The Synthesis of 2-Chloro-1-β-D-ribofuranosyl-5,6-dimethylbenzimidazole and Certain Related Derivatives (1)

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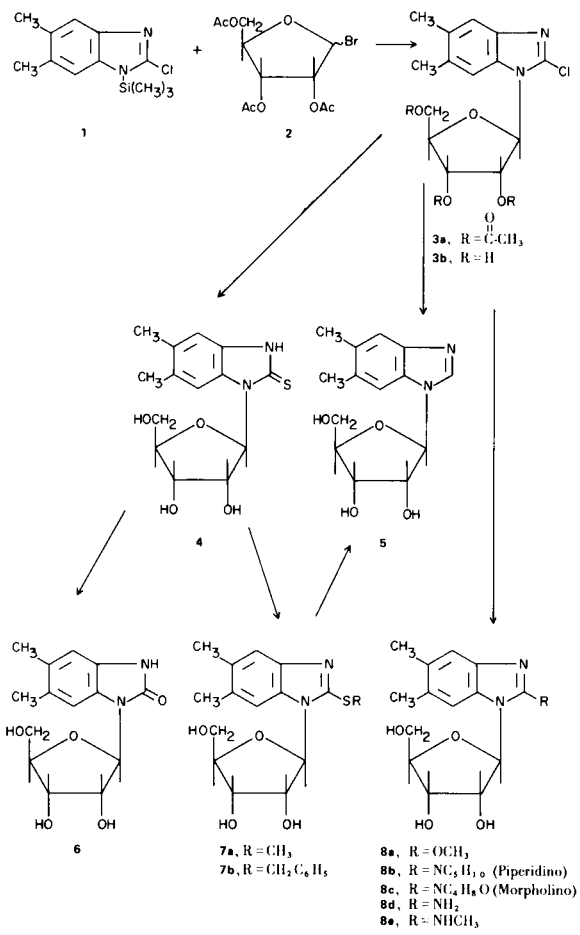
The synthesis of 2-chloro-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3b**) has been accomplished by a condensation of 1-trimethylsilyl-2-chloro-5,6-dimethylbenzimidazole (**1**) with 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide (**2**) followed by subsequent deacetylation. Nucleophilic displacement of the 2-chloro group from **3b** has furnished several interesting 2-substituted-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazoles. 1-(β-D-Ribofuranosyl)-5,6-dimethylbenzimidazole (**5**) and 1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole-2-thione (**4**) were prepared from **3b**. Alkylation of **4** furnished certain 2-alkylthio-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazoles and oxidation of **4** with alkaline hydrogen peroxide produced 1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole-2-one (**6**). The assignment of anomeric configuration for all nucleosides reported is discussed.

The isolation and characterization (2,3,4) of several benzimidazole nucleosides from vitamin B_{12} and vitamin B_{12} analogs has stimulated considerable interest in the chemical synthesis of these naturally occurring benzimidazole nucleosides and other closely related derivatives. It is of interest that all these benzimidazole nucleosides have possessed exocyclic substituents only on the benzene ring of the aglycon. A synthetic route for the preparation of 2-substitutedbenzimidazole nucleosides without any substituents on the benzene ring has been recently described (5a) from our Laboratory. However, this has furnished 2-substitutedbenzimidazole nucleosides without substituents on the benzene ring. This prompted the present investigation and we now wish to report the first successful preparation of 2-substituted-5,6-dimethylbenzimidazole nucleosides using the silylation procedure (5b).

The silylation of 2-chloro-5,6-dimethylbenzimidazole with hexamethyldisilazane under anhydrous conditions using a catalytic amount of ammonium sulfate furnished a syrup which was assumed to be the silylated derivative (**1**). Since this material (**1**) is extremely susceptible to hydrolysis (cleavage of the Si-N bond), no attempt was made at purification and **1** was always prepared immediately before utilization in the condensation reaction. The condensation of 1-trimethylsilyl-2-chloro-5,6-dimethylbenzimidazole (**1**) with 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide (**2**) in the presence of a catalytic amount of sodium iodide at 120° for 20 minutes afforded a 68.4% yield of 2-chloro-1-(2′,3′,5′-tri-*O*-acetyl-β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3a**) as a syrup. Removal of the blocking groups from the carbohydrate moiety of **3a** was accomplished with methanolic ammonia at room temperature to furnish 2-chloro-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3b**) in 70% yield. An assignment of anomeric configuration for ribofuranosides, excluding conformational changes, can be made by utilization of pmr spectroscopy (coupling constants) only for the β-anomer and then only if the coupling constant ($J_{1,2}$) for the anomeric proton is less than 3.5 cps (7-9). The pmr spectrum of **3b** in dmso-d_6 revealed a $J_{1,2}$ of 6.0 cps which definitely precluded the use of the above method for the assignment of anomeric configuration.

Removal of the 2-chloro group from 2-chloro-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3b**) was effected catalytically (10% palladium on powdered charcoal) to afford a 67.5% yield of 1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**5**). The preparation of **5** has been described (6) previously by the condensation of 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in dry dioxane solution with an excess of 5,6-dimethylbenzimidazole. The nucleoside material (**5**) prepared from **3b**, has a melting point of 191-193° and a specific rotation $[\alpha]_D^{25}$ -52.3° (C=1, pyridine); $[\alpha]_D^{25}$ -29.9° (C=1, methanol). This is very similar to the physicochemical properties reported (6) [m.p. 191-193°; $[\alpha]_D^{20}$ -51.9 (C=2.01, pyridine); $[\alpha]^{20}$ -30.2 (C=1.95, methanol)] for this nucleoside prepared by other methods. The ultraviolet



absorption spectra (Table 1) observed for **5** was found to be in accord with that reported (10) previously and the above data established the site of ribosidation and β-configuration for all nucleosides reported herein.

Displacement of the 2-chloro group of **3b** was accomplished with thiourea in ethanol at reflux temperature to furnish a 70.5% yield of 1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole-2-thione (**4**). There was observed an absorption band in the infrared spectrum (potassium bromide) at 1605 cm^{-1} which was assigned as C=S stretching and part of a -N-C=S system (11) which indicated that **4** exists in the thione rather than the thiol form. The absence of a band at 2550-2600 cm^{-1} usually attributable (12) to -SH stretching and the appearance of an absorption peak in the pmr spectrum at δ 12.8 (1 proton which was assigned to N-3 of **4**) provided additional support for the thione form. Alkylation of **4** has occurred on the exocyclic sulfur atom and furnished certain 2-alkylthio-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazoles. Treatment of **4** in aqueous ammonium hydroxide solution with methyl iodide at room temperature furnished a good yield of 2-methylthio-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**7a**). The site of methylation was initially assigned on the basis of ultraviolet absorption (hypsochromic shift) and pmr spectroscopy (based on the chemical shift between a methyl group on an exocyclic mercapto group and a ring nitrogen, value observed being δ 2.8). This initial assignment of methylation was corroborated when desulfurization of **7a** with Raney nickel in absolute ethanol furnished 1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**5**) identical in all respects with **5** prepared from **3b**. Alkylation of **4** with benzyl chloride in an aqueous ammonium hydroxide solution produced 2-benzylthio-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**7b**) in 77.5% yield. The position of alkylation was established by ultraviolet absorption and pmr spectra. Treatment of **4** with 30% hydrogen peroxide in an aqueous ammoniacal solution at room temperature effected a facile conversion of sulfur to oxygen and furnished 1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole-2-one (**6**). The infrared spectrum (potassium bromide) of **6** revealed an absorption band at 1710 cm^{-1} which is similar to the C=O absorption band observed for a 5-membered cyclic ureide.

It has been reported previously (13) that the ease of nucleophilic displacement of the 2-chloro group from 2-chlorobenzimidazoles is greatly facilitated by a substituent at *N*-1. Nucleophilic substitution has now been observed to proceed readily utilizing **3b** as starting material to produce several 2-substituted-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazoles. Treatment of **3b** with sodium methoxide in absolute methanol under anhydrous conditions at reflux temperature produced a good yield of 2-methoxy-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**8a**). Treatment of **3b** with piperidine and morpholine in absolute ethanol at reflux temperature has afforded 2-(*N*-piperidino)-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**8b**) and 2-(*N*-morpholino)-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**8c**), respectively. Treatment of **3b** with methanolic ammonia at 150° in a sealed reaction vessel has furnished a good yield of 2-amino-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**8d**). 2-Methylamino-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**8e**) was prepared in good yield from **3b** and aqueous methylamine solution (40%) at reflux temperature.

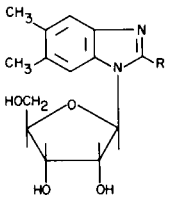
EXPERIMENTAL (14)

2-Chloro-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3b**).

A mixture of dry 2-chloro-5,6-dimethylbenzimidazole (15) (5.4 g.), freshly distilled hexamethyldisilazane (6 g.) and a few crystals of ammonium sulfate (approximately 50 mg.) was heated at reflux temperature under anhydrous conditions with stirring for 15 hours. The unreacted hexamethyldisilazane was removed under

TABLE I

Ultraviolet Absorption Spectra of Certain 2-Substituted-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazoles (a)



Compound	R	pH 1 λ Max nm	pH 1 ε	Methanol λ Max nm	Methanol ε	pH 11 λ Max nm	pH 11 ε
3b	Cl	281	9380	248	8130	248	8440
		290	8755	280	6255	280	6880
				289	6880	289	6880
5	H	277	8895	250	5840	250	5560
		285	9175	280	4170	280	4450
				287	5285	287	5000
4	SH	250	12400	224	20150	226	20150
		300	23870	254	11800	260	11160
		310	26980	313	31000	308	21700
7a	SCH_3	242	9718	254	9400	254	9400
		290	18140	261 (b)	8750	261 (b)	8750
		300	18790	290	13280	290	13600
				299	13930	299	14260
7b	$S\text{-}CH_2\text{-}C_6H_5$	301	15600	255	9200	255	7200
				261 (b)	8800	261 (b)	7200
				291 (b)	15600	291.5 (b)	12800
				299	16000	299	13200
6	OH	285	11750	255	10300	255	8820
				285	11750	286	11200
8a	OCH_3	278	7700	240	6470	240	7700
		283	7700	283	5855	283	5855
				288	5550	288	5550
8b	NC_5H_{10}	240	12640	251	10470	251	10470
		286 (b)	16960	292	10470	292	10820
		295	17700				
8c	NC_4H_8O	240	14160	250	10530	250	10890
		285	16330	292	9800	292	10160
		294	16700				
8d	NH_2	282	7840	245	7035	245	7035
				288	8790	288	7325
8e	$NHCH_3$	285	11350	250	7980	249	8290
				291	9520	291	9210

(a) Ultraviolet absorption spectra were obtained with a Beckman DK-2 Ultraviolet Spectrophotometer. (b) Shoulder.

reduced pressure to afford a syrup which solidified on cooling and was assumed to be 1-trimethylsilyl-2-chloro-5,6-dimethylbenzimidazole (**1**). This material was extremely susceptible to hydrolysis and was used in the following fusion reaction without further purification. 1-Trimethylsilyl-2-chloro-5,6-dimethylbenzimidazole (**1**, 5.05 g.) was thoroughly mixed with 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide (16) (**2**, 7.5 g.) and a catalytic amount of sodium iodide (25 mg.). The mixture was heated at 120° (oil bath temperature) for 20 minutes *in vacuo* (1.5 mm) with efficient stirring. The reaction mixture was cooled to room temperature and dissolved in chloroform (250 ml.). The insoluble solid material (0.6 g.) was removed by filtration and discarded. The filtrate was washed with cold saturated aqueous sodium bicarbonate (4 x 100 ml. portions) and then with cold water (4 x 100 ml. portions). The chloroform phase was dried over anhydrous sodium sulfate and then evaporated *in vacuo* at 35° to a brown syrup. The residual syrup was dissolved in methanol (100 ml.), charcoal added and the charcoal then removed by filtration and the filtrate evaporated to dryness under reduced pressure. The syrup (**3a**, 6 g., 68.4%) was dissolved in methanolic ammonia (methanol saturated with ammonia at 0°, 250 ml.) and this solution was then allowed to stand at room temperature for 30 hours with occasional shaking. The solution was filtered and the filtrate evaporated *in vacuo* on a steam bath to a syrup. The syrup was triturated with cold water (0°, 50 ml.) for one hour. The solid which had separated was removed by filtration, dissolved in the minimum amount of ethanol (25°) and absorbed on a column (5 cm x 20 cm) of neutral alumina (150 g, Merck). A mixture of ethanol and water (65:35, v/v) was used as eluent with 20 ml. fractions being collected to give chromatographically pure 2-chloro-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3b**, 3.0 g., 70.2%) in fractions 10-25. A small sample was recrystallized from a mixture of ethanol and water (1:1, v/v) for analysis m.p. 182°, $[\alpha]_D^{25}$ -67.90° (C=1, ethanol).

Anal. Calcd. for $C_{14}H_{17}ClN_2O_4$: C, 53.75; H, 5.44; N, 8.96; Cl, 11.36. Found: C, 53.84; H, 5.45; N, 8.77; Cl, 11.54.

1-(β-D-Ribofuranosyl)-5,6-dimethylbenzimidazole-2-thione (**4**).

To a solution of 2-chloro-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3b**, 1.0 g.) in absolute ethanol (25 ml.) was added 0.25 g. of thiourea. The mixture was heated at reflux temperature under anhydrous conditions for 2 hours and then allowed to stand at room temperature for 18 hours. A small amount of solid material was removed by filtration and the filtrate evaporated *in vacuo* over a hot water bath to a foam. The foam was triturated with cold water (10 ml.) for one hour and the solid material which had separated was collected by filtration and washed with cold water (2 x 5 ml. portions). The nucleoside crystallized from aqueous ethanol as colorless needles, 0.7 g. (70.5%). A small sample was recrystallized from water containing a small amount of ethanol for analysis, m.p. 241-242°, $[\alpha]_D^{25}$ -15.06° (C=0.5, ethanol).

Anal. Calcd. for $C_{14}H_{18}N_2O_4S$: C, 54.19; H, 5.80; N, 9.03; S, 10.32. Found: C, 53.97; H, 5.90; N, 8.97; S, 10.24.

2-Methylthio-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**7a**).

1-(β-D-Ribofuranosyl)-5,6-dimethylbenzimidazole-2-thione (**4**, 1.0 g.) was suspended in cold water (20 ml.) and concentrated aqueous ammonium hydroxide (4 ml.) was added with stirring to effect a clear solution. Methyl iodide (0.5 ml.) was then added to this solution and the stirring continued at room temperature. After 10 minutes a colorless solid began to separate from the solution. The stirring was continued for an additional 2 hours and the reaction mixture then allowed to stand at 5° for 18 hours. The crystalline material was collected by filtration, washed with cold water (5 x 10 ml. portions) and then crystallized from water to afford 0.8 g. (76.5%) of **7a**. A small sample was recrystallized once more from water for analysis m.p. 150°, $[\alpha]_D^{25}$ -45.0° (C=1, ethanol).

Anal. Calcd. for $C_{15}H_{20}N_2O_4S$: C, 55.56; H, 6.17; N, 8.64; S, 9.87. Found: C, 55.34; H, 6.01; N, 8.44; S, 9.65.

1-(β-D-Ribofuranosyl)-5,6-dimethylbenzimidazole (**5**).

Method 1.

2-Chloro-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3b**, 1.0 g.) was dissolved in a solution of water (40 ml.) and concentrated aqueous ammonium hydroxide (2 ml.) containing a few drops of ethanol. To this solution was added 10% palladium on powdered carbon (0.3 g.) and the mixture hydrogenated at 40 psi and room temperature for 5 hours. The catalyst was then removed by filtration on a celite pad and the catalyst washed with hot water (3 x 5 ml.). The combined filtrate and washings were evaporated to dryness *in vacuo* over a hot water bath and the residual material crystallized from a mixture of ethanol and water (8:2, v/v) to furnish **5** as colorless needles, 0.6 g. (67.5%). A small sample was recrystallized from the same solvent mixture for analysis m.p. 191-193°, $[\alpha]_D^{25}$ -52.3° (C=1, pyridine); $[\alpha]_D^{25}$ -29.9° (C=1, methanol).

Anal. Calcd. for $C_{14}H_{18}N_2O_4$: C, 60.43; H, 6.47; N, 10.07. Found: C, 60.42; H, 6.57; N, 10.21.

The following physicochemical constants have been reported (6) for 1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole: m.p. 190-192° and $[\alpha]_D^{20}$ -51.9° (C=2.01 pyridine), $[\alpha]_D^{20}$ -30.2° (C=1.95, methanol).

Method 2.

2-Methylthio-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**7a**, 1.0 g.) was dissolved in 25 ml. of absolute ethanol. Raney nickel (2 g.) was added to this solution and the resulting mixture heated at reflux temperature with the exclusion of moisture. After 2 hours an additional amount of Raney nickel (0.5 g.) was added and the heating continued for an additional 8 hours. The reaction mixture was cooled to room temperature and the Raney nickel removed by filtration. The catalyst was washed with hot ethanol (2 x 10 ml. portions) and the combined filtrate and washings were evaporated to dryness *in vacuo* to afford a solid. This solid material was crystallized from a mixture of ethanol and water (8:2, v/v) as needles, 0.55 g. (64%), m.p. 191-192°, $[\alpha]_D^{25}$ -52.2° (C=1, pyridine). A mixed melting point with the nucleoside prepared by Method 1 was 190-192°.

Anal. Calcd. for $C_{14}H_{18}N_2O_4$: C, 60.43; H, 6.47; N, 10.07. Found: C, 60.48; H, 6.51; N, 10.18.

2-Benzylthio-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**7b**).

1-(β-D-Ribofuranosyl)-5,6-dimethylbenzimidazole-2-thione (**4**, 1.0 g.) was dissolved in cold water (10 ml.) containing 25 ml. of concentrated ammonium hydroxide. To this solution was added benzyl chloride (1 ml.) with stirring while maintaining the reaction temperature below 25°. After 10 minutes a solid material began to separate from the reaction solution. The mixture was stirred for an additional 4 hours and then allowed to stand at 5° for 15 hours. The solid was collected by filtration, washed thoroughly with cold water and dried *in vacuo* over potassium hydroxide pellets. The dry residue was crystallized from a mixture of ethanol and ethyl acetate as needles, 1.0 g. (77.5%). A small

sample was recrystallized from the same solvent mixture for analysis, m.p. 208°, $[\alpha]_D^{25}$ -8° (C=0.5, 75% aqueous ethanol).

Anal. Calcd. for $C_{21}H_{24}N_2O_4S$: C, 63.00; H, 6.00; N, 7.00; S, 8.00. Found: C, 62.90; H, 5.96; N, 6.97; S, 8.04.

1-(β-D-Ribofuranosyl)-5,6-dimethylbenzimidazole-2-one (**6**).

1-(β-D-Ribofuranosyl)-5,6-dimethylbenzimidazole-2-thione (**4**, 1.0 g.) was dissolved in cold water (10 ml.) containing concentrated ammonium hydroxide (2.5 ml.). To this clear solution was added 30% aqueous hydrogen peroxide (1.5 ml.) slowly with stirring, while maintaining the reaction temperature below 25°. The reaction solution was stirred for 5 hours at room temperature then evaporated to dryness *in vacuo*. The resulting residue was dissolved in absolute ethanol (50 ml.) and again evaporated to dryness *in vacuo*. This process was repeated until the last traces of hydrogen peroxide had been removed. The dry residue was suspended in absolute methanol (50 ml.) and stirred for one hour. The insoluble material (40 mg.) was removed by filtration and discarded. The filtrate was evaporated to dryness *in vacuo* to afford a syrup and this syrup was then dissolved in methanol and the volume reduced to 5 ml. Acetone (10 ml.) was added and the solution allowed to stand at 5° for 18 hours. The needles which had separated were collected by filtration and dried *in vacuo* over phosphorus pentoxide, 0.45 g. (47.5%), m.p. > 210°, $[\alpha]_D^{25}$ -21° (C=1, ethanol).

Anal. Calcd. for $C_{14}H_{18}N_2O_5$: C, 57.15; H, 6.12; N, 9.52. Found: C, 57.63; H, 6.31; N, 9.67.

2-Methoxy-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**8a**).

2-Chloro-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3b**, 0.625 g.) was dissolved in 0.5 M methanolic sodium methoxide (10 ml.) and the solution heated at reflux temperature for 2.5 hours under anhydrous conditions. The reaction mixture was then allowed to stand at room temperature for 12 hours. The sodium chloride was removed by filtration and the *p*H of the filtrate adjusted to 7 with 6*N* hydrochloric acid. The solution was evaporated to dryness *in vacuo* over a hot water bath and the resulting residue dissolved in absolute ethanol and again evaporated to dryness. This process was repeated until a dry residue was obtained and this residue was then extracted with hot acetone (50 ml.). The acetone was removed *in vacuo* and the residual material was crystallized from methanol to furnish **8a** as colorless needles, 0.40 g. (65%). A small sample was recrystallized from methanol for analysis, m.p. 205°, $[\alpha]_D^{25}$ -51.1 (C=1, ethanol).

Anal. Calcd. for $C_{15}H_{20}N_2O_5$: C, 58.43; H, 6.49; N, 9.09. Found: C, 58.26; H, 6.50; N, 8.89.

2-(*N*-Piperidino)-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**8b**).

2-Chloro-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3b**, 0.6 g.) was dissolved in absolute ethanol (10 ml.) containing 0.4 g. of piperidine. The solution was heated at reflux temperature for 15 hours under anhydrous conditions and then allowed to stand at 5° for 12 hours. The solid material that had separated from solution was collected by filtration, washed with cold water (5 x 5 ml.) and crystallized from ethanol as colorless needles, 0.45 g. (65%). A small sample was recrystallized from ethanol for analysis, m.p. 233°, $[\alpha]_D^{25}$ -11.8° (C=1, ethanol).

Anal. Calcd. for $C_{19}H_{27}N_3O_4$: C, 63.16; H, 7.48; N, 11.63. Found: C, 62.98; H, 7.47; N, 11.63.

2-(*N*-Morpholino)-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**8c**).

2-Chloro-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3b**, 0.6 g.) was dissolved in absolute ethanol (10 ml.) containing 0.4 g. of freshly distilled morpholine. The solution was heated at reflux temperature for 35 hours under anhydrous conditions and then allowed to stand at room temperature for 15 hours. The reaction mixture was evaporated to dryness *in vacuo* over a hot water bath and the residual syrup dissolved in absolute ethanol (25 ml.). The evaporation procedure was repeated until the last traces of morpholine had been removed. The solid residue was collected, washed with 5% aqueous ethanol (2 x 5 ml.) and crystallized from ethanol for analysis, m.p. 243-244°, $[\alpha]_D^{25}$ -22.5° (C=1, ethanol).

Anal. Calcd. for $C_{18}H_{25}N_3O_5$: C, 59.51; H, 6.88; N, 11.57. Found: C, 59.33; H, 6.75; N, 11.31.

2-Amino-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**8d**).

2-Chloro-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3b**, 1.50 g.) was dissolved in methanolic ammonia (methanol saturated with ammonia at 0°, 150 ml.) and the solution then heated in a steel reaction vessel at 150° for 10 hours. A small amount of solid material was removed by filtration and discarded. The filtrate was evaporated *in vacuo* to a syrup and this syrup triturated with methanol (20 ml.) for one hour. The solid was collected by filtration and crystallized from methanol as pale yellow needles, 0.70 g. (49.8%). A small sample was recrystallized from methanol for analysis, m.p. 135°, $[\alpha]_D^{25}$ -3.6° (C=0.5, ethanol).

Anal. Calcd. for $C_{14}H_{19}N_3O_4$: C, 57.33; H, 6.49; N, 14.34. Found: C, 57.68; H, 6.53; N, 14.51.

2-Methylamino-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**8e**).

2-Chloro-1-(β-D-ribofuranosyl)-5,6-dimethylbenzimidazole (**3b**, 0.6 g.) was dissolved in 40% aqueous methylamine (20 ml.) and this solution heated at reflux temperature for 2 hours. The reaction mixture was allowed to stand at 5° for 18 hours and the colorless solid material that had separated was collected by filtration. The solid material was washed with ice cold water (5 x 5 ml.) and crystallized as needles from water containing a few drops of ethanol 0.40 g. (68%). A small sample was recrystallized from a water-ethanol mixture for analysis m.p. 254-255°, $[\alpha]_D^{25}$ -2.2° (C=1, ethanol).

Anal. Calcd. for $C_{15}H_{21}N_3O_4$: C, 58.64; H, 6.84; N, 13.68. Found: C, 58.42; H, 7.07; N, 13.25.

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(14) All nucleosides prepared in the present study were found to be chromatographically homogeneous in three solvent systems. PMR spectra were obtained on a Varian A-60 instrument using tetramethylsilane as an internal standard and the infrared spectra were obtained with a Beckman IR-5A spectrometer. Melting points were observed on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Optical rotations were obtained with a Perkin-Elmer Model 141 automatic digital readout polarimeter. Elemental analyses were performed by M-H-W Laboratories, Garden City, Michigan and Heterocyclic Chemical Corp., Harrisonville, Missouri.

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