# Branched-Chain N-Sugar Nucleosides. 2. Nucleosides of 3-C-Cyanomethyl-, Carboxamidomethyl-, and N,N-Dimethylcarboxamidomethyl-3-deoxyribofuranose. Synthesis of a Homolog of the Amino Sugar Nucleoside Moiety of Puromycin[1]

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*Received July 10, 1972*

The synthesis of novel N-containing branched-chain ribo sugar nucleosides is described. Periodate oxidation of 3-*C*-cyanomethyl-3-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (**1**) followed by sodium borohydride reduction of the resulting aldehydo sugar afforded 3-*C*-cyanomethyl-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**2**) in 90% yield. Utilizing a parallel set of reactions to those described in the previous paper,[2a] the 6-chloro-3′-(cyanomethyl)ribofuranosylpurine nucleoside **6** was prepared. Treatment of the latter with dimethylamine–water–methanol gave 6-*N*,*N*-dimethylamino-9-[3′-deoxy-3′-*C*-(*N*,*N*-dimethylcarbamoylmethyl)-β-D-ribofuranosyl]purine (**7**) in 72% yield. Sublimation of the latter compound afforded the novel γ-lactone nucleoside, 6-*N*,*N*-dimethylamino-9-[3′-*C*-(carboxymethyl-2′,3′-γ-lactone)-3′-deoxy-β-D-ribofuranosyl]purine (**8**) in 73% yield. Treatment of **8** with liquid ammonia yielded the branched-chain 3′-carbamoylmethyl ribo nucleoside **9** in quantitative yield. Reaction of the lactone **8** with ethyl glycinate in *N*,*N*-dimethylformamide afforded a nucleoside peptide 6-*N*,*N*-dimethylamino-9-[3′-*C*-(carbomethyl-*N*-glycine ethyl ester)-3′-deoxy-β-D-ribofuranosyl]purine (**10**) in 72% yield. Selective de-O-acylation of **6** at −10° yielded the 3′-*C*-cyanomethyl ribo nucleoside **11** in 67% yield. Catalytic hydrogenation of **11** in the presence of acetic anhydride and ethanol followed by de-O-acetylation of the blocked nucleoside gave, in about 90% yield, crystalline 6-*N*,*N*-dimethylamino-9-[3′-(2″-acetamidoethyl)-3′-deoxy-β-D-ribofuranosyl]purine (**12**).

In the previous report[2a] from this laboratory the synthesis of 6-*N*,*N*-dimethylamino-9-(3′-*C*-*N*,*N*-dimethylcarbamoylmethyl-3′-deoxy-β-D-allofuranosyl)-purine from a cyanomethyl nucleoside was described. Attempts to degrade the allo carbamoyl nucleoside to a ribo nucleoside by classical procedures[2b,3] failed to give a crystalline product, although its structure was supported by nmr, ir, and mass spectrometry. Although lithium aluminum hydride reduction of the 3-*C*-cyanomethyl allo nucleoside gave the expected 3-*C*′-aminoethyl allo nucleoside (as evidenced by its nmr spectrum), the amino sugar nucleoside could not be freed from inorganic ions. As a consequence, a new approach for the synthesis of an ethyl homolog of the amino sugar nucleoside moiety of puromycin[4] was sought. This paper deals mainly with this synthesis and, in addition, the preparation of a branched-chain 3′-*C*-carbamoylmethyl and a nucleoside peptide analog are described. The reasons for the synthesis of these novel classes of branched-chain N-sugar nucleosides were presented in the preceding paper.[2a] Other authors[5] have also given reasons for the great interest in the potential biological activity of puromycin analogs.

Periodate oxidation of the previously described 3-*C*-cyanomethyl-3-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (**1**) followed by immediate sodium borohydride reduction of the resulting aldehydo sugar afforded crystalline 3-*C*-cyanomethyl-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**2**) in 90% yield. The latter compound was readily converted into its 5-*O*-benzoate ester **3** in 80% yield. Acetolysis of the 1,2-*O*-isopropylidene group of **3** with a 90% solution of trifluoroacetic acid at room temperature followed by acetylation yielded crystalline 1,2-di-*O*-acetyl-5-*O*-benzoyl-3-*C*-cyanomethyl-3-deoxy-β-D-ribofuranose (**4**) in 78% yield and the 2,3-γ-lactone **4a** (about 5% yield). The β-anomeric configuration of **4** and **4a** was assigned on the same basis as described previously.[2a]

Treatment of the cyanomethyl branched-chain ribo sugar **4** with anhydrous hydrogen bromide in dichloromethane afforded the bromo sugar, which was immediately condensed with chloromercuri-6-benzamidopurine in anhydrous toluene to afford, after silica gel column chromatography, amorphous 6-benzamido-9-(2′-*O*-acetyl-5′-*O*-benzoyl-3′-*C*-cyanomethyl-3′-deoxy-β-D-ribofuranosyl)purine (**5**) in 40% yield.

Fusion of the β anomer **4** with 6-chloropurine at 160° afforded, after column chromatography on silica gel, the crystalline 6-chloropurine nucleoside (**6**) in 66% yield. Treatment of **6** with 25% aqueous dimethylamine and methanol at room temperature for 4 hr readily de-O-acetylated **6** and aminated the cyanomethyl group to yield 6-*N*,*N*-dimethylamino-9-(3′-deoxy-3′-*C*-*N*,*N*-dimethylcarbamoylmethyl-β-D-ribofuranosyl)purine (**7**) in 72% yield, identical (nmr and mass spectrum) with compound **10** described in the previous paper.[2a] Compound **7** was readily acetylated to yield a diacetyl derivative which failed to crystallize. Attempts to remove all traces of moisture from **7** by drying under vacuum at about 60° led to a gradual decrease in its nitrogen content, indicating deamination. Surprisingly, the allo homolog of **7**, described in the previous report,[2a] was stable when heated under similar conditions. Sublimation of **7** at temperatures of 180–210° led to complete dehydroamination, resulting in the formation, after crystallization, of the novel branched-chain 2′,3′-γ-lactone nucleoside **8** in 73% yield. Its ir spectrum (1770 $cm^{-1}$, lactone), nmr, molecular weight (319), and elemental analysis were in complete accord with the structure **8**. The lactone **8** was readily reconverted in quantitative yield into the *N*,*N*-dimethylcarbamoylmethyl nucleoside **7** by treatment with dimethylamine at 0° for 4 hr. When the γ-lactone **8** was allowed to react with anhydrous liquid ammonia for 6 hr, then the branched-chain 3′-*C*-carbamoylmethyl ribo nucleoside **9** was produced in 95% yield. Surprisingly, the carbamoylmethyl-

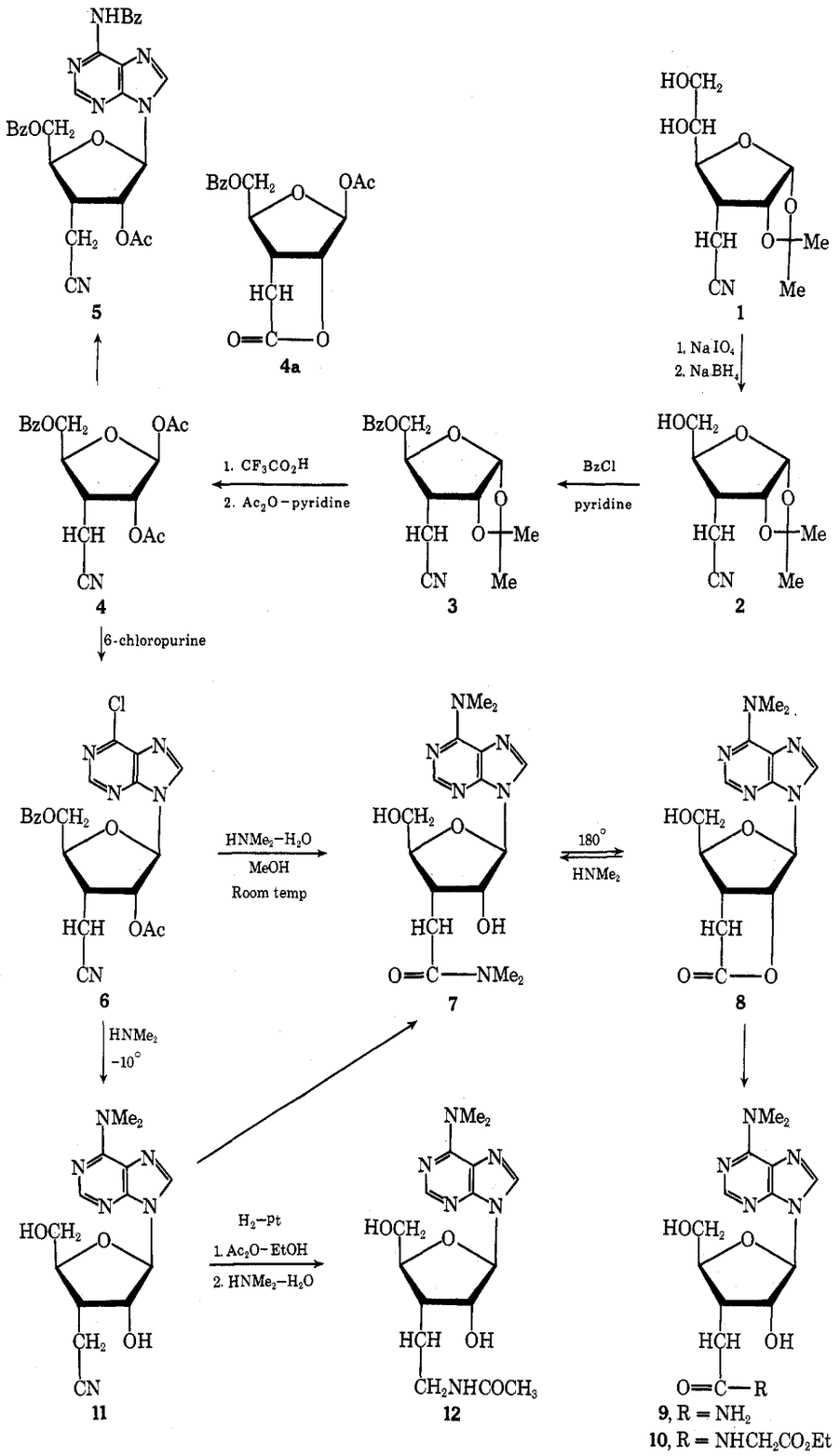
(1) Preliminary communication: Abstracts, Third International Congress of Heterocyclic Chemistry, Sendai, Japan, Aug 1971, p 106.

(2) (a) A. Rosenthal and D. Baker, *J. Org. Chem.*, **38**, 193 (1973); (b) A. Rosenthal and L. Nguyen, *ibid.*, **34**, 1029 (1969).

(3) A. Rosenthal and M. Sprinzl, *Can. J. Chem.*, **47**, 4477 (1969).

(4) J. J. Fox, K. A. Watanabe, and A. Block, *Progr. Nucl. Acid Res. Mol. Biol.*, **5**, 251 (1966).

(5) L. V. Fisher, W. W. Lee, and L. Goodman, *J. Med. Chem.*, **13**, 775 (1970), and references cited therein.




nucleoside **9** had much greater thermal stability than the *N,N*-dimethylcarbamoylmethyl nucleoside **7**. Again, nmr and ir fully supported structure **9** and, in addition, a very satisfactory elemental analysis of crystalline **9** was obtained. The great utility of the γ-lactone nucleoside **8** was demonstrated by its ready conversion into the crystalline nucleoside peptide **10**, by treatment with ethyl glycinate in anhydrous *N,N*-dimethylformamide at room temperature for 30 hr.

Lithium aluminum hydride reduction of the carbamoylmethyl ribo nucleoside **9** gave only a trace amount of a branched-chain aminoethyl ribo nucleoside **12**. As a consequence, efforts were then directed toward finding a procedure for preferentially de-O-acylating the blocked cyanomethyl ribo nucleoside **6** without hydrolyzing or aminating the cyano group. Treatment of **6** with anhydrous liquid ammonia gave, on work-up, a complex mixture of products. Use of methanolic sodium methoxide for de-O-acylating also

proved to be unsatisfactory because a complex mixture of nucleosides was obtained. Selective de-O-acylation of **6** was finally achieved by treatment of the 6-chloropurine cyano nucleoside **6** with anhydrous dimethylamine at −10° for 20 days. Concomitant replacement of the 6-chloro substituent on purine by the *N,N*-dimethylamino group also took place to afford, after chromatography and crystallization, 6-*N,N*-dimethylamino-9-(3′-*C*-cyanomethyl-3′-deoxy-β-D-ribofuranosyl)purine (**11**) in 67% yield. Treatment of **11** with methanolic aqueous dimethylamine at room temperature for 12 hr gave the *N,N*-dimethylcarbamoylmethyl nucleoside **7** in quantitative yield.

Catalytic reduction of the branched-chain cyanomethyl ribo nucleoside **11** over platinum in the presence of acetic anhydride and ethanol gave a mixture of two acetylated amino nucleosides in about 90% yield which were separated by column chromatography on silica gel. The faster moving component was the triacetate of the branched-chain amino ethyl ribo nucleoside **12**, whereas the slower moving component (in about equal yield) was the 5′-*O*-acetyl derivative of **12** (on the basis of its nmr spectrum in DMSO-$d_6$: one doublet at $\tau$ 4.18, assigned to C-2′ OH, disappeared on addition of $D_2O$). Treatment of either component with aqueous dimethylamine readily afforded crystalline 6-*N,N*-dimethylamino-9-[3′-(2′′-acetamidomethyl)-3′-deoxy-β-D-ribofuranosyl]purine (**12**). Interestingly, the presence of the ethanol and acetic anhydride in the hydrogenation mixture did not prevent acetylation of the hydroxyl groups. Catalytic reduction of **6** or **11** in the absence of acetic anhydride gave a complex mixture of products which were very difficult to separate.

## Experimental Section

**3-*C*-Cyanomethyl-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (2).**—To a well-stirred solution of 3-*C*-cyanomethyl-3-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (**1**)[2a] (1.5 g) in ethanol (40 ml) was added a saturated solution of sodium hydrogen carbonate (2 ml) followed by sodium metaperiodate solution (1.32 g in 70 ml of water). After the solution was stirred for 3 hr the excess sodium metaperiodate was destroyed by the addition of a few drops of ethylene glycol. The resoluting aldehydo sugar was immediately reduced with sodium borohydride (0.120 g). After the solution had stood for 4 hr, acetone (0.5 ml) was added and the mixture was stirred for an additional 0.5 hr. After the residue was removed by filtration, the filtrate was extracted with methylene chloride (4 × 100 ml). The combined extracts were dried over sodium sulfate, filtered, and evaporated under reduced pressure to yield 1 g (90%) of **2**. Crystallization of this product from ether gave pure **2**: mp 70°; $[\alpha]^{22}D$ +97° (*c* 1.1, chloroform); $\tau^{CDCl_3}$ 4.23 (d, $J_{1,2}$ = 4 Hz, H-1), 5.34 (t, $J_{2,3}$ = 4 Hz, H-2).

*Anal.* Calcd for $C_{10}H_{15}NO_4$: C, 56.4; H, 7.05; N, 6.57. Found: C, 56.6; H, 6.99; N, 6.67.

**5-*O*-Benzoyl-3-*C*-cyanomethyl-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (3).**—To a solution of 4.55 g of **2** in 25 ml of anhydrous pyridine was added 2 ml of benzoyl chloride. After the reaction mixture was kept at room temperature for 24 hr, a mixture of ice and water was added causing precipitation of solid **3**. Recrystallization of this solid from ethanol and then from ether–petroleum ether (bp 30–65°) gave 5.4 g (80%) of pure **3**: mp 110°; $[\alpha]^{22}D$ +59° (*c* 1.8, chloroform); $\tau^{CDCl_3}$ 4.1 (d, $J_{1,2}$ = 4 Hz, H-1), 5.22 (t, H-2); ir 2250 $cm^{-1}$ (C≡N).

*Anal.* Calcd for $C_{17}H_{19}NO_5$: C, 64.26; H, 6.03; N, 4.45. Found: C, 64.11; H, 5.93; N, 4.31.

**1,2-Di-*O*-acetyl-5-*O*-benzoyl-3-*C*-cyanomethyl-3-deoxy-β-D-ribofuranose (4) and 1-*O*-Acetyl-5-*O*-benzoyl-3-*C*-(carboxymethyl-2,3-γ-lactone)-3-deoxy-β-D-ribofuranose (4a).**—The benzoate **3** (4.40 g) was hydrolyzed with 90% trifluoroacetic acid (50 ml) for 10 min and the resulting syrup was acetylated with acetic anhydride (15 ml) and pyridine (15 ml) for 18 hr. The product, worked up as described previously,[2a] was crystallized from ethanol to give 2 g of pure β anomer **4**. The mother liquor was evaporated to dryness and the residue was chromatographed on 120 g of silica gel using 3:1 benzene–ethyl acetate as developer to afford a fast-moving fraction **4a** (0.4 g, 5%) and 1.9 g (38%) of a 3:7 mixture of α,β anomers of **4**. Pure **4** had mp 117°; $[\alpha]^{22}D$ −21.9° (*c* 1.5, chloroform); ir 2250 $cm^{-1}$ (C≡N); $\tau^{CDCl_3}$ 3.83 (s, H-1), 4.7 (d, H-2).

*Anal.* Calcd for $C_{18}H_{19}NO_7$: C, 59.82; H, 5.31; N, 3.81. Found: C, 59.56; H, 5.17; N, 3.53.

**4a** was recrystallized from ethanol: mp 137°; $[\alpha]^{24}D$ −96° (*c* 1.6, chloroform); ir (Nujol), 1700, 1780 $cm^{-1}$ (C=O); $\tau^{CDCl_3}$ 3.6 (s, 1 H, H-1), 5.0 (d, 1 H, H-2), 5.5–5.9 (m, 3 H, H-5 and H-4), 6.7–7.5 (m, $CH_2CO_2$ and H-3), 8.0 (s, 3 H, Ac).

*Anal.* Calcd for $C_{16}H_{16}O_7$: C, 60.00; H, 5.04. Found: C, 59.80; H, 5.18.

**6-Benzamido-9-(2′-*O*-acetyl-5′-*O*-benzoyl-3′-*C*-cyanomethyl-3′-deoxy-β-D-ribofuranosyl)purine (5).**—*Hydrogen bromide* was bubbled into a 0° solution of 1,2-di-*O*-acetyl-5-*O*-benzoyl-3-*C*-cyanomethyl-3-deoxy-β-D-ribofuranose (**4**) (0.500 g) in anhydrous dichloromethane (25 ml) for 15 min. The reaction mixture was kept at 0° for 1 hr and then at room temperature for 15 min. The solution was then evaporated to a syrup and the last traces of hydrogen bromide were removed by coevaporation with dry toluene. The resultant syrup was redissolved in toluene (10 ml) and added to a suspension of chloromercuri-6-benzamidopurine (0.658 g) and Celite (0.500 g) in toluene (50 ml) which had been previously dried by distilling off 20 ml of toluene from the mixture. When the addition was completed the mixture was refluxed for 1 hr and then worked up as previously described.[2a] The material resulting from this procedure (0.508 g) was chromatographed on silica gel using benzene–ethyl acetate–ethanol (5:5:1) as developer to afford nucleoside **5** (0.298 g, 40% yield) as an amorphous foam: $[\alpha]^{22}D$ +3.1° (*c* 1.2, chloroform); ir film 2250 $cm^{-1}$ (C≡N); $\tau^{CDCl_3}$ 0.75–1.00 (b, 1 H, HNC=O), 1.46 (s, 1 H, H-2 or H-8), 7.26 (d, 2 H, $-CH_2C{\equiv}N$), 7.83 (s, 3 H, $O{=}CCH_3$).

*Anal.* Calcd for $C_{28}H_{24}N_6O_6$: C, 62.22; H, 4.48; N, 15.55. Found: C, 61.99; H, 4.80; N, 15.50.

**6-Chloro-9-(2′-*O*-acetyl-5′-*O*-benzoyl-3′-*C*-cyanomethyl-3′-deoxy-β-D-ribofuranosyl)purine (6).**—A thoroughly dried, finely powdered mixture of 0.72 g of **4** and 0.33 g of anhydrous 6-chloropurine was heated in an oil bath at 160° at 30 Torr for 5 min followed by further heating at 160° at 1 Torr for 40 min. The melt was extracted with 40 ml of dichloromethane and the extract was then filtered. Evaporation of the filtrate gave a residue which was chromatographed on 45 g of grade II silica using 2:1 benzene–ethyl acetate as developer to afford 0.600 g (66%) of nucleoside. Crystallization of this solid from ethanol gave pure nucleoside **6**: mp 136.5–137°; $[\alpha]^{22}D$ +16° (*c* 1.5, chloroform); ir (Nujol) 2250 $cm^{-1}$ (C≡N); $\tau^{CDCl_3}$ 1.75 and 1.50 (H-2 and H-8), 3.96 (d, 1 H, $J_{1',2'}$ = 1 Hz, H-1′), 7.2 (d, 2 H, $CH_2CN$), 7.78 (s, 3 H, OAc).

*Anal.* Calcd for $C_{21}H_{18}N_5O_5Cl$: C, 55.33; H, 3.98; N, 15.35. Found: C, 55.00; H, 3.60; N, 15.14.

**6-*N,N*-Dimethylamino-9-[3′-deoxy-3′-*C*-(*N,N*-dimethylcarbamoylmethyl)-β-D-ribofuranosyl]purine (7).**—To a solution of 6-chloro-9-(2′-*O*-acetyl-5′-*O*-benzoyl-3′-*C*-cyanomethyl-3′-deoxy-β-D-ribofuranosyl)purine (**6**) (0.102 g in 7 ml of methanol) was added dropwise a 25% aqueous solution of dimethylamine (2 ml). After the reaction mixture was allowed to stand for 4 hr, the solvent was evaporated and the residue was chromatographed on a column of tlc silica gel using dichloromethane–methanol (93:7) as developer to afford the amide nucleoside **7** (0.064 g, 72% yield) as a syrup which crystallized after standing for over a month, mp 82–84°. This compound was homogeneous on paper ($R_f$ 0.68, butanol–ethanol–water, 40:19:11), and on silica tlc ($R_f$ 0.42, dichloromethane–methanol, 9:1): $\tau^{CDCl_3}$ 1.80 (s, 2, H-2 and H-8), 6.10 (d, 1, $J_{1',2'}$ = 3.5 Hz, H-1′), 4.43 (s, 2-3, C-5′ OH and C-2′ OH), 5.3 (two d, 2, $J_{2',3'}$ = 3.5 Hz, H-2′), 5.7–6.3 (m, 3, H-4′ and C-5′ $CH_2$), 6.53 [s, 6, $N(Me)_2$], 6.96, 7.08 [2 τ s, 6, $O{=}CN(Me)_2$], 7.1–7.6 (m, 3, H-3′, $CH_2CO$); on addition of $D_2O$, the peak at τ 4.43 disappeared and the singlet at 1.80 became two singlets; uv (two max) 275 mμ ($H_2O$); ir (film) 3200–3500 (OH), 1640 $cm^{-1}$ (C=O). The nmr spectrum of **7** was the same as that of compound **10** described in the previous paper. The analysis given is that of **10**.[2a]

*Anal.* Calcd for $C_{16}H_{24}N_6O_4 \cdot {}^1/_2H_2O$): C, 51.30; H, 6.65; N, 22.50. Found: C, 50.86; H, 6.43; N, 22.40; mol wt 364 (mass spectroscopy).

Attempts to dry the compound under reduced pressure at about 50° led to a slow conversion of **7** into the lactone **8**.

**6-*N*,*N*-Dimethylamino-9-[2′,5′-di-*O*-acetyl-3′-*C*-(*N*,*N*-dimethylcarbamoylmethyl)-3′-deoxy-β-D-ribofuranosyl]purine.**—A solution of **7** (0.050 g) in pyridine (0.5 ml) and acetic anhydride (0.5 ml) was stored at room temperature for 20 hr. The reaction mixture was then diluted with ice water (10 ml) and extracted with chloroform (3 × 20 ml). After the chloroform extracts were dried over sodium sulfate and evaporated, the residue was chromatographed on a column of tlc silica to yield 0.055 g (40%) of the title nucleoside as a syrup, $[\alpha]^{25}D$ −25° (*c* 1, chloroform).

*Anal.* Calcd for $C_{20}H_{28}N_6O_6$: C, 53.64; H, 6.29; N, 18.74. Found: C, 53.90; H, 6.31; N, 18.65.

**6-*N*,*N*-Dimethylamino-9-[3′-*C*-(carboxymethyl-2′,3′-γ-lactone)-3′-deoxy-β-D-ribofuranosyl]purine (8).**—Sublimation of 6-*N*,*N*-dimethylamino-9-(3′-*C*-*N*,*N*-dimethycarbamoylmethyl-3′-deoxy-β-D-ribofuranosyl)purine (**7**) (0.030 g) at 210° (0.1 Torr) afforded after crystallization from ethyl acetate the title lactone nucleoside (**8**) (0.019 g,73%): mp 198–199° (with sublimation); $[\alpha]^{22}D$ − 57.5° (*c* 1.1, chloroform); uv max 274 mμ (ε 14,500, methanol); CD max 274 (θ −10,000, methanol); ir (KBr) 1770 $cm^{-1}$ (C=O); $\tau^{CDCl_3}$ 1.73, 2.23 (2 s, 2H, H-2, H-8), 6.48 [s, 6H, N(Me)$_2$]; $\tau^{DMSO\text{-}d_6}$ 4.93 (t, 1 H, C-5′ OH). The hydroxyl absorption disappeared on addition of $D_2O$; molecular weight from mass spectrum 319.

*Anal.* Calcd for $C_{14}H_{17}N_5O_4$: C, 52.65; H, 5.37; N, 21.93. Found: C, 52.43; H, 5.54; N, 21.83.

**Amidation of Lactone 8 to Yield Amide Nucleoside 7.**—6-*N*,*N*-Dimethylamino-9-[3′-*C*-(carboxymethyl-2′,3′-γ-lactone)-3′-deoxy-β-D-ribofuranosyl]purine (**8**) (0.030 g) was dissolved in dimethylamine (3 ml) and allowed to stand at 0° for 4 hr. After evaporation of the dimethylamine from the reaction mixture the branched-chain *N*,*N*-dimethylcarbamoylmethyl nucleoside (**7**) (0.034 g, quantitative yield) was recovered having an ir and nmr identical with those of the product obtained by treatment of **6** with aqueous dimethylamine. The product crystallized after standing at room temperature for over a month.

**6-*N*,*N*-Dimethylamino-9-[3′-*C*-(carbamoylmethyl)-3′-deoxy-β-D-ribofuranosyl]purine (9).**—The lactone nucleoside **8** (0.030 g) was allowed to react with liquid ammonia (3 ml) for 6 hr and the ammonia was then allowed to slowly evaporate. The resultant residue was crystallized from ethanol to afford the amide nucleoside **9** (0.030 g, 95%): mp 207°; $[\alpha]^{23}D$ − 29.9° (*c* 0.5, water); ir (Nujol) 1650 $cm^{-1}$ (C=O); $\tau^{DMSO\text{-}d_6}$ 2.60, 3.13 (b, 2 H, O=CNH$_2$), 4.08 (d, 1 H, C-2′ OH(, 4.83 (t, 1 H, C-5′ OH); uv max 275 mμ (ε 14,000, $H_2O$); CD max 275 (θ −6000).

*Anal.* Calcd for $C_{14}H_{20}N_6O_4$: C, 49.99; H, 5.99; N, 24.98. Found: C, 49.59; H, 5.94; N, 24.72.

**6-*N*,*N*-Dimethylamino-9-[3′-*C*-(carbomethyl-*N*-glycine ethyl ester)-3′-deoxy-β-D-ribofuranosyl]purine (10).**—The lactone **8** (0.040 g) was dissolved in a mixture of *N*,*N*-dimethylformamide (0.75 ml) and ethyl glycinate (0.25 ml) and stirred at room temperature for 30 hr. The volatile material was removed by distillation (50°, 0.1 Torr) and the remaining residue column was chromatographed on tlc silica gel using dichloromethane–methanol (9:1) as developer to afford after crystallization from ethyl acetate the title peptide nucleoside (**10**) (0.038 g, 72%): mp 155–157°; $[\alpha]^{25}D$ − 49° (*c* 1.3, chloroform); uv $\lambda_{max}$ 275 mμ (ε 14,600, water); CD $\lambda_{max}$ 275 mμ (θ −8500, water); ir (KBr) 1730 (C=O ester), 1650 $cm^{-1}$ (C=O amide); $\tau^{CDCl_3}$ 1.83, 2.00 (2 s, 2 H, H-2, H-8), 7.18 (b, 1 H, NH), 4.10 (d, 1 H, H-1), 8.70 (t, 3 H, $CH_3$ of ethyl ester).

*Anal.* Calcd for $C_{18}H_{26}N_6O_6$: C, 51.10; H, 6.21; N, 19.89. Found: C, 50.92; H, 6.19; N, 19.61.

**6-*N*,*N*-Dimethylamino-9-(3′-*C*-cyanomethyl-3′-deoxy-β-D-ribofuranosyl)purine (11).**—6-Chloro-9-(2′-*O*-acetyl-5′-*O*-benzoyl-3′-(*C*-cyanomethyl)-3′-deoxy-β-D-ribofuranosyl)purine (**6**) (0.268 g) was dissolved in anhydrous dimethylamine (30 ml) and stored at −10° for 20 days. The dimethylamine was then evaporated and the residue was triturated with ether (5 ml). The material remaining after the ether was decanted was taken up in ethanol and allowed to stand at 0° for 24 hr. A portion of the title nucleoside (0.094 g) crystallized directly out of this solution and a further 0.060 g (67% yield) was obtained by chromatography of the mother liquor on a column of tlc silica gel using dichloromethane–ethanol (93:7) as developer. Recrystallization of the nucleoside from ethanol or sublimation gave pure **11**: mp 206°; $[\alpha]^{25}D$ −39.4° (*c* 0.6, ethanol); uv $\lambda_{max}$ 275 mμ (ε 15,800, water); CD $\lambda_{max}$ 275 (θ −6100, water ); ir (KBr) 2230 $cm^{-1}$ (C≡N); $\tau^{DMSO\text{-}d_6}$ 1.70, 1.76 (2 s, 2 H, H-2, H-8), 3.98 (d, 1 H, H-1′), 6.80 [s, 6 H, N(Me)$_2$].

*Anal.* Calcd for $C_{14}H_{18}N_6O_3$: C, 52.82; H, 5.70; N, 26.40. Found: C, 52.64; H, 5.64; N, 26.42.

**6-*N*,*N*-Dimethylamino-9-[3′-deoxy-3′-*C*-(*N*,*N*-dimethylcarbamoylmethyl)-β-D-ribofuranosyl]purine (7) from 11.**—6-*N*,*N*-Dimethylamino-9-(3′-*C*-cyanomethyl-3′-deoxy-β-D-ribofuranosyl)purine (**11**) (0.020 g) was dissolved in a mixture of methanol (4 ml) and 25% aqueous dimethylamine (2 ml). After the reaction mixture was left to stand at room temperature for 12 hr the solvent was evaporated to yield **7** (0.023 g, quantitative yield) as a syrup which crystallized after standing at room temperature. The product was identical by ir and nmr with the product obtained by treatment of **6** with a methane–water–dimethylamine mixture except for an additional HO peak in its nmr at τ 7.3. The product was not stable, mp 82–85°.

*Anal.* Calcd for $C_{16}H_{24}N_6O_4 \cdot H_2O$: C, 50.35; H, 6.82; N, 21.95. Found: C, 49.86; H, 6.58; N, 21.31.

**6-*N*,*N*-Dimethylamino-9-[3′-(2″-acetamidoethyl)-3′-deoxy-β-D-ribofuranosyl]purine (12).**—6-*N*,*N*-Dimethylamino-9-(3′-*C*-cyanomethyl-3′-deoxy-β-D-ribofuranosyl)purine (**11**) (0.030 g) was dissolved in a mixture of acetic anhydride (2 ml) and absolute ethanol (2 ml) and hydrogenated over platinum oxide (20 mg) at 60 psi for 4 hr. The catalyst was then removed by filtration and the solvent was evaporated to afford 0.040 g of syrup. Examination of this product by tlc showed that it contained two components, $R_f$ 0.18 and 0.10 in dichloromethane–ethyl acetate–ethanol (5:5:1). These two components were separated by column chromatography on tlc silica gel using the above developer, to afford 0.017 g of the faster component [$\tau^{DMSO\text{-}d_6}$ 2.14 (broad t, 1 H, NH), 7.85, 8.04, 8.20 (3 s, 9 H, 3 Ac), no hydroxyl signals] and 0.019 g (about 90% total yield of two components) of the slower component [$\tau^{DMSO\text{-}d_6}$ 2.22 (broad t, 1 H, NH), 4.18 (d, 1 H, C-2′ OH), 7.98, 8.17 (2 s, 6 H, 2 Ac)]. Upon addition of $D_2O$ the doublet at τ 4.18 disappeared. The slower moving component was dissolved in 25% aqueous dimethylamine (1 ml) solution and allowed to stand for 3 hr at room temperature. After evaporation of the solvent, the remaining material crystallized on trituration with dichloromethane. Reaction of the faster moving component under the same conditions afforded the identical product. Recrystallization of these products from isopropyl alcohol–water gave pure **12** (0.023 g, 63%): mp 193–194°; $[\alpha]^{25}D$ −1.0° (*c* 0.9, ethanol); $\lambda_{max}^{H_2O}$ 274 mμ (ε 23,900); $\tau^{DMSO\text{-}d_6}$ 1.56, 1.76 (2 s, 2 H, H-2, H-8), 2.19 (t, 1 H, NH), 4.0 (s, 1 H, H-1′), 8.23 (s, 3 H, NAc).

*Anal.* Calcd for $C_{16}H_{24}N_6O_4 \cdot {}^1/_2H_2O$: C, 51.47; H, 6.74; N, 22.47. Found: C, 51.38; H, 6.38; N, 22.07.

**Registry No.**—**2,** 37108-29-5; **3,** 37108-30-8; **4,** 37108-31-9; **4a,** 37108-32-0; **5,** 37108-33-1; **6,** 37157-03-2; **7,** 37108-20-6; **8,** 37108-35-3; **9,** 37108-36-4; **10,** 37108-37-5; **11,** 37108-38-6; **12,** 37108-11-5; 6-*N*,*N*-dimethylamino-9-[2′,5′-di-*O*-acetyl-3′-*C*-(*N*,*N*-dimethylcarbamoylmethyl)-3′-deoxy-β-D-ribofuranosyl]-purine, 37108-12-6.

**Acknowledgment.**—The authors thank the National Research Council of Canada for financial assistance.