Registry No.—**1**, 28528-49-6; **2**, 25575-32-0; **4**, 65-46-3; **5a**, 26790-12-5; **5b**, 10212-25-6; **6**, 32659-29-3; **7**, 32659-30-6; **9**, 147-94-4; **10**, 32659-31-7; **11**, 32830-01-6; **12**, 3257-75-8.

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Nucleoside Peptides. III. The Synthesis of *N*-[1-(9-Adenyl)-β-D-ribofuranuronosyl] Derivatives of Certain Amino Acids and Peptides

MASAJIRO KAWANA, ROBERT J. ROUSSEAU,* AND ROLAND K. ROBINS

ICN Nucleic Acid Research Institute, Irvine, California 92664

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Benzyl esters of several amino acids and peptides have now been successfully coupled with 1-(9-adenyl)-2,3-*O*-isopropylidene-β-D-ribofuranuronic acid (**1**) by the DCC method to afford *N*-[1-(9-adenyl)-2,3-*O*-isopropylidene-β-D-ribofuranuronosyl]amino acid and peptide benzyl esters. Concomitant acylurea side-product formation was inhibited by the addition of *N*-hydroxysuccinimide. The title compounds were produced in excellent yields when the isopropylidene and benzyl blocking groups were removed by acid hydrolysis and catalytic hydrogenolysis, respectively. These procedures provide a general method for the attachment of the amino terminus of an amino acid or peptide to a carboxylic acid moiety of a nucleoside.

Recently there has been a great deal of interest in the isolation and synthesis of nucleoside amino acids and peptides.[1-3] Reasons for the preparation and study of this class of compounds has been outlined in an earlier publication submitted from these laboratories.[4] Most syntheses of nucleoside peptides have involved either the coupling of an amino[1,2,4] or hydroxyl[5] group of a nucleoside to the carboxyl group of a blocked amino acid or displacement of a leaving group on a nucleoside by the amino group of an amino acid.[6] In one report[7] purine and pyrimidine ribofuranuronic acids have been coupled to unblocked high molecular weight polypeptides in yields ranging from 2 to 10%. The work described in this article has provided a general method for the coupling of the amino terminus of an amino acid or peptide to a free carboxylic acid moiety of a nucleoside in good yield.

1-(9-Adenyl)-2,3-*O*-isopropylidene-β-D-ribofuranuronic acid (**1**) was selected as the nucleoside reagent because of its solubility properties and ease of preparation.[8a,b] *N*,*N*′-Dicyclohexylcarbodiimide (DCC) was chosen to effect coupling, since it has been known to provide peptide linkages in high yield with little or no racemization.[9] When **1** was coupled to various amino acid benzyl esters by the action of DCC, yields ranging from 40 to 50% of the desired products (**2**) were obtained (Scheme I). Purification was complicated by the presence of a second product (**3**), 15–30% yields, from which **2** could not be readily separated. Consideration of the mechanism of action of DCC proposed by Khorana and coworkers[10,11] led to the assumption that this by-product could be the acylurea adduct[12,13] of **1** and DCC. This assumption was substantiated by elemental analysis. Examination of its infrared spectrum, which exhibited a strong band at 1640 cm^{-1} (-NHCONH, ~1660 cm^{-1}),[14] suggested that this by-product was actually *N*-acylurea (**3**) rather than the *O*-acylisourea.[10]

Attempts to suppress the formation of acylurea by-product by changing the solvent medium to methylene chloride[12] were without success. Addition of *N*-hydroxysuccinimide (NHS) with DCC has been shown to improve the yields in peptide syntheses[15] without increasing racemization;[16] therefore **1** was coupled to glycine benzyl ester in the presence of DCC and NHS and gave a 91% yield of *N*-[1-(9-adenyl)-2,3-*O*-isopropylidene-β-D-ribofuranuronosyl]glycine benzyl ester (**2a**). Under these conditions only a trace of the side product was detected in the reaction mixture. Similarly, compounds **2b**, **2c**, and **2d** benzyl ester were prepared in high yield by treating **1** with the benzyl esters of L-alanine, L-phenylalanine, and L-glutamic acid (Scheme I).

Hydrolysis of the isopropylidene blocking groups with 88% formic acid was very slow at room temperature. When the temperature was raised to 60–65° the reaction was complete in 2–4 hr. *N*-[1-(9-Adenyl)-β-D-ribofuranuronosyl]glycine benzyl ester (**4a**), -L-alanine benzyl ester (**4b**), -L-phenylalanine benzyl ester (**4c**), and -L-glutamic acid dibenzyl ester (**4d**) were produced in good yields by this procedure. Facile hydrogenolysis of the benzyl blocking groups of **4a–d** was accomplished utilizing palladium on charcoal as catalyst. The title compounds *N*-[1-(9-adenyl)-β-D-ribofuran-

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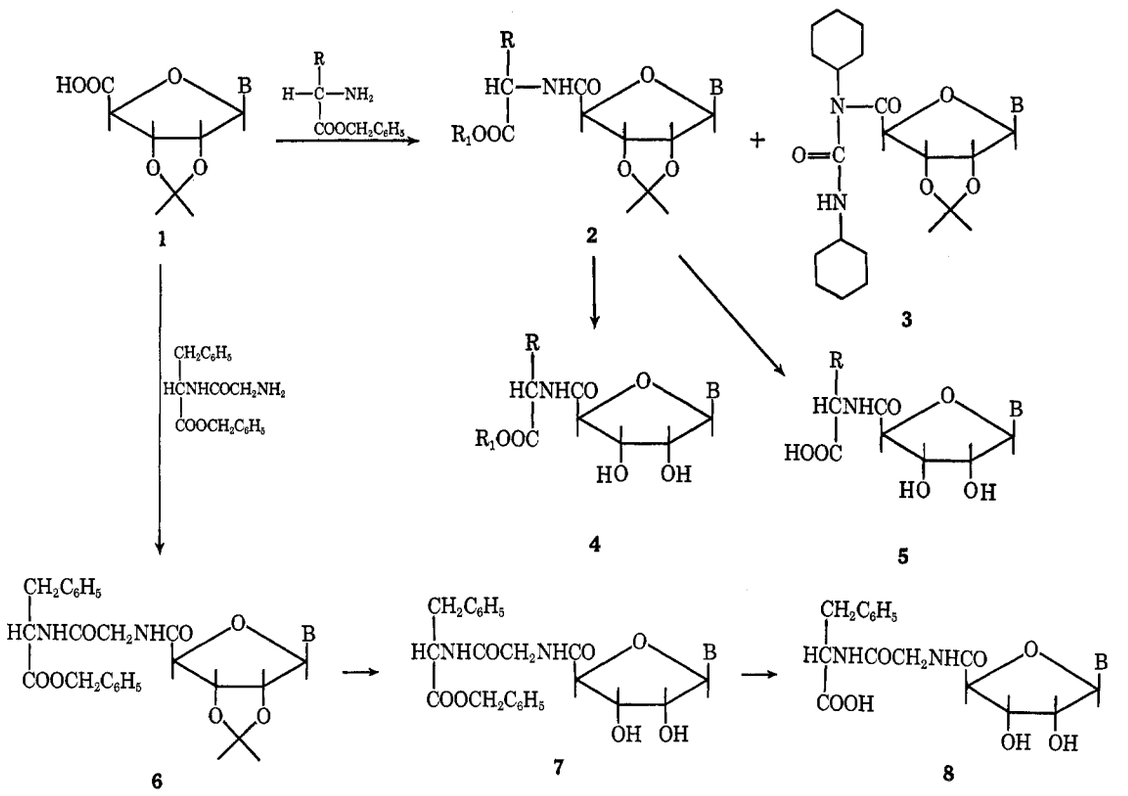
SCHEME I



B = 9-β-adenyl
a, R = H; $R_1 = CH_2C_6H_5$
b, R = CH_3; $R_1 = CH_2C_6H_5$
c, R = $CH_2C_6H_5$; $R_1 = CH_2C_6H_5$
d, R = CH_2CH_2COOH; $R_1 = CH_2C_6H_5$
e, R = $(CH_2)_4NHCbz$; $R_1 = CH_3$
f, R = $(CH_2)_4NHCbz$; R1 = H
g, R = $(CH_2)_4NH_2$

uronosyl]glycine (**5a**), *N*-[1-(9-adenyl)-β-D-ribofuranuronosyl]-L-alanine (**5b**), *N*-[1-(9-adenyl)-β-D-ribofuranuronosyl]-L-phenylalanine (**5c**), and *N*-[-1-(9-adenyl)-β-D-ribofuranuronosyl]-L-glutamic acid (**5d**) were produced by this method in yields of 58, 71, 89, and 73%, respectively.

When **1** was coupled to N^{ϵ}-carbobenzyloxy-L-lysine methyl ester, N^{α}-[1-(9-adenyl)-2,3-*O*-isopropylidene-β-D-ribofuranuronosyl]-N^{ϵ}-carbobenzyloxy-L-lysine methyl ester (**2e**) was formed in 91% yield. Removal of the methyl ester with potassium hydroxide gave **2f** while subsequent treatment with 88% formic acid removed the isopropylidene blocking group and afforded N^{α}-[1-(9-adenyl)-β-D-ribofuranuronosyl]-N^{ϵ}-carbobenzyloxy-L-lysine (**4f**). Attempts to remove the carbobenzyloxy group by catalytic hydrogenolysis were unsuccessful, since **4f** was insoluble in the common solvents used for hydrogenolysis. The desired product, N^{α}-[1-(9-adenyl)-β-D-ribofuranuronosyl]-L-lysine (**5g**), was prepared in 79% yield by catalytic hydrogenolysis of **2e** in 88% formic acid.

The dipeptide, glycyl-L-phenylalanine benzyl ester, was also coupled with **1** in the presence of DCC and NHS. This afforded a 93% yield of *N*-[1-(9-adenyl)-2,3-*O*-isopropylidene-β-D-ribofuranuronosyl]glycyl-L-phenylalanine benzyl ester (**6**). Removal of the isopropylidene and benzyl blocking groups gave the desired product *N*-[1-(9-adenyl)-β-D-ribofuranuronosyl]-glycyl-L-phenylalanine (**8**) in good yield.

Confirmation that little or no racemization of the amino acid moieties had occurred was ascertained by tlc, since the products at each step were found to be homogenous in several solvent systems.

Experimental Section[17]

General Procedure A for the Preparation of 2a–d (Table I).—DCC (453 mg, 2.2 mmol) was added to a mixture of 1-(9-adenyl)-2,3-*O*-isopropylidene-β-D-ribofuranuronic acid[8a] (**1**, 642 mg, 2.0 mmol), the appropriate blocked amino acid (glycine benzyl ester,[18] 330 mg, 2.0 mmol, for **2a**; L-alanine benzyl ester,[18] 396 mg, 2.0 mmol, for **2b**; L-phenylalanine benzyl ester,[19] 510 mg, 2.0 mmol, for **2c**; L-glutamic acid dibenzyl ester,[19] 654 mg, 2.0 mmol, for **2d**), and NHS (230 mg, 2.0 mmol) in DMF (5 ml). The mixture was stirred at room temperature for 5 hr. Acetic acid (60 mg) was added to decompose the excess DCC. The crystalline residue was filtered and washed with dichloromethane (40 ml), washed successively with water (30 ml), 5% Na_2CO_3 (20 ml), and water (five 30-ml portions), and dried ($MgSO_4$). After evaporation of the solvent the residue was treated with a small amount of dichloromethane, and the undissolved material was collected and discarded. The filtrate was evaporated to dryness to give crude product. The analytical samples were obtained either by silica gel column chromatography or recrystallization according to the conditions given in Table I. Table II gives physical constants.

(17) Physical properties were determined with the following instruments: melting points, Thomas–Hoover apparatus (uncorrected); uv spectra, Cary 15 uv spectrometer (pH 1, pH 11, and MeOH); specific rotations, Perkin-Elmer Model 141 polarimeter; and ir spectra, Perkin-Elmer Model 257 (KBr). Where indicated by elemental analyses, solvation was verified by nmr spectroscopy in absolute DMSO-d_6 and in the case of hydration, by exchange with addition of D_2O and reintegration of the spectral area where the D_2O peak had occurred.

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TABLE I

Compd	Method	Purification	Yield, %	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found,[d] % C	Found,[d] % H	Found,[d] % N
2a	A	Column chromatography[a]	91	$C_{22}H_{24}N_6O_6 \cdot 0.5H_2O$[17]	55.34	5.27	17.60	55.41	5.16	17.55
2b	A	EtOAc[b]	63	$C_{23}H_{26}N_6O_6$	57.25	5.43	17.41	56.99	5.72	17.18
2c	A	EtOAc–*n*-heptane[b]	71	$C_{29}H_{30}N_6O_6$	62.35	5.41	15.05	62.28	5.34	15.07
2d	A	Column chromatography[a]	92	$C_{32}H_{34}N_6O_8 \cdot H_2O$	59.25	5.59	12.95	59.27	5.61	12.94
4a	B	MeOH[b]	56	$C_{19}H_{20}N_6O_6$	53.26	4.70	19.61	53.23	5.09	19.64
4b	B	EtOH–H_2O[b]	82	$C_{20}H_{22}N_6O_6 \cdot H_2O$	52.17	5.27		52.40	5.56	
4c	B	Column chromatography[c]	67	$C_{26}H_{26}N_6O_6$	60.22	5.05	16.20	60.22	4.95	15.97
4d	B	Column chromatography[c]	72	$C_{29}H_{30}N_6O_8$	58.97	5.12	14.23	58.99	5.24	14.36
5a	C	MeOH[b]	58	$C_{12}H_{14}N_6O_6$	42.60	4.17	24.84	42.69	4.58	24.58
5b	C	EtOH–H_2O[b]	71	$C_{13}H_{16}N_6O_6$	44.32	4.57	23.85	44.61	4.71	24.01
5c	C	EtOH–H_2O[b]	89	$C_{19}H_{20}N_6O_6 \cdot 0.5H_2O$	52.17	4.83	19.21	52.21	4.86	19.28
5d	C	EtOH–H_2O[b]	73	$C_{15}H_{18}N_6O_8$	43.90	4.42	20.48	43.87	4.54	20.51

[a] Silica gel column, packed and eluted with EtOAc–*n*-heptane–$CHCl_3$ (8:1:1). [b] Recrystallization solvent. [c] Silica gel column, packed and eluted with EtOAc–$CHCl_3$–EtOH (6:3:1). [d] Compounds were dried (P_2O_5) *in vacuo* at 56° for 4 hr before analytical determinations.

TABLE II

PHYSICAL CONSTANTS OF CERTAIN *N*-[1-(9-ADENYL)-β-D-RIBOFURANURONOSYL] AMINO ACIDS AND PEPTIDES

Compd	Mp, °C	$\lambda_{max}^{pH\ 1}$, nm (ε)	$\lambda_{max}^{pH\ 11}$, nm (ε)	λ_{max}^{MeOH}, nm (ε)	Chromatographic mobilities[a]: 5% NH_4HCO_3	EtOH–1 *N* NH_4OAc (7:3)	*n*-PrOH–conc NH_4OH–H_2O (6:3:1)
2a	Glass	257 (13,300)	258 (13,400)	259 (16,400)			
2b	~90	255 (15,800)	257 (17,700)	257 (16,000)			
2c	134–135	257 (13,200)	257 (13,700)	259 (14,500)			
2d	Glass	257 (13,200)	258 (11,600)	258 (13,900)			
4a	109–110	256 (14,500)	258 (15,500)	259 (15,400)			
4b	139 softens 148 dec	255 (14,400)	257 (19,900)	258 (14,800)			
4c	Glass	258 (13,100)	258 (14,400)	259 (14,800)			
4d	Glass	258 (11,900)	259 (9,600)	260 (13,900)			
5a		257 (17,400)	258 (18,100)	258 (17,800)	0.62	0.29	0.39
5b	262–263	256 (16,500)	259 (17,100)	259 (16,000)	0.70	0.37	0.45
5c		257 (14,300)	259 (14,900)	254 (15,700)	0.69	0.48	0.59
5d	229–232	257 (14,400)	258 (14,700)	259 (14,800)	0.80	0.18	0.23

[a] Chromatograms were developed by the descending technique utilizing Whatman No. 1 chromatographic paper and spots were detected with short-wave uv light.

General Procedure B (Table I) for the Removal of Isopropylidene Groups. Preparation of Compounds 4a–d.—A solution of the respective isopropylidene blocked compounds (**2a–d**) in 88% formic acid (6 ml) was heated at 60–65° (bath temperature) for 3–4 hr. The solvent was removed by repeated coevaporation with EtOH–MeOH *in vacuo* to give an amorphous residue. The residue was treated according to Table I.

General Procedure C (Table I) for the Removal of the Benzyl Blocking Groups by Catalytic Hydrogenation. Preparation of Compounds 5a–d.—A cooled solution of the respective benzyl ester compound (**4a–d**, 2.0 mmol) in the appropriate solvent under nitrogen atmosphere was hydrogenated using Pd/C (150 mg) at room temperature and on a Parr apparatus at 45 psi for 20 hr. The resulting precipitate was dissolved by heating [water (40 ml) had to be added to dissolve the precipitate in the preparation of **5b**], the catalyst was removed by filtration (Celite pad) and washed with methanol, and the filtrate and washings were evaporated to dryness. The residue was recrystallized from the appropriate solvent (Table I).

***N*-[1-(9-Adenyl)-2,3-*O*-isopropylidene-β-D-ribofuranuronosyl]-*N*,*N*′-dicyclohexylurea (3).**—A mixture of **1** (1.9 g, 6 mmol) and L-phenylalanine benzyl ester[19] (1.5 g, 6 mmol) in DMF (20 ml) was treated with DCC (1.36 g, 6.6 mmol) in the absence of NHS in a manner similar to that used in the preparation of **2a**. A solution of the crude product in $CHCl_3$ was chromatographed over a silica gel column (200 g, 4.2 cm). Elution was effected with ethyl acetate–*n*-heptane–chloroform (8:1:1), and 100-ml fractions were collected. Fractions 7–16 contained **2c** (1.85 g, 55%). Fractions 23–24 were combined, and the solvent was removed to give **3** (680 mg, 22%) as an amorphous foam, which was crystallized from isopropyl alcohol: mp 210–211° (sintered); $[\alpha]^{25}D$ +0.3° (*c* 2, $CHCl_3$); $\lambda_{max}^{pH\ 1}$ 257 nm (ε 15,700), $\lambda_{max}^{pH\ 11}$ 259 (15,200), λ_{max}^{MeOH} 259 (16,100); ir 1640 cm^{-1} (–NHCONH–).

Anal. Calcd for $C_{26}H_{37}N_7O_5$: C, 59.18; H, 7.06; N, 18.58. Found: C, 59.23; H, 7.17; N, 18.60.

N^{α}-[1-(9-Adenyl)-2,3-*O*-isopropylidene-β-D-ribofuranuronosyl]-N^{ϵ}-carbobenzyloxy-L-lysine Methyl Ester (2e).—A mixture of **1** (321 mg, 1 mmol), N^{ϵ}-carbobenzyloxy-L-lysine methyl ester[20] (294 mg, 1 mmol), and NHS (115 mg, 1 mmol) in DMF (5 ml) was treated with DCC (227 mg, 1.1 mmol) in a manner similar to that used in the preparation of **2a**; aqueous saturated $NaHCO_3$ was used instead of 5% Na_2CO_3. The crude product (**2e**, 560 mg, 91%) was obtained as a colorless solid, which could be utilized in further reactions.

The analytical sample was prepared by purification with a silica gel column using ligroin–ethyl acetate–methanol (6:3:1) to elute the desired product. The uv-absorbing fractions were collected and concentrated to yield an amorphous solid (dried over P_2O_5 at 80° *in vacuo* for 4 hr): $[\alpha]^{25}D$ −9.0° (*c* 1, $CHCl_3$); $\lambda_{max}^{pH\ 1}$ 257 nm (ε 14,300), $\lambda_{max}^{pH\ 11}$ 259 (14,000), λ_{max}^{MeOH} 259 (14,300).

Anal. Calcd for $C_{28}H_{35}N_7O_8 \cdot H_2O$: C, 54.62; H, 6.05; N, 15.92. Found: C, 55.01; H, 6.22; N, 15.52.

***N*-[1-(9-Adenyl)-2,3-*O*-isopropylidene-β-D-ribofuranuronosyl]-N^{ϵ}-carbobenzyloxy-L-lysine (2f).**—To a solution of **2e** (230 mg, 0.37 mmol) in methanol (5 ml) was added a solution of KOH

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(34 mg) in methanol (5 ml) and water (0.2 ml), and the mixture was stirred at room temperature. After 24 hr, KOH (11 mg) was added, and the stirring was continued for another 6 hr; the reaction was monitored by a silica gel tlc using chloroform–methanol (9:1). After evaporation of the solvent, the residue was taken in water (10 ml), and the undissolved material was removed by filtration. The filtrate was cooled in an ice–water bath, stirred, and acidified to pH 3.5–4 with 20% formic acid. The resulting precipitate was filtered, washed with water, and dried over P_2O_5.

This compound was crystallized from ethanol–water to give fine needles of **2f** (120 mg, 56%): mp 224–226° dec; $[\alpha]^{25}D$ −16.5° (*c* 1, DMSO); $\lambda_{max}^{pH\ 1}$ 256 nm (ϵ 13,800), $\lambda_{max}^{pH\ 11}$ 259 (13,800), λ_{max}^{MeOH} 259 (13,900).

Anal. Calcd for $C_{27}H_{33}N_7O_8$: C, 55.56; H, 5.69; N, 16.80. Found: C, 55.63; H, 5.63; N, 16.98.

N^{α}-[1-(9-Adenyl)-β-D-ribofuranuronosyl]-N^{ϵ}-carbobenzyloxy-L-lysine (4f).—A solution of **2f** (250 mg, 0.43 mmol) in 88% formic acid (3 ml) was heated at 60–65° (bath temperature) for 2.3 hr. The solvent was removed by repeated coevaporation with ethanol. The residue was dissolved in refluxing ethanol (10 ml) and the wall of the vessel was scratched to induce crystallization of **4f** (200 mg, 86%). This compound was recrystallized from DMF–water and dried at 110° over P_2O_5 *in vacuo* for 10 hr to afford an analytically pure sample: mp 230° (partly melted), 244–246° dec; $[\alpha]^{25}D$ −23.9° (*c* 1, DMSO); $\lambda_{max}^{pH\ 1}$ 257 nm (ϵ 13,700), $\lambda_{max}^{pH\ 11}$ 259 (13,900), $\lambda_{max}^{pH\ 7}$ 259 (13,900).

Anal. Calcd for $C_{24}H_{29}N_7O_8$: C, 53.03; H, 5.37; N, 18.03. Found: C, 52.90; H, 5.52; N, 18.10.

N^{α}-[1-(9-Adenyl)-β-D-ribofuranuronosyl]-L-lysine (5g).—To a cooled solution of **2f** (430 mg, 0.74 mmol) in 88% formic acid (20 ml) was added 10% palladium on charcoal (150 mg) under nitrogen atmosphere. The mixture was treated with hydrogen at room temperature with a Parr apparatus at 45 psi for 18 hr. The catalyst was removed *via* filtration utilizing a Celite pad. Then it was washed with cold water. The combined filtrate and washings were concentrated to dryness by coevaporation with ethanol. The resulting amorphous solid was dissolved in water (1 ml), and ethanol (15 ml) was added to give a gummy precipitate, which was scratched until a solid was obtained. After the mixture had been allowed to stand at 5° overnight, the solid was collected, washed with ethanol, and dried to yield 260 mg (79%) of **5g**.

The analytical sample was obtained by reprecipitation from ethanol–water to give an amorphous solid (dried over P_2O_5 at 80° *in vacuo* for 4 hr); $[\alpha]^{25}D$ −19.3° (*c* 1, H_2O); $\lambda_{max}^{pH\ 1}$ 256 nm (ϵ 14,800), $\lambda_{max}^{pH\ 11}$ 259 (14,600), λ_{max}^{MeOH} 258 (14,800).

Anal. Calcd for $C_{16}H_{23}N_7O_6 \cdot 2H_2O$: C, 43.14; H, 6.11; N, 22.01. Found: C, 43.23; H, 6.14; N, 21.83.

N-[1-(9-Adenyl)-2,3-O-isopropylidene-β-D-ribofuranuronosyl]-glycyl-L-phenylananine Benzyl Ester (6).—A mixture of glycyl-L-phenylalanine[21] (6.17 g, 28 mmol), *p*-toluenesulfonic acid monohydrate (5.4 g, 28.6 mmol), benzene (50 ml), and benzyl alcohol (50 ml) was refluxed into a Dean–Stark distillation apparatus.[22] After the azeotropic distillation of water had ceased (1.5 hr) the solution was allowed to cool to room temperature, diethyl ether (800 ml) was added, and the cloudy mixture was allowed to stand at 4° overnight. The excess solvents were decanted and the residual syrup was twice crystallized from ethanol–petroleum ether (bp 30–60°) to give glycyl-L-phenylalanine benzyl ester *p*-toluenesulfonate salt (3.5 g). This salt (2.96 g, 6.1 mmol) was added to a solution of Na_2CO_3 (647 mg) in water (40 ml) and the solution was extracted with dichloromethane (three 40-ml portions) and dried ($MgSO_4$) and the organic phase was evaporated *in vacuo*. The residue was treated with **1** (1.93 g, 6.0 mmol), NHS (690 mg, 6.0 mmol), and DCC (1.36 g, 6.6 mmol), in a manner similar to that used in the preparation of **2a**, affording 3.5 g (93%) of the crude product **6**.

The analytical sample was obtained by silica gel chromatography using ethyl acetate–chloroform–methanol (6:3:1) as a developer. The uv-absorbing band yielded an amorphous foam (dried over P_2O_5 at 80° *in vacuo* for 5 hr): $[\alpha]^{25}D$ −15.7° (*c* 1, $CHCl_3$); $\lambda_{max}^{pH\ 1}$ 257 nm (ϵ 14,600), $\lambda_{max}^{pH\ 11}$ 259 (15,000), λ_{max}^{MeOH} 259 (14,900).

Anal. Calcd for $C_{31}H_{33}N_7O_7 \cdot 0.5H_2O$: C, 59.60; H, 5.48; N, 15.69. Found: C, 59.47; H, 5.45; N, 15.72.

N-[1-(9-Adenyl)-β-D-ribofuranuronosyl]glycyl-L-phenylalanine Benzyl Ester (7).—A solution of **6** (2.8 g, 4.48 mmol) in 88% formic acid (24 ml) was heated at 60–65° (bath temperature) for 2 hr. The solvent was removed by coevaporation with ethanol to give an amorphous foam, which was dissolved in a small amount of chloroform–methanol. The solution was applied to a silica gel column (200 g, 4.2 cm) packed with ethyl acetate–chloroform–methanol (5:3:2). Elution was effected with the same solvent system, 50-ml fractions being collected. Fractions 15–19 were combined and evaporation of the solvent gave colorless solids (1.5 g, 56%).

The analytical sample was obtained by crystallization from ethanol: mp 138–140°; $[\alpha]^{25}D$ −36.5° (*c* 1, DMSO); $\lambda_{max}^{pH\ 1}$ 257 nm (ϵ 14,500), $\lambda_{max}^{pH\ 11}$ 259 (14,500), λ_{max}^{MeOH} 260 (15,100).

Anal. Calcd for $C_{28}H_{29}N_7O_7 \cdot 1.5H_2O$: C, 55.80; H, 5.35; N, 16.27. Found: C, 55.79; H, 5.44; N, 16.50.

N-[1-(9-Adenyl)-β-D-ribofuranuronosyl]glycyl-L-phenylalanine (8).—The benzyl ester (**7**, 500 mg, 0.83 mmol) was dissolved in hot methanol (150 ml). To the cooled solution was added a suspension of 10% palladium on charcoal (300 mg) in water (10 ml), and the mixture was hydrogenated at room temperature on a Parr apparatus at 45 psi for 20 hr. The catalyst was removed by filtration with a Celite pad and washed with methanol. The combined filtrate and washings were evaporated to dryness to give a colorless solid in a yield of 370 mg (92%).

The analytical sample was prepared by recrystallization twice from ethanol–water and dried over P_2O_5 at 110° *in vacuo* for 2 hr: mp 242–244° dec; $[\alpha]^{25}D$ −30.8° (*c* 1, DMSO); $\lambda_{max}^{pH\ 1}$ 258 nm (ϵ 14,300), $\lambda_{max}^{pH\ 11}$ 260 (14,400), λ_{max}^{MeOH} 259 (15,700).

Anal. Calcd for $C_{21}H_{23}N_7O_7$: C, 51.95; H, 4.77; N, 20.19. Found: C, 51.89; H, 4.82; N, 20.37.

Registry No.—**1**, 19234-66-3; **2a**, 32730-49-7; **2b**, 32730-50-0; **2c**, 32827-42-2; **2d**, 32730-51-1; **2e**, 32730-46-4; **2f**, 32730-47-5; **3**, 32730-45-3; **4a**, 32730-52-2; **4b**, 32730-53-3; **4c**, 32827-43-3; **4d**, 32730-54-4; **4f**, 32730-48-6; **5a**, 32730-55-5; **5b**, 32730-56-6; **5c**, 32721-40-7; **5d**, 32721-41-8; **5g**, 32721-36-1; **6**, 32721-37-2; **7**, 32721-38-3; **8**, 32721-39-4.

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