55%) identical to that obtained before.

The slower band yielded compound **10** (0.1 g, 21%) as a foam: UV λ_{max} (EtOH) 255 nm (ε 8,240); IR (Nujol) 3310, 3175 ($CONH_2$), 1735 cm^{-1} (CO_2CH_3); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.33, 1.53 (2s, 6H, isopropylidene), 2.37 (m, 2H, H-5'), 3.36, 3.40 (2t, 1H, $J_{5',6'}$ = 7.1 Hz, H-6'), 3.67, 3.70 (2s, 3H, CO_2CH_3), 4.10 (m, 1H, H-4'), 4.66, 4.68 (2t, 1H, $J_{2',3'} = J_{3',4'}$ = 4.6 Hz, H-3'), 4.96, 4.98 (2dd, 1H, $J_{1',2'}$ = 2.0 Hz, H-2'), 5.09 (s, 2H, $CH_2C_6H_5$), 5.49, 6.10 (2bs, 2H, $CONH_2$), 5.55 (d, 1H, H-1'), 5.80 (d, 1H, $J_{5,6}$ = 8 Hz, H-5), 7.15, 7.18 (d, 1H, $J_{5,6}$ = 8 Hz, H-6), 7.22-7.44 (m, 5H, C_6H_5).

Anal. Calcd. for $C_{23}H_{27}N_3O_8$: C, 58.35; H, 5.71; N, 8.88. Found: C, 58.39; H, 6.00; N, 8.90.

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