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Studies on the Oxidation of "Reversed Nucleosides" in Oxygen. III.[1] Synthesis of Eritadenine Analogues of Purines and Pyrimidines[2]

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Reaction of methyl 5-O-tosyl-2,3-O-isopropylidene-β-D-ribofuranoside (**1**) with the sodium salts of purines, (**2**) and (**3**), and pyrimidines, (**12**), (**13**), and (**14**) derivatives in DMF afforded the corresponding "reversed nucleosides." 6-Alkylaminopurine analogues were prepared by the reaction of the 6-methylthiopurine derivative (**4**) with the amines. After removal of the protective groups, the reversed nucleosides were oxidized by oxygen in dilute alkaline solution to afford easily eritadenine analogues as major products.

The novel synthesis of eritadenine (**40**, R=NH_2, R_1=H), a hypocholesterolemic alkaloidal substance from *Lentinus edodes* Sing.,[4] by the oxidation of reversed nucleosides, 5-(6-aminopurin-9H-9-yl)-5-deoxy-D-ribofuranose and -arabofuranose, in oxygen has been previously reported.[1,5] It was hoped that extension of this useful reaction to some other reversed nucleosides would provide the corresponding eritadenine analogues with interesting pharmacological activity. In this paper we wish to report the synthesis of some reversed nucleosides of purine and pyrimidine derivatives and the oxidation of them in oxygen affording eritadenine analogues.

Reaction of methyl 5-O-tosyl-2,3-O-isopropylidene-β-D-ribofuranoside (**1**)[6] with the sodium salt of 6-methylthiopurine (**2**)[7] in dimethyl formamide (DMF) gave three isomeric reversed nucleosides, which were separated by column chromatography. The N(9)-substituted compound (**4**), one of them, was obtained in 83.5% yield as a major product. The structures of another two minor products were determined to be the N(7)-substituted (**5**) and the N(3)-substituted (**6**) compounds by means of ultraviolet (UV) spectral data.[8] However, the N(1)-substituted compound could not be detected in the reaction mixture. On the other hand, reaction of **1** with the sodium salt of purine (**3**)[9] under similar conditions gave a mixture of the N(9)-isomer (**7**) and the N(7)-isomer (**8**). Both isomers were purified by chromatographic separation with silica gel in 58% and 28% yield, respectively. These structures were confirmed by means of UV spectral data,[10] and also by the fact that the desulfurization[9] of **4** and **5** with Raney-Ni gave **7** and **8**, respectively. None of the other position isomers could be detected in the reaction mixture.

1) Part II: N. Takamura, N. Taga, T. Kanno, and M. Kawazu, *J. Org. Chem.*, **38**, 2891 (1973).
2) Presented at the 91th Annual Meeting of Pharmaceutical Society of Japan, Fukuoka, April 1971.
3) Location: *2-2-50, Kawagishi, Toda, Saitama.*
4) *a*) I. Chibata, K. Okumura, S. Takeyama, and K. Kotera, *Experientia*, **25**, 1237 (1969); *b*) T. Kamiya, Y. Saito, M. Hashimoto, and H. Seki, *Tetrahedron Letters*, **1969**, 4729; *c*) *Idem*, *Tetrahedron*, **28**, 899 (1972).
5) M. Kawazu, T. Kanno, S. Yamamura, T. Mizoguchi, and S. Saito, *J. Org, Chem.*, **38**, 2887 (1973).
6) N.J. Leonard and K.L. Carraway, *J. Heterocyclic Chem.*, **3**, 485 (1966).
7) G.B. Elion, E. Bugi, and G.H. Hithings, *J. Am. Chem. Soc.*, **74**, 411 (1952).
8) *a*) F. Bergman, G. Levin, A. Kalmus, and H. Kwietny-Govrin, *J. Org. Chem.*, **26**, 1504 (1961); *b*) D.J. Brown and P.W. Ford, *J. Chem. Soc.* (*C*), **1969**, 2620; *c*) I. Okumura, T. Oine, Y. Yamada, M. Tomie, T. Adachi, T. Nagura, M. Kawazu, T. Mizoguchi, and I. Inoue, *J. Org. Chem.*, **36**, 1573 (1971), and references therein.
9) A.G. Beaman, *J. Am. Chem. Soc.*, **76**, 5633 (1954).
10) *a*) A. Bendich, P.J. Russell Jr. and J.J. Fox, *J. Am. Chem. Soc.*, **76**, 6073 (1954); *b*) L.B. Townsend and R.K. Robins, *J. Heterocyclic Chem.*, **3**, 241 (1966).

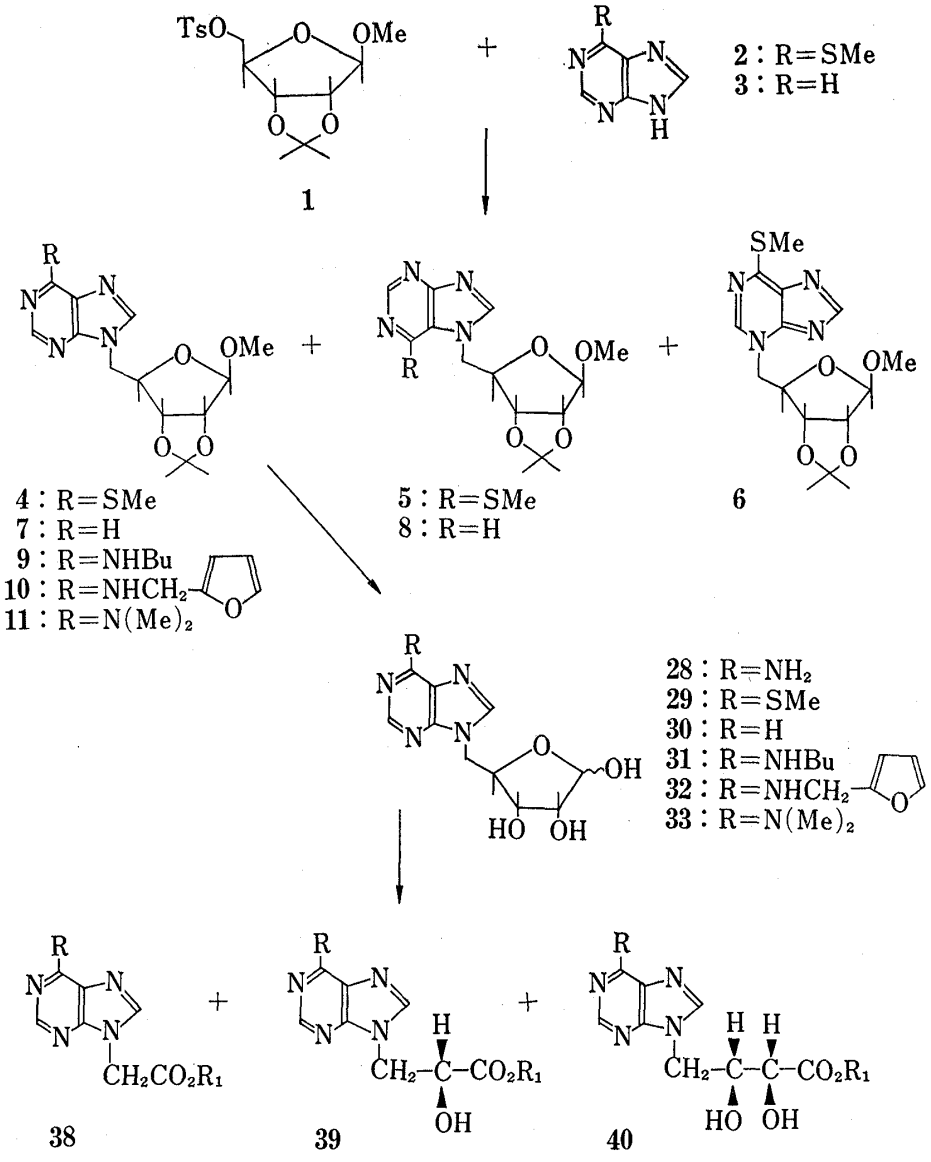


Chart 1

In order to prepare several 6-alkylamino derivatives of purine reversed nucleosides, the reaction of **4** with suitable alkylamines employing the method of Elion, *et al.*[7] was carried out. The mother compound **4** was heated in a sealed-tube with *n*-butylamine, furfurylamine[11] and 40% aqueous dimethylamine to give the corresponding 6-butylamino (**9**), -furfurylamino (**10**) and -dimethylamino (**11**) derivatives (Table I). The compounds **9** and **11** were obtained in good yield, but the yield of **10** decreased on account of the instability of furfurylamine under the reaction conditions.

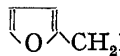
Reaction of **1** with the sodium salts of uracil (**12**), thymine (**13**) and cytosine (**14**) in a similar manner to that described above gave mixtures of several products, respectively, which were separated by chromatography on silica gel. The structures of these products were confirmed by comparing these UV spectra with those of suitable model compounds in the literature.[12] The alkylation of these pyrimidines gave mainly the N(1)-monosubstituted

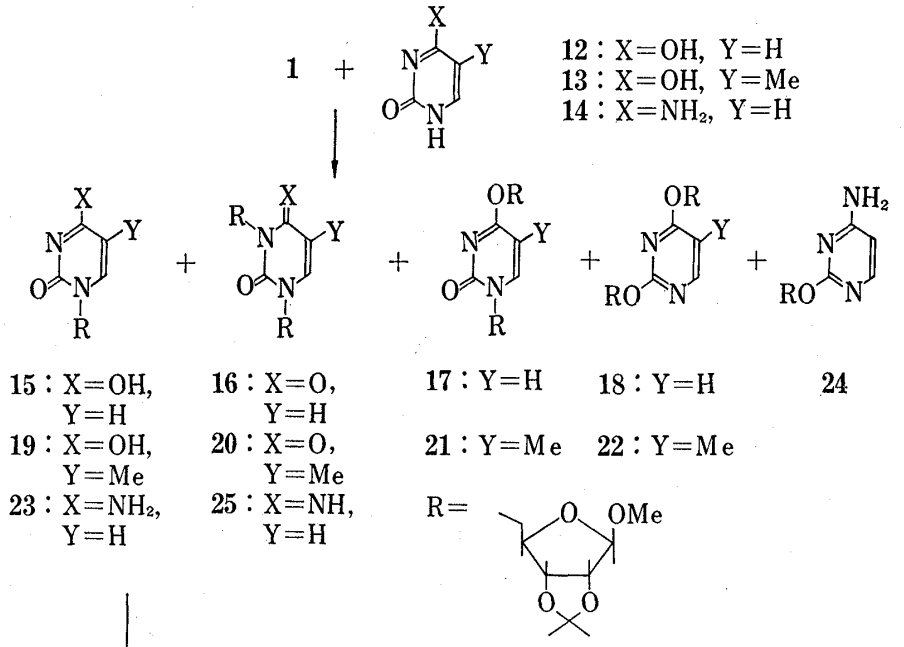
11) Furfurylamine was prepared in 51% yield by the reduction of α-furfuraldoxime with lithium aluminum hydride in anhydrous THF.

12) *a*) D. Shugar and J.J. Fox, *Biochem. Biophys. Acta*, **9**, 199 (1952); *b*) E. Wittenburg, *Chem. Ber.*, **99**, 2391 (1966); *c*) D.F. Brown and J.M. Lyall, *Australian J. Chem.*, **15**, 851 (1962); *d*) G.W. Kenner, C.B. Reese, and Sir A.R. Todd, *J. Chem. Soc.*, **1955**, 855; *e*) J.L. Wong and D.S. Fuchs, *J. Org. Chem.*, **35**, 3736 (1970).

compounds, (**15**),[13] (**19**) and (**23**), accompanied with small amounts of some disubstituted compounds (Table II). However, the N(3)-monosubstituted compounds were not detected in these reaction mixtures. In the reaction of **12** or **13**, three disubstituted compounds, the

Table I. Reaction of 4 with Amines

Amines	Solvent	Reaction		Product	Yield (%)
		Temp.(°C)	Time(hr)		
$BuNH_2$	BuOH	200	60	**9**	99
	BuOH	200	64	**10**	55
40%aq.$NHMe_2$	EtOH	170	30	**11**	98



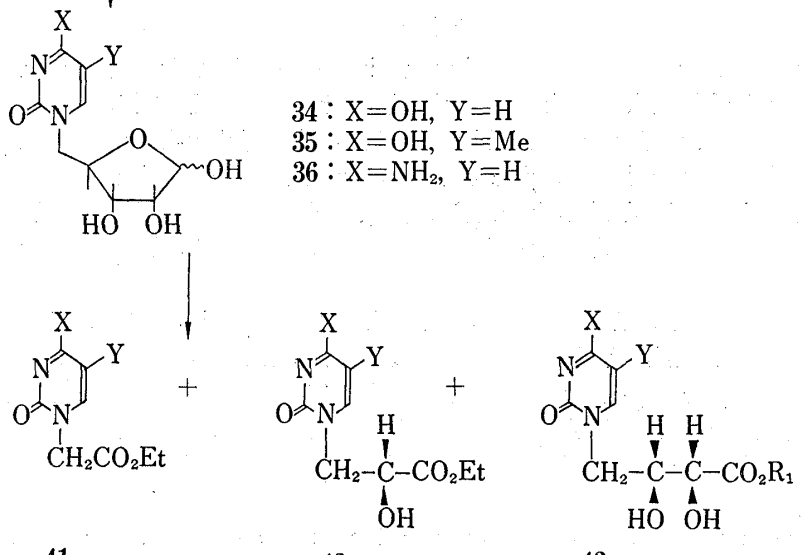


Chart 2

13) S. Fukatsu, Y. Takeda, and S. Umezawa, *Bull. Chem. Soc. Japan*, **46**, 3165 (1973).

Table II. Product Composition in the Reaction of **1** with the Sodium Salts of Pyrimidines

Pyrimidines	Yield of product isomers (%)				
	N(1)	O(2)	N(1)N(3)	N(1)O(4)	O(2)O(4)
12	43	—	10	2	2.9
13	47	—	19	0.5	1.9
14	43	23	2.5	—	—

N(1)N(3)-, the N(1) O(4)- and the O(2)O(4)-disubstituted pyrimidines, were obtained, respectively. In the reaction of **14**, however, one disubstituted compound which was found to be the N(1)N(3)-disubstituted derivative (**25**) was obtained in a low yield, and also the O(2)-monosubstituted compound (**24**) was isolated in 23% yield.

Reaction of **1** with the sodium salt of benzimidazole (**26**) in a similar manner to that described above afforded the N(1)-substituted derivative (**27**) in a good yield.

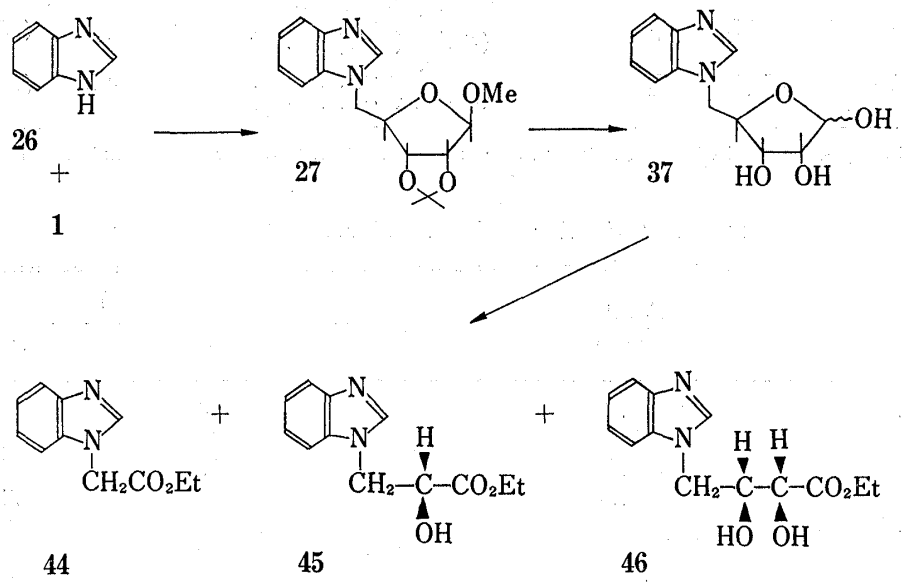


Chart 3

Hydrolysis to remove the protective groups of these masked reversed nucleosides with dilute hydrochloric acid was satisfactorily carried out to give **29**, **30**, **31**, **32**, **33**, **34**, **35**, **36** and **37**, respectively. These results are listed in Table III.

The oxidation of these reversed nucleosides in dilute alkaline solution under an oxygen atmosphere was carried out employing previously reported conditions (see Experimental Section). After oxidation, the eritadenine analogue crystallized was collected by filtration. Esterification of the residue obtained from the filtrate followed by chromatography on silica gel gave three products, (A), (B) and (C). These results and the comparative data[5] obtained previously for **28** are summarized in Table IV.

In the case of the 6-methylthiopurine derivative (**29**), however, six products were obtained. Three of them were 6-methylthiopurine derivatives, (**38**, R=SMe, R_1=Et), (**39**, R=SMe, R_1=Et) and (**40**, R=SMe, R_1=Et). Another three products were hypoxanthine derivatives,[14] (**38**, R=OH, R_1=Et), (**39**, R=OH, R_1=Et) and (**40**, R=OH, R_1=Et). The physical data

14) It is known[15] that a 6-methylthiopurine derivative is hydrolyzed under alkaline conditions to give a hypoxanthine derivative.

15) J.W. Jones and R.K. Robins, *J. Am. Chem. Soc.*, **84**, 1914 (1962).

Table III. Properties and Elemental Analyses of Reversed Nucleosides

Compound	mp(°C)[a]	Formula	Analysis (%) Found (Calcd.) C	H	N	Yield (%)	$[\alpha]_D$ (temp., c)
29	174—175	$C_{11}H_{14}O_4N_4S$[b]	44.40 (44.30)	4.68 (4.73)	18.73 (18.79)	80	+29° (24, 0.5)[c]
30	146—148	$C_{10}H_{12}O_4N_4$	47.76 (47.62)	4.80 (4.80)	22.10 (22.22)	95	+41.6° (24, 0.5)[d]
31	142—143	$C_{14}H_{21}O_4N_5$	51.77 (52.00)	6.41 (6.55)	21.38 (21.66)	64	+28° (26, 0.5)[c]
32	149—153	$C_{15}H_{17}O_5N_5 \cdot 1/4H_2O$	51.17 (51.13)	5.06 (5.01)	19.63 (19.89)	56	+89.4° (26, 0.28)[d]
33	155—157	$C_{12}H_{17}O_4N_5 \cdot 1/4H_2O$	48.08 (48.03)	5.85 (5.88)	23.24 (23.38)	68	+32° (26, 0.3)[c]
34	175—178	$C_9H_{12}O_6N_2$	44.35 (44.26)	5.03 (4.95)	11.35 (11.47)	87	+47.4° (22, 0.5)[c]
35	108—110	$C_{10}H_{14}O_6N_2 \cdot 1/4H_2O$	45.66 (45.67)	5.86 (5.56)	10.40 (10.66)	58	+75° (25, 0.6)[d]
36	173—175	$C_9H_{13}O_5N_3 \cdot 1/5H_2O$	43.89 (43.79)	5.50 (5.47)	17.28 (17.03)	64	+58° (25, 1.0)[c]
37	152—153	$C_{12}H_{14}O_4N_2$	57.29 (57.59)	5.58 (5.64)	11.17 (11.20)	91	+56° (24, 0.5)[d]

a) decomposition *b*) elemental analysis of S; Found: 10.59%, Calcd.: 10.73% *c*) in H_2O *d*) in EtOH

Table IV. Oxidation of Reversed Nucleosides by Oxygen

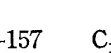
Starting material	Total yield (%)	Product ratio (%) A[a]	B[b]	C[c]
28[d]	87.8	4	4	92
29	51.9[e]	6	16	78
	41.7[f]	5	15	80
	10.2[g]	9	20	71
30	34.8	12	25	63
31	51.5	15	16	69
32	42.8	10	16	74
33	42.4	13	18	69
34	69.8	10	11	79
35	66.4	13	21	66
36	49.4	5	20	75
37	37.1	25	34	41

a) acetic acid derivative
b) α-hydroxypropionic acid derivative
c) eritadenine analogue
d) this had been reported in ref 2).
e) total data of *f*) and *g*)
f) product of 6-methylthiopurin-9H-9-yl derivative
g) product of hypoxanthin-9H-9-yl derivative

and elemental analyses compatible with the structures of them are given in the Experimental Section.

In the case of the oxidation of purine derivative (**30**), the solution turned red-brown. A similar phenomenon was also observed in the case of benzimidazole derivative (**37**). The imidazole ring in these compounds may be considered to decompose under these conditions. As the result, the oxidation of **30** and **37** did not proceed so well as that of another reversed nucleosides. In particular, in the case of **37** the product ratios of ethyl acetate derivative (**44**) and ethyl α-hydroxypropionate derivative (**45**) increased and that of eritadenine analogue (**46**) significantly decreased.

Table V. Properties and Elemental Analyses of Eritadenine Analogues

Compound	mp (°C)	Formula	Analysis (%) Found (Calcd.) C	H	N	Yield[a] (%)	$[\alpha]_D$ (temp., c)
40: R=SMe, R_1=Et	syrup	$C_{12}H_{16}O_4N_4S$				33.4	+25° (27, 1.0)[b]
40: R=OH, R_1=Et	216—218[c]	$C_{11}H_{14}O_5N_4$	46.66 (46.81)	4.99 (5.00)	19.86 (19.85)	7.2	+28° (27, 1.0)[b]
40: R=H, R_1=Et	136—137	$C_{11}H_{14}O_4N_4$	49.69 (49.62)	5.35 (5.30)	21.05 (21.04)	22.0	+45° (24, 1.0)[d]
40: R=BuNH, R_1=H	190—191[c]	$C_{13}H_{19}O_4N_5\cdot H_2O$	47.35 (47.66)	6.16 (6.46)	21.10 (21.38)	14.0	+30° (25, 1.0)[e]
40: R=BuNH, R_1=iso-Bu	156—157	$C_{17}H_{27}O_4N_5$	55.77 (55.87)	7.43 (7.45)	19.41 (19.17)	21.5	+19° (25, 0.5)[d]
40: R=  , R_1=Et	156—157	$C_{16}H_{19}O_5N_5$	52.98 (53.18)	4.99 (5.30)	19.23 (19.38)	31.8	+14.5° (25, 1.0)[b]
40: R=NMe_2, R_1=H	196—199[c]	$C_{11}H_{15}O_4N_5\cdot 1/4H_2O$	46.50 (46.19)	5.50 (5.47)	24.25 (24.49)	16.6	+27.5° (26, 0.4)[b]
40: R=NMe_2, R=iso-Bu	syrup	$C_{15}H_{23}O_4N_5$				12.5	
43: X=OH, Y=R_1=H	225—226[c]	$C_8H_{10}O_6N_2$	41.65 (41.74)	4.51 (4.38)	12.31 (12.17)	47.0	+51.4° (24, 0.35)[e]
43: X=OH, Y=H, R_1=Et	82— 83	$C_{10}H_{14}O_6N_2$	46.27 (46.51)	5.51 (5.47)	10.87 (10.85)	8.0	+49° (24, 0.5)[d]
43: X=OH, Y=Me, R_1=Et	166—168	$C_{11}H_{16}O_6N_2\cdot 1/4H_2O$	47.87 (47.74)	6.07 (6.01)	10.25 (10.12)	44.1	+49° (27, 1.0)[b]
43: X=NH_2, Y=H, R_1=Et	201—203[c]	$C_{10}H_{15}O_5N_3\cdot 1/2H_2O$	44.81 (45.11)	5.87 (6.06)	15.72 (15.78)	37.0	+75° (28, 1.0)[f]
46	158—160	$C_{13}H_{16}O_4N_2$	58.84 (59.08)	6.02 (6.10)	10.63 (10.60)	15.2	+40° (20, 1.0)[d]

a) Calcd. on the basis of reversed nucleoside *b*) in MeOH *c*) decomposition *d*) in EtOH *e*) in H_2O *f*) in DMSO

The oxidation of 6-alkylaminopurine derivatives, **31**, **32** and **33**, gave three products in the almost same ratio, respectively. And the main products were eritadenine analogues, (**40**, R=BuNH, R_1=H and isoBu), (**40**, R=furfurylamino, R_1=Et) and (**40**, R=NMe_2, R_1=H and isoBu), respectively.

The pyrimidine derivatives, **34**, **35** and **36**, were oxidized under similar conditions to afford also the three products, eritadenine analogues, (**43**, X=OH, Y=H, R_1=H),[16] (**43**, X=OH, Y=Me, R_1=Et) and (**43**, X=NH_2, Y=H, R_1=Et), as the main products.

Thus the reversed nucleosides were easily oxidized in dilute alkaline solution under an oxygen atmosphere to afford eritadenine analogues (C) (Table V). However, in comparison with the reaction of 6-aminopurine derivative (**28**) previously reported,[5] the total yield was rather low and the ratios of the minor products (A, B) increased slightly in these cases (see Table IV).

Further works on the mechanism of the oxidation are in progress.

Experimental

Melting points were taken on a Yanagimoto capillary melting point apparatus Model MP-1 and are uncorrected. IR spectra were recorded on a Hitachi IR-E or IR-215 spectrophotometer. UV spectra were measured on a Hitachi 323 spectrophotometer. NMR spectra were taken at 60 MHz with tetramethylsilane

16) T. Kamiya, Y. Saito, M. Hashimoto, and H. Seki, *J. Heterocyclic Chem.*, **9**, 359 (1972).

as an internal standard unless otherwise indicated using a Model JEOL ME-60 spectrometer. Mass spectra were measured using Hitachi RMS-4 mass spectrometer. Optical rotations were measured with a Yanagimoto polarimeter Model OR-20. Organic extracts were dried over anhyd. Na_2SO_4. All evaporations were performed on rotary evaporators *in vacuo*.

General Procedure for the Reaction of the Sodium Salts of the Pyrimidine or Purine Derivatives with Methyl 5-O-TOsyl-2,3-O-isopropylidene-β-D-ribofuranoside (1)——The sodium salts of purine or pyrimidine derivatives were prepared by stirring a suspension of an equimolar amount of the purine or pyrimidine derivatives and sodium hydride (in mineral oil) in DMF (3—5 ml/mmole of the purines or pyrimidines) at room temperature for 1 hr and warming at 50—60° for 1 hr. After cooling, a solution of **1** (0.9—1.0 mole equivalent) in DMF (4—5 ml/mmole) was added dropwise. The mixture was stirred and warmed at 100° for 10 hr. The DMF was evaporated at 80—90°. The resulting residue was treated in the appropriate manner for the respective reaction.

Reaction of the Sodium Salt of 6-Methylthiopurine (2)——A mixture of the sodium salt of **2** (2.65 g), **1** (5.5 g) and DMF (110 ml) was allowed to react and treated in the manner described in the general procedure. H_2O (70 ml) was added to this resulting residue. The solution was extracted with $CHCl_3$. The $CHCl_3$ extracts were washed with H_2O, dried and evaporated to give 5.7 g of a crude mixture. This mixture was purified by chromatography on Al_2O_3 (grade II—III, 250 g). The first part of elution with 50% benzene-$CHCl_3$ gave 4.5 g (83.5%) of methyl 5-(6-methylthiopurin-9H-9-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (**4**). Recrystallization from isopropyl ether afforded an analytical sample of **4** as colorless prisms: mp 84—85° $[\alpha]_D^{24}$ +10° (c=0.5, $CHCl_3$). IR λ_{max}^{Nujol} cm^{-1}: 1569. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 8.70 (1H, s), 8.00 (1H, s), 5.01 (1H, s, C_1-H), 4.72 (2H, s, C_5-2H), 4.80—4.20 (3H, m), 3.40 (3H, s, OCH_3), 2.74 (3H, s, SCH_3), 1.44 (3H, s), 1.28 (3H, s). *Anal.* Calcd. for $C_{15}H_{20}O_4N_4S$: C, 51.13; H, 5.72; N, 15.90. Found: C, 51.43; H, 5.72; H, 15.84. The second part of elution with 50% benzene–$CHCl_3$ gave 0.16 g (3%) of methyl 5-(6-methylthiopurin-3H-3-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (**6**). Recrystallization from AcOEt-isopropyl ether gave colorless crystalline powder: mp 92—95°. $[\alpha]_D^{20}$ +59° (c=1.0, $CHCl_3$). IR λ_{max}^{Nujol} cm^{-1}: 1595, 1555. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 8.45 (1H, s), 8.39 (1H, s), 5.06 (1H, s, C_1-H), 5.0—4.6 (5H, m), 3.47 (3H, s, OMe), 2.81 (3H, s, SMe), 1.44 (3H, s), 1.32 (3H, s). *Anal.* Calcd. for $C_{15}H_{20}O_4N_4S \cdot 1/3H_2O$: C, 50.27; H, 5.81; N, 15.63. Found: C, 50.24; H, 5.78; N, 15.41. The last part of elution with benzene–$CHCl_3$ (1:1) and with $CHCl_3$ gave 0.6 g (9.3%) of methyl 5-(6-methylthiopurin-7H-7-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (**5**). Two recrystallizations from benzene afforded an analytical sample of **5** as colorless needles: mp 167—168°. $[\alpha]_D^{24}$ +66° (c=0.5, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1567, 1539. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 8.90 (1H, s), 8.15 (1H, s), 5.07 (1H, s, C_1-H), 4.77 (2H, s, C_5-2H), 4.90—4.50 (3H, m), 3.48 (3H, s, OMe), 2.79 (3H, s, SMe), 1.47 (3H, s), 1.33 (3H, s). *Anal.* Calcd. for $C_{15}H_{20}O_4N_4S$: C, 51.13; H, 5.72; N, 15.90. Found: C, 51.35; H, 5.71; N, 16.04.

Reaction of the Sodium Salt of Purine (3)——A mixture of the sodium salt of **3** (5.0 g), **1** (14.9 g) and DMF (300 ml) was allowed to react and treated in the manner described in the general procedure. The resulting residue was dissolved in H_2O (100 ml). The solution was extracted with $CHCl_3$. The $CHCl_3$ extracts were washed with H_2O, dried and evaporated to give 11 g of a mixture of two products. This was chromatographed on Al_2O_3 (grade II—III, 300 g). Elution with 50% benzene–AcOEt gave 6.85 g (58%) of methyl 5-(purin-9H-9-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (**7**). Recrystallization from isopropyl ether afforded an analytical sample of **7** as colorless needles: mp 72—72.5°. $[\alpha]_D^{20}$ −12° (c=0.5, EtOH). IR ν_{max}^{Nujol} cm^{-1}: 1592, 1574, 1502. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 9.18 (1H, s), 9.02 (1H, s), 8.22 (1H, s), 5.06 (1H, s, C_1-H), 4.9—4.2 (5H, m), 3.42 (3H, s, OMe), 1.45 (3H, s), 1.31 (3H, s). *Anal.* Calcd. for $C_{14}H_{18}O_4N_4$: C, 54.89; H, 5.92; N, 18.29. Found: C, 55.14; H, 5.84; N, 18.59. Elution with 2% MeOH–$CHCl_3$ gave 3.34 g (28%) of methyl 5-(purin-7H-7-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (**8**). Recrystallization from benzene–isopropyl ether afforded an analytical sample of **8** as colorless needles: mp 118—119°. $[\alpha]_D^{20}$ 0° (c=0.37, EtOH). IR ν_{max}^{Nujol} cm^{-1}: 1602, 1557. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 9.23 (1H, s), 9.12 (1H, s), 8.42 (1H, s), 5.10 (1H, s, C_1-H), 4.78 (2H, s, C_5-2H), 4.75—4.35 (3H, m), 3.45 (3H, s, OMe), 1.48 (3H, s), 1.34 (3H, s). *Anal.* Calcd. for $C_{14}H_{18}O_4N_4$: C, 54.89; H, 5.92; N, 18.29. Found: C, 55.15; H, 5.84; N, 18.35.

Reaction of the Sodium Salt of Uracil (12)——A mixture of the sodium salt of **12** (5.0 g), **1** (14.5 g) and DMF (300 ml) was allowed to react and treated in the manner described in the general procedure. To the resulting solid was added H_2O (80 ml), and insoluble crystals were filtered and washed with ether. The crystals were purified by fractional crystallizations from MeOH to afford 3.19 g (mp 175—178°) of methyl 5-(uracil-1H-1-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (**15**).[13] The H_2O solution was extracted with ether and then $CHCl_3$. The both extracts were washed with H_2O and dried. The $CHCl_3$ extracts were evaporated and crystallized from benzene–AcOEt to give 1.28 g of **15**. The total yield of **15** was 5.19 g (43%). Recrystallization from MeOH afforded an analytical sample of **15** as colorless prisms: mp 179—180°. $[\alpha]_D^{22}$ +31° (c=0.5, MeOH). IR ν_{max}^{Nujol} cm^{-1}: 1730 (sh.) 1695. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 9.87 (1H, broad s, >N–H), 7.28 (1H, d, J=8 Hz), 5.72 (1H, d, J=8 Hz), 5.00 (1H, s, C_1-H), 4.68 (2H, s), 4.60—3.80 (3H, m), 3.41 (3H, s, OMe), 1.47 (3H, s), 1.33 (3H, s). *Anal.* Calcd. for $C_{13}H_{18}O_6N_2$: C, 52.34; H, 6.80. N, 9.39. Found: C, 52.47; H, 6.05; N, 9.43. The ether extracts were eva-

Table VI. UV Absorption Properties

Compound	Solvent	λ_{max} ($\varepsilon \times 10^{-3}$) mμ	$\lambda_{max}^{a)}$ ($\varepsilon \times 10^{-3}$) mμ	$\lambda_{max}^{b)}$ ($\varepsilon \times 10^{-3}$) mμ
4	EtOH	283 (26.1)	284 (25.6)	283 (25.5)
		291 (25.6)	291 (25.3)	291 (24.2)
5	EtOH	291.5(14.2)	291.5(14.6)	291.5(13.8)
		299 (12.2)	299 (13.8)sh[c)]	299 (11.7)sh
6	EtOH	239.5(13.0)	239 (21.8)	240 (11.9)
			280 (20.7)	
		316 (17.4)	319.5(29.6)	316 (16.6)
7	EtOH	264 (8.1)	264 (7.4)	264 (7.5)
8	EtOH	267 (7.5)	265 (7.1)	267 (7.3)
9	EtOH	269 (17.2)	265 (18.8)	269 (17.0)
11	EtOH	276 (26.5)	270 (26.1)	276 (26.3)
15	EtOH	265 (11.0)	265 (11.0)	263 (7.6)
17	EtOH	280 (6.8)	280 (6.7)	279 (6.6)
18	EtOH	259 (6.9)	259 (7.5)	259 (6.7)
19	EtOH	270 (10.2)	270 (10.0)	268.5(7.2)
23	MeOH	274 (8.9)	285.5(14.3)	275 (8.7)
25	MeOH	221 (10.3)		223 (10.5)
		278 (8.8)	287 (11.4)	274 (8.1)
27	EtOH	248 (7.5)	245 (5.4)sh	249 (7.2)
		253 (7.4)	254 (5.5)	254 (7.2)
		266 (4.3)	262 (5.9)	266 (4.2)
		274.5(4.9)	269 (7.5)	275 (4.5)
		282 (5.1)	275.5(7.0)	282 (5.0)

a) 1N HCl–EtOH (or MeOH)=1: 99 *b*) 1N NaOH–EtOH (or MeOH)=1: 99 *c*) shoulder

porated to give 4.5 g of crude mixture. This mixture was chromatographed on Al_2O_3 (grade II—III, 200 g). Elution with benzene gave 564 mg (2.9%) of O(2)O(4)-bis(methyl 2,3-O-isopropylidene-5-deoxy-β-D-ribofuranos-5-yl)-uracil (**18**). Recrystallization from isopropyl ether afford an analytical sample of **18** as colorless prisms: mp 107—108°. IR ν_{max}^{Nujol} cm^{-1}: 1580. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 8.24 (1H, d, J=6.0 Hz), 6.45 (1H, d, J=6.0 Hz), 5.00 (2H, s), 4.95—4.20 (10H, m), 3.35 (6H, s, 2×OMe), 1.48 (6H, s), 1.34 (6H, s). *Anal.* Calcd. for $C_{22}H_{32}O_{10}N_2$: C, 54.54; H, 6.66; N, 5.78. Found: C, 54.44; H, 6.76; N, 5.81. Elution with AcOEt–benzene (1: 9) afforded 2.03 g (10%) of N(1)N(3)-bis(methyl 2,3-O-isopropylidene-5-deoxy-β-D-ribofuranos-5-yl)-uracil (**16**) as colorless viscous syrup. IR ν_{max}^{Liquid} cm^{-1}: 1695, 1650. UV λ_{max}^{EtOH} mμ: 266. NMR ($CDCl_3$) δ: 7.22 (1H, d, J=8.0 Hz), 5.75 (1H, d, J=8.0 Hz), 4.96 (2H, s), 4.90—3.90 (10H, m), 3.39 (3H, s, OMe), 3.36 (3H, s, OMe), 1.44 (6H, s), 1.30 (6H, s). Elution with AcOEt–benzene (1: 1) gave 385 mg (2%) of N(1)O(4)-bis(methyl 2,3-O-isopropylidene-5-deoxy-β-D-ribofuranos-5-yl)-uracil (**17**). Two recrystallizations from benzene afforded an analytical sample of **17** as colorless prisms: mp 168—169°. IR ν_{max}^{Nujol} cm^{-1}: 1645, 1625, 1530. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 7.49 (1H, d, J=8.0 Hz), 5.90 (1H, d, J=8.0 Hz), 4.96 (2H, s), 4.85—4.15 (10H, m), 3.39 (3H, s, OMe), 3.30 (3H, s, OMe), 1.46 (3H, s), 1.43 (3H, s), 1.25 (6H, s). *Anal.* Calcd. for $C_{22}H_{32}O_{10}N_2$: C, 54.54; H, 6.66; N, 5.78. Found: C, 54.56; H, 6.60; N, 6.04.

Reaction of the Sodium Salt of Thymine (**13**)——A mixture of the sodium salt of **13** (5 g), **1** (14.2 g) and DMF (260 ml) was allowed to react and treated in the manner described in the general procedure. H_2O (100 ml) was added to this resulting solids and insoluble precipitates were filtered and washed with ether to give 770 mg of **13**. The H_2O solution was extracted with ether and then $CHCl_3$. The both extracts were washed with H_2O and dried. The ether extracts were evaporated to give 8 g of a mixture of five components. This mixture was chromatographed on silica gel (400 g). The first part of elution with 5% AcOEt–benzene gave 326 mg (1.9%) of O(2)O(4)-bis(methyl 2,3-O-isopropylidene-5-deoxy-β-D-ribofuranos-5-yl)-thymine (**22**) as colorless syrup. IR ν_{max}^{Liquid} cm^{-1}: 1605, 1575. UV λ_{max}^{EtOH} mμ: 266. NMR ($CDCl_3$) δ: 7.95 (1H, s), 4.95 (2H, s), 4.90—4.10 (10H, m), 3.29 (6H, s, 2×OMe), 2.05 (3H, s, CH_3), 1.46 (6H, s), 1.30 (6H, s). The second part of elution with 5% AcOEt–benzene gave 87 mg (0.5%) of N(1)O(4)-bis(methyl 2,3-O-isopropylidene-5-deoxy-β-D-ribofuranos-5-yl)-thymine (**21**) as colorless syrup. IR ν_{max}^{Liquid} cm^{-1}: 1670, 1550. UV λ_{max}^{EtOH} mμ: 276. NMR ($CDCl_3$) δ: 7.40 (1H, s), 4.94 (1H, s), 4.90 (1H, s), 4.80—3.70 (10H, m), 3.30 (3H, s, OMe), 3.26 (3H, s, OMe), 1.94 (3H, s, CH_3), 1.44 (3H, s), 1.38 (3H, s), 1.28 (3H, s), 1.24 (3H, s). Elution with 10% AcOEt–benzene gave 3.23 g (19%) of N(1)N(3)-bis(methyl 2,3-O-isopropylidene-5-deoxy-β-D-ribofuranos-5-yl)-thymine (**20**) as colorless viscous syrup. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1690, 1655, 1640. UV λ_{max}^{EtOH} mμ: 271. NMR ($CDCl_3$) δ: 7.00 (1H, s), 4.93 (2H, s), 4.85—3.90 (10H, m), 3.35 (3H, s, OMe), 3.32 (3H, s, OMe), 1.90 (3H, s,

CH_3), 1.42 (6H, s), 1.28 (6H, s). Elution with AcOEt–benzene (1: 1) gave 2.45 g of methyl 5-(thymin-1H-1-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (**19**). And then the $CHCl_3$ extracts were evaporated to give 2.8 g of **19** also. Two recrystallizations from benzene–isopropyl ether afforded an analytical sample of **19** as colorless prisms: yield 4.95 g (47%); mp 132—133°. $[\alpha]_D^{25}$ +23° (c=1.0, MeOH). IR ν_{max}^{Nujol} cm^{-1}: 3160, 3020, 1671. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 9.65 (1H, broad s, >N–H), 7.10 (1H, s), 5.03 (1H, s, C_1-H), 4.70 (2H, s), 4.60—3.70 (3H, s), 3.41 (3H, s, OMe), 1.94 (3H, s, CH_3), 1.48 (3H, s), 1.34 (3H, s). *Anal.* Calcd. for $C_{14}H_{20}O_6N_2$: C, 53.84; H, 6.45; N, 8.97. Found: C, 53.66; H, 6.48; N, 8.87.

Reaction of the Sodium Salt of Cytosine (14)——A mixture of the sodium salt of **14** (3.0 g), **1** (10 g) and DMF (200 ml) was allowed to react and treated in the manner described in the general procedure. To the resulting solid was added H_2O (100 ml), and insoluble crystals were filtered and washed with ether to give 3.22 g (mp 254—260°) of methyl 5-(cytosin-1H-1-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (**23**). The H_2O solution was extracted with $CHCl_3$. The $CHCl_3$ extracts were washed with H_2O, dried and evaporated to afford 4.43 g of a mixture of five components. This mixture was chromatographed on silica gel (160 g). Elution with 3% MeOH–$CHCl_3$ afforded 1.83 g (23%) of methyl 5-(4-aminopyrimidin-2-O-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (**24**) as colorless viscous syrup. $[\alpha]_D^{26}$ −46° (c=1.0, $CHCl_3$). IR ν_{max}^{Liquid} cm^{-1}: 3450, 3340, 3200, 1630, 1590, 1560. UV λ_{max}^{MeOH} mμ: 228, 273. NMR ($CDCl_3$) δ: 8.05 (1H, d, J=5.5 Hz), 6.15 (1H, d, J=5.5 Hz), 5.67 (2H, broad s, exchangeable with D_2O, $-NH_2$), 5.04 (1H, s, C_1-H), 5.00—4.20 (5H, m), 3.35 (3H, s, OMe), 1.49 (3H, s), 1.31 (3H, s). Mass Spectrum m/e: 282 (M^+−15), 112 (M^+−185), 83 (M^+−214). Elution with 5% MeOH–$CHCl_3$ afforded 332 mg (2.5%) of N(1)N(3)-bis(methyl 2,3-O-isopropylidene-5-deoxy-β-D-ribofuranos-5-yl)-cytosine (**25**) as a colorless form. $[\alpha]_D^{26}$ −12° (c=1.0, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3320 (=NH), 1680, 1660, 1585. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 6.70 (1H, d, J=8.0 Hz), 5.57 (1H, d, J=8.0 Hz), 5.40 (1H, broad, exchangeable with D_2O, =NH), 5.00 (2H, s), 4.95—3.80 (10H, m), 3.39 (6H, s, 2×OMe), 1.44 (6H, s), 1.30 (6H, s): Mass Spectrum m/e: 483 (M^+), 392 (M^+−187), 264 (M^+−219). Elution with 10% MeOH–$CHCl_3$ afforded 243 mg of **23**. The total yield of **23** was 3.46 g (43%). Recrystallization from EtOH afforded an analytical sample of **23** as colorless prisms: mp 266—267°. $[\alpha]_D^{26}$ +52° (c=0.5, H_2O). IR ν_{max}^{Nujol} cm^{-1}: 3400, 3300, 3200, 1660, 1605. UV absorption properties are summarized in Table VI. NMR (DMSO-d_6) δ: 7.54 (1H, d, J=7.5 Hz), 7.10 (2H, broad s, exchangeable with D_2O, $-NH_2$), 5.67 (1H, d, J=7.5 Hz), 4.91 (1H, s, C_1-H), 4.85—3.4 (5H, m), 3.27 (3H, s, OMe), 1.34 (3H, s), 1.23 (3H, s). *Anal.* Calcd. for $C_{13}H_{19}O_5N_3$: C, 52.51; H, 6.44; N, 14.13. Found: C, 52.20; H, 6.17; N, 14.04.

Reaction of the Sodium Salt of Benzimidazole (26)——A mixture of the sodium salt of **26** (5.0 g), **1** (13.8 g) and DMF (280 ml) was allowed to react and treated in the manner described in the general procedure (In this experiment, the reaction time was enough for 5 hr.). H_2O (70 ml) was added to the resulting residue. The solution was extracted with benzene. The benzene extracts were washed with H_2O, dried and evaporated to give 13.5 g of a mixture. The mixture was chromatographed on Al_2O_3 (grade II—III, 200 g). Elution with benzene–$CHCl_3$ (1: 1) gave 12 g (quantitative) of methyl 5-(benzimidazol-1H-1-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (**27**) as syrup, which crystallized at room temperature after two months. Recrystallization from benzene–isopropyl ether afforded an analytical sample of **27** as colorless needles: mp 92—93°. $[\alpha]_D^{22}$ −3.0° (c=0.5, C_6H_6). IR ν_{max}^{Nujol} cm^{-1}: 1610. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 8.02 (1H, s), 7.85 (1H, m), 7.43 (3H, m), 5.05 (1H, s, C_1-H), 4.70 (2H, s, C_5-2H), 4.85—4.15 (3H, m), 3.40 (3H, s, OMe), 1.44 (3H, s), 1.28 (3H, s). *Anal.* Calcd. for $C_{16}H_{20}O_4N_2$: C, 63.14; H, 6.62; N, 9.21. Found: C, 62.99; H, 6.51; N, 9.04.

Methyl 5-(6-*n*-Butylaminopurin-9H-9-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (9)——A mixture of **4** (4.0 g), BuOH (30 ml), and $BuNH_2$ (3.93 g) was allowed to react in a sealed tube. After evaporation of BuOH, H_2O (20 ml) was added. The solution was extracted with ether. The ether extracts were washed with H_2O, dried and evaporated to give 4.2 g (99%) of **9**. Recrystallization from isopropyl ether–petroleum ether afforded an analytical sample of **9** as colorless prisms: mp 71—72°. $[\alpha]_D^{25}$ +12.5° (c=1.0, C_6H_6). IR ν_{max}^{Nujol} cm^{-1}: 3420, 3200 (>NH), 1620, 1585. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 8.47 (1H, s), 7.92 (1H, s), 6.25 (1H, broad t, J=5 Hz, exchangeable with D_2O, >N–H), 5.10 (1H, s, C_1-H), 5.0—4.2 (5H, m), 3.75 (2H, m), 3.44 (3H, s, OMe), 1.9—1.3 (4H, m), 1.46 (3H, s), 1.31 (3H, s), 0.95 (3H, broad t, J=7.5 Hz). *Anal.* Calcd. for $C_{18}H_{27}O_4N_5$: C, 57.28; H, 7.21; N, 18.56. Found: C, 57.12; H, 7.08; N, 18.35.

Methyl 5-(6-Furfurylaminopurin-9H-9-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (10)——A mixture of **4** (5.45 g), furfurylamine (6 g), and BuOH (30 ml) was allowed to react in a sealed tube. After BuOH had been evaporated, H_2O (20 ml) was added. The solution was extracted with ether. The ether extracts were washed with H_2O, dried and evaporated to give a mixture as viscous syrup. The mixture was chromatographed on silica gel (300 g). The first part of elution with 50% AcOEt–benzene afforded 857 mg (15%) of **4**. The second part of elution with 50% AcOEt–benzene gave 3.42 g (55%) of **10** as pale yellow syrup. $[\alpha]_D^{26}$ +13.7° (c=1.46, C_6H_6). IR ν_{max}^{Liquid} cm^{-1}: 3200 (>NH), 1615, 1580, 880 (furan ring). UV λ_{max}^{EtOH} mμ: 270. NMR ($CDCl_3$) δ: 8.44 (1H, s), 7.83 (1H, s), 7.47 (1H, broad t, exchangeable with D_2O, >N–H), 7.34 (1H, m), 6.31 (1H, s), 6.29 (1H, s), 5.03 (1H, s, C_1-H), 4.90 (2H, d, J=5.5 Hz, s on addition of D_2O, $-NH-CH_2-$), 4.80—4.0 (5H, m), 3.35 (3H, s, OMe), 1.43 (3H, s), 1.27 (3H, s). Mass Spectrum m/e: 401 (M^+).

Methyl 5-(6-Dimethylaminopurin-9H-9-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (11)——A mixture of **4** (3.8 g), 40% aqueous $NHMe_2$ solution (7.6 g), and EtOH (15 ml) was allowed to react in a sealed tube. After EtOH had been evaporated, H_2O (20 ml) was added. The solution was extracted with ether. The ether extracts were washed with H_2O, dried and evaporated to give 3.7 g (98%) of **11**. Two recrystallizations from isopropyl ether–petroleum ether afforded an analytical sample of **11** as colorless needles: mp 90—91°. $[\alpha]_D^{26}$ −8° (c=0.5, EtOH). IR λ_{max}^{Nujol} cm^{-1}: 1610, 1570, 1533. UV absorption properties are summarized in Table VI. NMR ($CDCl_3$) δ: 8.36 (1H, s), 7.83 (1H, s), 5.05 (1H, s, C_1-H), 4.90—4.10 (5H, m), 3.55 (6H, s, $-NMe_2$), 3.42 (3H, s, OMe), 1.45 (3H, s), 1.29 (3H, s). *Anal.* Calcd. for $C_{16}H_{23}O_4N_5$: C, 55.00; H, 6.64; N, 20.05. Found: C, 55.26; H, 6.48; N, 19.95.

Desulfurization of 5-(6-Methylthiopurin-9H-9-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (4)——A suspension of **4** (3.5 g) and Raney–Ni (25 g) in MeOH (100 ml) was refluxed with stirring for 1 hr. The Raney–Ni was filtered off and washed with hot MeOH several times. After evaporation of the filtrate, the crude material was chromatographed on Al_2O_3. Elution with 50% AcOEt–benzene gave 581 mg (19%) of **7**. Recrystallization from isopropyl ether afforded **7** as colorless needles (mp 71—72°). The IR spectrum of this product was identical with that of an authentic sample of **7**.

Desulfurization of 5-(6-Methylthiopurin-7H-7-yl)-2,3-O-isopropylidene-5-deoxy-β-D-ribofuranoside (5)——A suspension of **5** (1.0 g) and Raney–Ni (8 g) in MeOH (50 ml) was allowed to react and treated in the manner described above. The crude product (239 mg, 27%) was recrystallized from benzene–isopropyl ether to give **8** as colorless needles (mp 117—118°), which was identified with an authentic sample of **8**.

General Procedure for the Hydrolysis of the Masked "Reversed Nucleosides"——A solution of the masked "reversed nucleoside" and 6 N HCl (0.5 ml/lg) in H_2O (20 ml/lg) was stirred and warmed at 70—80° for 1—3 hr. After the reaction mixture had been cooled, the solution was passed through a column of Amberite IR-45 (OH^- form, dry, 3—5 g/1 ml of 6 N HCl). The eluate and washings were evaporated to dryness. The resulting solid was treated in the appropriate manner for the respective reaction.

5-(6-Methylthiopurin-9H-9-yl)-5-deoxy-D-ribofuranose (29)——A solution of **4** (3.5 g) and 6 N HCl (2 ml) in H_2O (80 ml) was treated in the manner described in the general procedure. The resulting solid was recrystallized from MeOH to afford an analytical sample of **29** as colorless prisms: yield 2.5 g; mp 174—175° (decomp.). IR λ_{max}^{Nujol} cm^{-1}: 3400 (–OH), 3120 (–OH), 1569. UV $\nu_{max}^{H_2O}$ mμ (ε): 286 (24000), 292.5 (24000). NMR (D_2O–NaOD) δ[17]: 8.70 (2H, s), 5.83 (1H, s), 4.90—3.95 (5H, m), 2.84 (3H, s, SCH_3).

5-(Purin-9H-9-yl)-5-deoxy-D-ribofuranose (30)——A solution of **7** (5.0 g) and 6 N HCl (3.5 ml) in H_2O (100 ml) was treated in the manner described in the general procedure. The resulting solid was crystallized with isopropyl alcohol to give 3.5 g of **30**. Two recrystallizations from isopropyl alcohol afforded an analytical sample of **30** as colorless granulars: mp 146—148° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3270 (–OH), 3070 (–OH), 1596, 1580, 1510. UV $\lambda_{max}^{H_2O}$ mμ (ε): 263 (7750). NMR (DMSO-d_6) δ: 9.25 (1H, s), 9.05 (1H, s), 8.52 (1H, s), 6.43 (1H, d, J=4.5 Hz, –OH), 5.00 (2H, m), 4.45 (2H, m), 4.05 (2H, m), 3.65 (2H, m).

5-(6-*n*-Butylaminopurin-9H-9-yl)-5-deoxy-D-ribofuranose (31)——A solution of **9** (4.2 g) and 6 N HCl (2.8 ml) in H_2O (80 ml) was treated in the manner described in the general procedure. The resulting solid was recrystallized from EtOH to afford an analytical sample of **31** as colorless prisms: yield 2.3 g; mp 142—143° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3340—3000 (–OH, >NH), 1620, 1580. UV $\lambda_{max}^{H_2O}$ mμ (ε): 268 (24200). NMR (DMSO-d_6) δ: 8.22 (1H, s), 8.08 (1H, s), 7.70 (1H, t, J=6 Hz), 6.40 (1H, broad), 5.00 (2H, broad s), 4.7—3.3 (8H, m), 1.8—0.7 (7H, m).

5-(6-Furfurylaminopurin-9H-9-yl)-5-deoxy-D-ribofuranose (32)——A solution of **10** (2.7 g) and 6 N HCl (0.8 ml) in H_2O (30 ml) was treated in the manner described in the general procedure. The resulting solid was recrystallized from isopropyl alcohol to afford an analytical sample of **32** pale yellow prisms: yield 1.5 g; mp 149—153° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3500 (–OH), 3340 (–OH), 3200 (>NH), 1619, 1587, 850. UV $\lambda_{max}^{H_2O}$ mμ (ε): 268 (23600), $\lambda_{max}^{1N\ HCl}$ mμ (ε): 267 (26000), $\lambda_{max}^{1N\ NaOH}$ mμ(ε): 268 (19600). NMR (DMSO-d_6–D_2O) δ: 8.48 (1H, s), 8.34 (1H, s), 7.75 (1H, m), 6.55 (2H, m), 5.4—4.8 (4H, m), 4.7—4.0 (4H, m).

5-(6-Dimethylaminopurin-9H-9-yl)-5-deoxy-D-ribofuranose (33)——A solution of **11** (4.0 g) and 6 N HCl (2.8 ml) in H_2O (80 ml) was treated in the manner described in the general procedure. The resulting solid was recrystallized from EtOH to afford an analytical sample of **33** as colorless granulars: yield 2.3 g; mp 155—157° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3360 (–OH), 1610. UV $\lambda_{max}^{H_2O}$ mμ (ε): 276 (24000). NMR (DMSO-d_6–D_2O) δ: 8.21 (1H, s), 8.06 (1H, s), 6.44 (1H, d, J=6 Hz, –OH), 4.97 (2H, broad d), 4.6—3.5 (6H, m), 3.43, 3.39 (3H, 3H, s, $-NMe_2$).

5-(Uracil-1H-1-yl)-5-deoxy-D-ribofuranose (34)——A solution of **15** (3.36 g) and 6 N HCl (1.7 ml) in H_2O (60 ml) was treated in the manner described in the general procedure. The resulting solid was recrystallized from MeOH to afforded an analytical sample of **34** as colorless prisms: yield 2.3 g; mp 175—178° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3400 (–OH), 3200 (–NH), 1670, 1650. UV $\lambda_{max}^{H_2O}$ mμ (ε): 265 (10700). NMR (DMSO-d_6) δ: 7.68 (1H, d, J=7.5 Hz), 5.72 (1H, d, J=7.5 Hz), 5.10 (3H, m), 4.00 (6H, broad m).

5-(Thymin-1H-1-yl)-5-deoxy-D-ribofuranose (35)——A solution of **19** (3.6 g) and 6 N HCl (1.8 ml) in H_2O (80 ml) was treated in the manner described in the general procedure. The resulting solid was recrystallized

17) Sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) was used as an internal standard.

from EtOH–isopropyl alcohol to afford an analytical sample of **35** as colorless prisms; yield 1.74 g; mp 108—110° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3500—3100 (–OH, >NH), 1665. UV $\lambda_{max}^{H_2O}$ mμ (ε): 271 (8950). NMR (DMSO-d_6) δ: 11.38 (1H, broad s, >N–H), 7.63 (1H, d, J=1.5 Hz), 6.67 (1H. d, J=5 Hz, exchangeable with D_2O), 5.20 (3H, m), 3.40 (1H, m), 1.94 (3H, s, $-CH_3$).

5-(Cytosin-1H-1-yl)-5-deoxy-D-ribofuranose (**36**)——A solution of **23** (3.4 g) and 6 N HCl (3 ml) in H_2O (80 ml) was treated in the manner described in the general procedure. The resulting solid was recrystallized from H_2O to afford an analytical sample of **36** as colorless prisms: yield 1.80 g; mp 173—175° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3360, 3310, 3180, 1660, 1590, 1575. UV $\lambda_{max}^{H_2O}$ mμ (ε): 274 (8950). NMR (DMSO-d_6) δ: 7.47 (1H, d, J=7.5 Hz), 7.00 (2H, broad, exchangeable with D_2O, $-NH_2$), 6.30 (1H, broad, OH), 5.63 (1H, d, J=7.5 Hz), 4.93 (3H, broad s), 4.2—3.4 (5H, m).

5-(Benzimidazol-1H-1-yl)-5-deoxy-D-ribofuranose (**37**)——A solution of **27** (12 g) and 6 N HCl (8 ml) in H_2O (200 ml) was treated in the manner described in the general procedure. The resulting solid was recrystallized from EtOH to afford an analytical sample of **37** as colorless prisms: yield 9.0 g; mp 152—153° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3360 (–OH), 3060 (–OH), 1610, 1504. UV $\lambda_{max}^{H_2O}$ mμ (ε): 247 (6240), 254 (6170), 265 (4050), 273 (4270), 280 (3700). NMR (DMSO-d_6) δ: 8.38 (1H, s), 8.00 (2H, m), 7.60 (2H, m), 5.33 (1H, s), 5.20—4.00 (8H, m).

General Procedure for the Oxidation of the "Reversed Nucleosides" by Oxygen——A reversed nucleoside and NaOH (2.5—3.0 molar equivalents) were dissolved in H_2O (200 ml/1 g of reversed nucleoside). This solution was stirred at room temperature under an oxygen atmosphere for 15—72 hr, and passed through a column of Amberlite IR-120 (H^+ form). The adsorbed substance was eluted with 1.4—2.8% NH_4OH. The eluate was evaporated to dryness at 50—60°. The resulting residue was treated in the appropriate manner for the respective reaction.

Oxidation of 5-(6-Methylthiopurin-9H-9-yl)-5-deoxy-D-ribofuranose (**29**)——A solution of **29** (2.0 g) and NaOH (950 mg) in H_2O (400 ml) and Amberlite IR-120 (wet 50 ml) were treated in the manner described in the general procedure. The resulting foams were dissolved in satd. EtOH–HCl, and refluxed for 2 hr. Then the solution was treated with Norite. After the evaporation of EtOH, further EtOH was added and evaporated off. This procedure was repeated three times. The residue was dissolved in EtOH and treated with dry Amberlite IR-45 (OH^- form) at room temperature in order to neutralize the solution. After removal of Amberlite IR-45 by filtration, the EtOH was evaporated. The resulting residue was chromatographed on silica gel. Elution with $CHCl_3$ gave 33 mg (2.0 %) of ethyl (6-methylthiopurin-9H-9-yl)acetate (**38**, R=SMe, R_1=Et). Recrystallization from isopropyl ether afforded an analytical sample of (**38**, R=SMe, R_1=Et) as colorless prisms: mp 114—115°. IR ν_{max}^{Nujol} cm^{-1}: 1750, 1739 (C=O), 1235, 1200 (C–O). UV λ_{max}^{EtOH} mμ (ε): 283 (21300), 290 (20900). NMR ($CDCl_3$) δ: 8.71 (1H, s), 8.02 (1H, s), 4.99 (2H, s, $-CH_2-$), 4.25 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 2.72 (3H, s, SMe), 1.28 (3H, t, J=7.5 Hz, $OCH_2C\underline{H}_3$). *Anal.* Calcd. for $C_{10}H_{12}O_2N_4S$: C, 47.60; H, 4.80; N, 22.21. Found: C, 47.48; H, 5.01; N, 22.33. Elution with 2% MeOH–$CHCl_3$ gave colorless solids 120 mg (6.3%) of ethyl 3-(6-methylthiopurin-9H-9-yl)-2(*R*)-hydroxypropionate (**39**, R=SMe, R_1=Et). Recrystallization from benzene–isopropyl ether afforded an analytical sample of (**39**, R=SMe, R_1=Et) as colorless prisms: mp 121—122°. $[\alpha]_D^{27}$ +10° (c=0.6, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3230 (–OH), 1730 (C=O), 1200 (C–O). UV λ_{max}^{EtOH} mμ (ε): 282.5 (23100), 290 (22700), $\lambda_{max}^{EtOH\text{-}1N\ HCl}$ mμ (ε): 283 (22800), 290 (22600), $\lambda_{max}^{EtOH\text{-}1N\ NaOH}$mμ (ε): 284 (23000), 291 (22400). NMR ($CDCl_3$) δ: 8.68 (1H, s), 8.06 (1H, s), 4.63 (3H, broad s), 4.21 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 4.22 (1H, s, exchangeable with D_2O, –OH), 2.68 (3H, s, SMe), 1.26 (3H, t, J=7.5 Hz, $OCH_2C\underline{H}_3$). *Anal.* Calcd. for $C_{11}H_{14}O_3N_4S$: C, 46.80; H, 5.00; N, 19.85. Found: C, 46.95; H, 5.25; N, 20.09. Elution with 2—5% MeOH—$CHCl_3$ gave 700 mg (33.4%) of ethyl 4-(6-methylthiopurin-9H-9-yl)-2(*R*),3(*R*)-dihydroxybutyrate (**40**, R=SMe, R_1=Et) as viscous syrup. IR ν_{max}^{Liquid} cm^{-1}: 3250 (–OH), 1740 (C=O), 1570, 1200 (C–O). UV λ_{max}^{EtOH} mμ: 283, 290. NMR ($CDCl_3$) δ: 8.60 (1H, s), 8.07 (1H, s), 5.0—4.0 (6H, m, 4H on the addition of D_2O), 4.25 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 2.61 (3H, s, SMe), 1.29 (3H, t, J=7.5 Hz, $OCH_2C\underline{H}_3$). Mass Spectrum *m/e*: 312 (M^+), 239 (M^+-73), 209 (M^+-103), 179 (M^+-133), 166 (M^+-146). Elution with 6% MeOH–$CHCl_3$ gave 13 mg (0.9%) of ethyl (6-hydroxypurin-9H-9-yl)acetate (**38**, R=OH, R_1=Et). Recrystallization from EtOH afforded colorless prisms: mp 225—227° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3050 (–OH), 1740 (C=O), 1660, 1205 (C–O). UV λ_{max}^{EtOH} mμ (ε): 245 (16600), 250 (16700). Mass Spectrum *m/e*: 222 (M^+), 177 (M^+-45), 150 (M^+-72), 149 (M^+-73). The first part of elution with 15% MeOH–$CHCl_3$ gave 36 mg (2.1%) of ethyl 3-(6-hydroxypurin-9H-9-yl)-2(*R*)-hydroxypropionate (**39**, R=OH, R_1=Et). Recrystallization from EtOH afforded colorless prisms: mp 218—220° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3200 (–OH), 1745 (C=O), 1690, 1210 (C–O). UV λ_{max}^{EtOH} mμ (ε): 245 (sh. 17200), 251 (17400). Mass Spectrum *m/e*: 252 (M^+), 226 (M^+-26), 207 (M^+-45), 179 (M^+-73), 149 (M^+-103). The second part of elution with 15% MeOH–$CHCl_3$ gave 136 mg (7.2%) of ethyl 4-(6-hydroxypurin-9H-9-yl)-2(*R*),3(*R*)-dihydroxybutyrate (**40**, R=OH, R_1=Et). Recrystallization from EtOH afforded an analytical sample of (**40**, R=OH, R_1=Et) as colorless prisms: mp 216—218° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3470—3100 (–OH), 1740 (C=O), 1700, 1220 (C–O). UV λ_{max}^{EtOH} mμ (ε): 246 (sh. 11500), 250.5 (11800), $\lambda_{max}^{EtOH\text{-}1N\ HCl}$ mμ (ε): 251 (9400), $\lambda_{max}^{EtOH\text{-}1N\ NaOH}$ mμ (ε): 256 (9860). NMR (DMSO-d_6) δ: 12.25 (1H, broad, –OH), 8.01 (1H, s), 7.96 (1H, s), 5.75 (1H, broad, –OH), 5.50 (1H, broad, –OH), 4.15 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 4.6—3.9 (4H, m), 1.25 (3H, t, J=7.5 Hz, $OCH_2C\underline{H}_3$).

Oxidation of 5-(Purin-9H-9-yl)-5-deoxy-D-ribofuranose (30)——A solution of **30** (2.1 g) and NaOH (952 mg) in H_2O (400 ml) and Amberlite IR-120 (wet 50 ml) were treated in the manner described in the general procedure. The resulting residue was esterified with satd. EtOH–HCl and worked up in the same manner described above. The crude products were purified by means of chromatography on silica gel. The first part of elution with 3% MeOH–$CHCl_3$ gave 67 mg (4.1%) of ethyl (purin-9H-9-yl)acetate (**38**, R=H, R_1=Et). Recrystallization from isopropyl ether afforded an analytical sample of (**38**, R=H, R_1=Et) as colorless needles: mp 119—120°. IR ν_{max}^{Nujol} cm^{-1}: 1750 (C=O), 1600, 1580, 1220 (C–O). UV λ_{max}^{EtOH} mμ (ε): 263 (8350). NMR ($CDCl_3$) δ: 9.14 (1H, s), 8.96 (1H, s), 8.17 (1H, s), 5.05 (2H, s, $-CH_2-$), 4.28 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 1.30 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$). *Anal.* Calcd. for $C_9H_{10}O_2N_4$: C, 52.42; H, 4.89; N, 27.17; O, 15.52. Found: C, 52.22; H, 4.92; N, 26.86; O, 15.69. The second part of elution with 3% MeOH–$CHCl_3$ gave 162 mg (8.7%) of ethyl 3-(purin-9H-9-yl)-2(*R*)-hydroxypropionate (**39**, R=H, R_1=Et) as viscous syrup. $[\alpha]_D^{24}$ +2.9° (c=1.2, EtOH). IR ν_{max}^{Liquid} cm^{-1}: 3300 (–OH), 1740 (C–O), 1595, 1580, 1200 (C–O). UV λ_{max}^{EtOH} mμ: 263. NMR ($CDCl_3$) δ: 9.03 (1H, s), 8.90 (1H, s), 8.26 (1H, s), 5.1—4.3 (4H, m), 4.20 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 1.25 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$). Mass Spectrum *m/e*: 236 (M^+), 207 (M^+-29), 163 (M^+-73), 134 (M^+-102), 133 (M^+-103). Elution with 10% MeOH–$CHCl_3$ gave 463 mg (22%) of ethyl 4-(purin-9H-9-yl)-2(R),3(R)-dihydroxybutyrate (**40**, R=H, R_1=Et). Two recrystallizations from EtOH–isopropyl ether afforded an analytical sample of (**40**, R=H, R_1=Et) as colorless prisms: mp 136—137°. IR ν_{max}^{Nujol} cm^{-1}: 3350 (–OH), 1735 (C–O), 1600, 1575, 1210 (C–O). UV λ_{max}^{EtOH} mμ (ε): 264 (7300), $\lambda_{max}^{EtOH\text{-}1N\ HCl}$mμ (ε): 263 (6000), $\lambda_{max}^{EtOH\text{-}1N\ NaOH}$ mμ (ε): 264 (7200). NMR ($CDCl_3$–DMSO-d_6) δ: 9.02 (1H, s), 8.88 (1H, s), 8.35 (1H, s), 5.5 (2H, broad, exchangeable with D_2O, 2×OH), 4.7—4.1 (4H, m), 4.17 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 1.27 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$).

Oxidation of 5-(6-*n*-Buthylaminopurin-9H-9-yl)-5-deoxy-D-ribofuranose (31)——A solution of **31** (2.5 g) and NaOH (910 mg) in H_2O (500 ml) and Amberlite IR-120 (wet 50 ml) were treated in the manner described in the general procedure. The resulting solid was recrystallized from MeOH three times to give 350 mg (14%) of 4-(6-*n*-buthylaminopurin-9H-9-yl)-2(*R*),3(*R*)-butyric acid (**40**, R=NHBu, R_1=H) monohydrate as colorless prisms: mp 190—191° (decomp.). IR ν_{max}^{Nujol} cm^{-1}- 3300 (–OH, >NH), 1700 (C=O), 1625, 1590. UV $\lambda_{max}^{H_2O}$ mμ (ε): 269 (25400), $\lambda_{max}^{1N\ HCl}$ mμ (ε): 265 (25700), $\lambda_{max}^{1N\ NaOH}$ mμ (ε): 269 (18300). NMR (D_2O–NaOD) δ[17]: 8.15 (1H, s), 8.13 (1H, s), 4.40 (4H, broad s), 3.50 (2H, m), 2.00—1.40 (4H, m), 1.15 (3H, m). The mother liquor of recrystallization was evaporated to dryness. The residue was esterified with satd. iso-BuOH–HCl, and then worked up in the same manner described above. The crude mixture was chromatographed on silica gel. The first part of elution with 2% MeOH–$CHCl_3$ gave 176 mg (7.5%) of isobutyl (6-*n*-butylaminopurin-9H-9-yl)-acetate (**38**, R=NHBu, R_1=isoBu). Recrystallization from isopropyl ether afforded an analytical sample of (**38**, R=NHBu, R_1=isoBu) as colorless needles: mp 112.5—113.5° IR ν_{max}^{Nujol} cm^{-1}: 3220 (>NH), 1730 (C=O), 1620, 1210 (C–O). UV λ_{max}^{EtOH} mμ (ε): 268 (22300). NMR ($CDCl_3$) δ: 8.33 (1H, s), 7.75 (1H, s), 5.90 (1H, m, exchangeable with D_2O, >N–H), 4.94 (2H, s, $-CH_2-$), 3.94 (2H, d, J=6 Hz, $-NH-C\underline{H}_2-$), 3.64 (2H, m), 2.0—0.8 (14H, m). *Anal.* Calcd. for $C_{15}H_{23}O_2N_5$: C, 58.99; H, 7.59; N, 22.94. Found: C, 58.72; H, 7.70; N, 22.96. The second part of elution with 2% MeOH–$CHCl_3$ gave 220 mg (8.5%) of isobutyl 3-(6-*n*-butylaminopurin-9H-9-yl)-2(*R*)-hydroxypropionate (**39**, R=NHBu, R_1=isoBu). Recrystallization from isopropyl ether afforded an analytical sample of (**39**, R=NHBu, R_1=isoBu) as colorless prisms: mp 101—102°, $[\alpha]_D^{25}$ +5° (c=0.5, EtOH). IR ν_{max}^{Nujol} cm^{-1}: 3320 (>NH), 3100 (–OH), 1728 (C=O), 1620, 1200 (C–O). UV λ_{max}^{EtOH} mμ (ε): 268 (25100). NMR ($CDCl_3$) δ: 8.28 (1H, s), 7.73 (1H, s), 6.05 (1H, m, exchangeable with D_2O, >N–H), 4.55 (3H, broad s), 3.94 (2H, d, J=6 Hz), 3.50 (2H, m), 2.0—0.8 (15H, m). *Anal.* Calcd. for $C_{16}H_{25}O_3N_5$: C, 57.29; H, 7.51; N, 20.88. Found: C, 57.17; H, 7.52; N, 20.94. Elution of 5% MeOH–$CHCl_3$ gave 608 mg (21.5%) of isobutyl 4-(6-*n*-butylaminopurin-9H-9-yl)-2(*R*),3(*R*)-dihydroxybutyrate (**40**, R=NHBu, R_1=isoBu). Recrystallization from benzene afforded an analytical sample of (**40**, R=NHBu, R_1=isoBu) as colorless prisms: mp 156—157°. IR ν_{max}^{Nujol} cm^{-1}: 3340 (>NH), 3100 (–OH), 1720 (C=O), 1620. UV λ_{max}^{EtOH} mμ (ε): 268 (26200). NMR ($CDCl_3$) δ: 8.30 (1H, s), 7.79 (1H, s), 6.20 (1H, broad, exchangeable with D_2O), 5.00 (1H, broad m, exchangeable with D_2O), 4.60—3.40 (9H, m), 2.20—0.75 (14H, m).

Oxidation of 5-(6-Furfurylaminopurin-9H-9-yl)-5-deoxy-D-ribofuranose (32)——A solution of **32** (2.68 g) and NaOH (1.10 g) in H_2O (540 ml) and Amberlite IR-120 (wet 50 ml) were treated in the manner described in the general procedure. The resulting foams were esterified with satd. EtOH–HCl and worked up in the manner described above. The crude material was chromatographed on silica gel. Elution with 1% MeOH–$CHCl_3$ gave 93 mg (4%) of ethyl (6-furfurylaminopurin-9H-9-yl)acetate (**38**, R=furfurylamino, R_1=Et). Two recrystallizations from MeOH afforded an analytical sample of (**38**, R=furfurylamino, R_1=Et) as colorless needles: mp 160—161° IR ν_{max}^{Nujol} cm^{-1}: 3275 (>NH), 1745 (C=O), 1630, 1230 (C–O). UV λ_{max}^{MeOH} mμ (ε): 214 (25600), 267 (19500). NMR (DMSO-d_6) δ: 8.28 (1H, s), 8.19 (1H, s), 8.4—8.1 (1H, m, exchangeable with D_2O), 7.57 (1H, m), 6.35 (2H, m), 5.10 (2H, s, $-CH_2-$), 4.80 (2H, broad d, J=6 Hz, s on the addition of D_2O, $-NH-C\underline{H}_2-$), 4.17 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 1.20 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$). *Anal.* Calcd. for $C_{14}H_{15}O_3N_5$: C, 55.80; H, 5.02; N, 23.25; O, 15.93. Found: C, 55.58; H, 4.91; N, 23.02; O, 15.76. Elution with 1—3% MeOH–$CHCl_3$ gave 179 mg (7%) of ethyl 3-(6-furfurylaminopurin-9H-9-yl)-2(*R*)-hydroxypropionate (**39**, R=furfurylamino, R_1=Et). Two recrystallizations from AcOEt–ether afforded colorless prisms: mp 103—104°. $[\alpha]_D^{25}$ +1.8° (c=0.5, MeOH). IR λ_{max}^{Nujol} cm^{-1}: 3370 (>NH), 3100 (–OH), 1750 (C–O), 1630,

1215 (C–O). UV ν_{max}^{MeOH} mμ (ε): 213 (21700), 268 (18300). NMR ($CDCl_3$) δ: 8.41 (1H, s), 7.38 (1H, s), 7.40 (1H, broad s), 6.88 (1H, broad t, J=6 Hz, exchangeable with D_2O, –CH_2N<u>H</u>–), 6.32 (2H, d), 5.30 (1H, broad, exchangeable with D_2O), 4.80 (2H, d, J=6 Hz, s on the addition of D_2O, –NH–C<u>H</u>$_2$–), 4.58 (3H, broad s), 4.17 (2H, q, J=7 Hz –O<u>CH</u>$_2$CH$_3$), 1.23 (3H, t, J=7 Hz, OCH$_2$C<u>H</u>$_3$). *Anal.* Calcd. for $C_{15}H_{17}O_4N_5$: C, 54.34; H, 5.17; N, 21.14; O, 19.32. Found: C, 54.16; H, 5.19; N, 20.89; O, 19.65. Elution with 3—5% MeOH–$CHCl_3$ gave 888 mg (31.8%) of ethyl 4-(6-furfurylaminopurin-9H-9-yl)-2(*R*),3(*R*)-dihydroxybutyrate (**40**, R=furfurylamino, R_1=Et). Recrystallization from MeOH afforded an analytical sample of (**40**, R=furfurylamino, R_1=Et) as colorless prisms: mp 156—157°. IR ν_{max}^{Nujol} cm^{-1}: 3390 (>NH), 3150 (–OH), 1740 (C=O), 1635, 1200 (C–O). UV λ_{max}^{MeOH} mμ (ε): 212 (27000), 268 (19000). NMR (DMSO-d_6) δ: 8.26 (1H, s), 8.08 (1H, s), 8.12 (1H, broad t, J=6 Hz, exchangeable with D_2O, –CH_2N<u>H</u>–), 6.30 (2H, m), 5.90 (1H, broad, exchangeable with D_2O, OH), 5.50 (1H, broad, exchangeable with D_2O, OH), 4.79 (2H, broad d, J=6 Hz, s on the addition of D_2O, –NH–C<u>H</u>$_2$–), 4.06 (2H, q, J=7 Hz, O<u>CH</u>$_2$CH$_3$), 4.5—3.8 (4H, m), 1.16 (3H, t, J=7 Hz, OCH$_2$C<u>H</u>$_3$).

Oxidation of 5-(6-Dimethylaminopurin-9H-9-yl)-5-deoxy-D-ribofuranose (33)——A solution of 33 (3.15 g) and NaOH (1.25 g) in H_2O (600 ml) and Amberlite IR-120 (wet 50 ml) were treated in the manner described in the general procedure. The crude products were crystallized from isopropyl alcohol to give 500 mg of 4-(6-dimethylaminopurin-9H-9-yl)-2(*R*),3(*R*)-dihydroxybutyric acid (**40**, R=NMe_2, R_1=H) as colorless prisms: mp 196—199° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3200 (–OH), 1600. UV λ_{max}^{EtOH} mμ (ε): 274 (24200), $\lambda_{max}^{1N\ HCl}$ mμ (ε): 269 (20000), $\lambda_{max}^{1N\ NaOH}$ mμ (ε): 277 (21200). NMR (D_2O) δ[17]: 8.15 (1H, s), 8.13 (1H, s), 4.40 (4H, broad m), 3.42 (6H, s –NMe_2). The mother liquor of crystallization was evaporated. The residue was esterified with satd. isoBuOH–HCl, and then worked up in the same manner described above. The crude material was chromatographed on silica gel. The first part of elution with 2% MeOH–$CHCl_3$ gave 170 mg (5.7%) of isobutyl (6-dimethylaminopurin-9H-9-yl)acetate (**38**, R=NMe_2, R_1=isoBu). Recrystallization from isopropyl ether afforded an analytical sample of (**38**, R=NMe_2, R_1=isoBu) as colorless prisms: mp 83—84°. IR ν_{max}^{Nujol} cm^{-1}: 1718 (C=O), 1600, 1570. UV λ_{max}^{EtOH} mμ (ε): 275 (10200). NMR ($CDCl_3$) δ: 8.35 (1H, s), 7.80 (1H, s), 4.96 (2H, s, –CH_2–), 3.97 (2H, d, J=7 Hz, O<u>CH</u>$_2$CH(CH$_3$)$_2$), 3.53 (6H, s, –NMe_2), 1.90 (1H, m, OCH$_2$–C<u>H</u>–(CH$_3$)$_2$), 0.90 (6H, d, J=7 Hz, –CH(C<u>H</u>$_3$)$_2$). *Anal.* Calcd. for $C_{13}H_{19}O_2N_5$: C, 56.30; H, 6.91; N, 25.26. Found: C, 56.11; H, 6.89; N, 25.41. The second part of elution with 2% MeOH–$CHCl_3$ gave 250 mg (7.6%) of isobutyl 3-(6-dimethylaminopurin-9H-9-yl)-2(*R*)-hydroxypropionate (**39**, R=NMe_2, R_1=isoBu). Recrystallization from benzene afforded an analytical sample of (**39**, R=NMe_2, R_1=isoBu) as colorless prisms: mp 168—169°. IR ν_{max}^{Nujol} cm^{-1}: 3160 (–OH), 1720 (C=O), 1610, 1203 (C–O). UV λ_{max}^{EtOH} mμ (ε): 275 (9450). NMR ($CDCl_3$) δ: 8.28 (1H, s), 7.75 (1H, s), 4.55 (3H, m), 4.30 (1H, broad m, exchangeable with D_2O), 3.85 (2H, d, J=7 Hz, O<u>CH</u>$_2$–CH(CH$_3$)$_2$), 3.48 (6H, s, –NMe_2), 1.90 (1H, broad m, OCH$_2$C<u>H</u>(CH$_3$)$_2$), 0.85 (6H, d, J=7 Hz, –CH(C<u>H</u>$_3$)$_2$). *Anal.* Calcd. for $C_{14}H_{21}O_3N_5$: C, 54.71; H, 6.89; N, 22.79. Found: C, 54.45; H, 6.98; N, 22.84. The third part of elution with 2% MeOH–$CHCl_3$ gave 450 mg (12.5%) of isobutyl 4-(6-dimethylaminopurin-9H-9-yl)-2(*R*),3(*R*)-dihydroxybutyrate (**40**, R=NMe_2, R_1=isoBu) as colorless syrup. IR ν_{max}^{Liquid} cm^{-1}: 3160 (–OH), 1725 (C=O), 1595, 1210 (C–O). UV λ_{max}^{EtOH} mμ: 275. NMR ($CDCl_3$) δ: 8.25 (1H, s), 7.79 (1H, s), 5.3—4.7 (2H, broad m, exchangeable with D_2O, 2×OH), 4.42 (3H, m), 4.23 (1H, m), 4.00 (2H, d, J=7 Hz, O<u>CH</u>$_2$CH(CH$_3$)$_2$), 3.51 (6H, s, –NMe_2), 1.90 (1H, m, OCH$_2$C<u>H</u>(CH$_3$)$_2$), 0.95 (6H, d, J=6 Hz, –CH(C<u>H</u>$_3$)$_2$). Mass Spectrum *m/e*: 337 (M^+), 280 (M^+−57), 236 (M^+−101), 206 (M^+−131), 176 (M^+−161), 163 (M^+−174).

Oxidation of 5-(Uracil-1H-1-yl)-5-deoxy-D-ribofuranose (34)——A solution of 34 (2.25 g) and NaOH (1.15 g) in H_2O (200 ml) and Amberlite IR-120 (wet 40 ml) were treated in the manner described in the general procedure. The crude products were crystallized from EtOH to give 1.0 g of 4-(uracil-1H-1-yl)-2(R),3(R)-dihydroxybutyric acid (**43**, X=OH, Y=R_1=H).[16] Two recrystallizations from MeOH afforded an analytical sample of (**43**, X=OH, Y=R_1=H) as colorless prisms: mp 225—226° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3280 (>NH), 3150 (–OH), 1705 (C=O), 1678, 1645. UV $\lambda_{max}^{H_2O}$ mμ (ε): 267 (10000), $\lambda_{max}^{1N\ HCl}$ mμ (ε): 267 (8940), $\lambda_{max}^{1N\ NaOH}$ mμ (ε): 266 (8960). The mother liquor of the EtOH crystallization was evaporated. The residue was esterified with satd. EtOH–HCl (60 ml) and worked up in the manner described above. The crude material was purified by means of chromatography on silica gel. The first part of elution with 5% EtOH–$CHCl_3$ gave 124 mg (6.8%) of ethyl (uracil-1H-1-yl)acetate (**41**, X=OH, Y=H). Recrystallization from benzene afforded an analytical sample of (**41**, X=OH, Y=H) as colorless prisms: mp 137—138°. IR ν_{max}^{Nujol} cm^{-1}: 1728 (C=O), 1695, 1622, 1228 (C–O). UV λ_{max}^{EtOH} mμ (ε): 262 (9600). NMR ($CDCl_3$) δ: 10.25 (1H, broad, exchangeable with D_2O, >NH), 7.28 (1H, d, J=8 Hz, C_6-H), 5.82 (1H, d, J=8 Hz, C_5-H), 4.52 (2H, s, –CH_2–), 4.43 (2H, q, J=7 Hz, O<u>CH</u>$_2$CH$_3$), 1.31 (3H, t, J=7 Hz, –CH_2C<u>H</u>$_3$). Mass Spectrum *m/e*: 198 (M^+), 153 (M^+−45), 126 (M^+−72), 125 (M^+−73). The second part of elution with 5% EtOH–$CHCl_3$ gave 168 mg (8%) of ethyl 3-(uracil-1H-1-yl)-2(R)-hydroxypropionate (**42**, X=OH, Y=H) as colorless viscous syrup. IR ν_{max}^{Liquid} cm^{-1}: 3440 (–OH, >NH), 1710 (C=O), 1675, 1220 (C–O). UV λ_{max}^{EtOH} mμ: 264. NMR ($CDCl_3$) δ: 10.30 (1H, broad, exchangeable with D_2O, >NH), 7.38 (1H, d, J=8 Hz, C_6-H), 5.64 (1H, d, J=8 Hz, C_5-H), 4.7—3.7 (6H, m), 1.26 (3H, t, J=7 Hz, –CH_2–C<u>H</u>$_3$). Mass Spectrum *m/e*: 228 (M^+), 155 (M^+−73), 126 (M^+−102), 125 (M^+−103). The third part of elution with 5% EtOH–$CHCl_3$ gave 205 mg (8%) of ethyl 4-(uracil-1H-1-yl)-2(*R*),3(*R*)-dihydroxybutyrate (**43**, X=OH, Y=H, R_1=Et). Recrystallization from isopropyl ether afforded an analytical sample of (**43**, X=OH, Y=H, R_1=Et) as colorless prisms: mp 82—83°. IR ν_{max}^{Nujol} cm^{-1}: 3250 (–OH, >NH), 1730 (C=O), 1665, 1230 (C–O). UV λ_{max}^{EtOH} mμ (ε): 265 (9900). NMR (DMSO-d_6) δ: 7.70 (1H,

d, J=7.5 Hz, C_6-H), 5.73 (1H, d, J=7.5 Hz, C_5-H), 6.10—5.50 (2H, m), 4.33 (2H, q, J=7 Hz, $-C\underline{H}_2-CH_3$), 4.5—3.8 (4H, m), 1.41 (3H, t, J=7 Hz, $-CH_2-C\underline{H}_3$).

Oxidation of 5-(Thymin-1H-1-yl)-5-deoxy-D-ribofuranose (35)——A solution of **35** (2.15 g) and NaOH (1.18 g) in H_2O (430 ml) and Amberlite IR-120 (wet 50 ml) were treated in the manner described in the general procedure. The resulting residue was esterified with satd. EtOH–HCl, and worked up in the same manner described above. The crude products were chromatographed on silica gel. The eluate with $CHCl_3$ gave 152 mg (8.6%) of ethyl (thymin-1H-1-yl)acetate (**41**, X=OH, Y=CH_3). Recrystallization from EtOH afforded an analytical sample of (**41**, X=OH, Y=CH_3) as colorless prisms: mp 172—173°. IR ν_{max}^{Nujol} cm^{-1}: 3150—3020 (–NH), 1730 (C–O), 1690, 1655, 1240 and 1220 (C–O). UV λ_{max}^{EtOH} mμ (ε): 267 (6800). NMR ($CDCl_3$–DMSO-d_6) δ: 7.16 (1H, broad s, C_6-H), 4.42 (2H, s, $-CH_2-$), 4.19 (2H, q, J=7 Hz, O–$C\underline{H}_2CH_3$), 1.85 (3H, broad s, $-CH_3$), 1.25 (3H, t, J=7 Hz, O–$CH_2C\underline{H}_3$). *Anal.* Calcd. for $C_9H_{12}O_4N_2$: C, 50.94; H, 5.70; N, 13.20. Found: C, 50.86; H, 5.75; N, 13.13. Elution with 1—2% MeOH–$CHCl_3$ gave 278 mg (13.7%) of ethyl 3-(thymin-1H-1-yl)-2(*R*)-hydroxypropionate (**42**, X=OH, Y=CH_3). Recrystallization from EtOH afforded colorless prisms: mp 147—149°. $[\alpha]_D^{27}$ +20° (c=0.6, MeOH). IR ν_{max}^{Nujol} cm^{-1}: 3370 (>NH), 3160 (–OH), 1720—1710 (C=O), 1690, 1670, 1230 (C–O). UV λ_{max}^{EtOH} mμ (ε): 270 (6900). NMR (DMSO-d_6) δ: 7.39 (1H, broad s, C_6-H), 5.80 (1H, d, J=6 Hz, exchangeable with D_2O, –OH), 4.4—3.6 (6H, m), 1.72 (3H, broad s, $-CH_3$), 1.18 (3H, t, J=7 Hz, $-CH_2-C\underline{H}_3$). *Anal.* Calcd. for $C_{10}H_{14}O_5N_2$: C, 49.58; H, 5.83; N, 11.57. Found: C, 49.88; H, 6.00; N, 11.61. Elution with 2—5% MeOH–$CHCl_3$ gave 1.0 g of ethyl 4-(thymin-1H-1-yl)-2(R),3(R)-dihydroxybutyrate (**43**, X=OH, Y=CH_3, R_1=Et) as colorless powder: mp 166—168°. IR ν_{max}^{Nujol} cm^{-1}: 3300 (>NH), 3060 (–OH), 1745 (C=O), 1680, 1230 (C–O). UV λ_{max}^{EtOH} mμ (ε): 270 (10000), $\lambda_{max}^{EtOH\text{-}1N\ HCl}$ mμ (ε): 271 (9800), $\lambda_{max}^{EtOH\text{-}1N\ NaOH}$ mμ (ε): 269 (7000). NMR (DMSO-d_6) δ: 7.28 (1H, broad s, C_6-H), 5.6—5.5 (2H, m, exchangeable with D_2O, 2×OH), 4.4—3.6 (6H, m), 1.79 (3H, broad s, $-CH_3$), 1.25 (3H, t, J=7 Hz, $-CH_2-C\underline{H}_3$).

Oxidation of 5-(Cytosin-1H-1-yl)-5-deoxy-D-ribofuranose (36)——A solution of **36** (2.0 g) and NaOH (1.15 g) in H_2O (400 ml) and Amberlite IR-120 (wet 60 ml) were treated in the manner described in the general procedure. The resulting foams were esterified with satd. EtOH–HCl and worked up in the same manner described above. The crude products were purified by means of chromatography on silica gel. The first part of elution of 10% MeOH–$CHCl_3$ gave 43 mg (2.6%) of ethyl (cytosin-1H-1-yl)acetate (**41**, X=NH_2, Y=H). Recrystallization from EtOH afforded colorless prisms: mp 237—239° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3350 and 3080 ($-NH_2$), 1740 (C=O), 1660, 1630. UV λ_{max}^{MeOH} mμ (ε): 272 (8000). *Anal.* Calcd. for $C_8H_{11}O_3N_3$: C, 48.72; H, 5.62; N, 21.31. Found: C, 48.72; H, 5.67; N, 21.30. The second part of elution with 10% MeOH–$CHCl_3$ gave 187 mg (9.8%) of ethyl 3-(cytosin-1H-1-yl)-2(*R*)-hydroxypropionate (**42**, X=NH_2, Y=H). Recrystallization from MeOH afforded an analytical sample of (**42**, X=NH_2, Y=H) as colorless prisms, mp 220—221° (decomp.). $[\alpha]_D^{28}$ +25° (c=0.6, DMSO). IR ν_{max}^{Nujol} cm^{-1}: 3360 and 3180 ($-NH_2$, –OH), 1725 (C=O), 1650, 1610, 1260 and 1220 (C–O). UV λ_{max}^{MeOH} mμ (ε): 274 (8300). NMR (DMSO-d_6) δ: 7.39 (1H, d, J=7 Hz, C_6-H), 6.96 (2H, broad s, exchangeable with D_2O, $-NH_2$), 5.80 (1H, broad, exchangeable with D_2O, –OH), 5.60 (1H, d, J=7 Hz, C_5-H), 4.05 (2H, q, J=7 Hz, O–$C\underline{H}_2CH_3$), 4.5—3.5 (3H, m), 1.17 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$). *Anal.* Calcd. for $C_9H_{13}O_4N_3$: C, 47.57; H, 5.77; N, 18.49. Found: C, 47.32; H, 5.85; N, 18.53. Elution with 10—20% MeOH–$CHCl_3$ gave 777 mg (37%) of ethyl 4-(cytosin-1H-1-yl)-2(*R*),3(*R*)-dihydroxybutyrate (**43**, X=NH_2, Y=H, R_1=Et). Recrystallization from MeOH afforded colorless prisms: mp 201—203° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3420—3330 ($-NH_2$, –OH), 1725 (C=O), 1660, 1640, 1600, 1235 (C–O). UV λ_{max}^{MeOH} mμ (ε): 275 (8760), $\lambda_{max}^{MeOH\text{-}1N\ HCl}$ mμ (ε): 286 (13700), $\lambda_{max}^{MeOH\text{-}1N\ NaOH}$ mμ (ε): 275 (8150). NMR (DMSO-d_6) δ: 7.36 (1H, d, J=7 Hz, C_6-H), 6.95 (2H, broad s, exchangeable with D_2O, $-NH_2$), 5.64 (1H, d, J=7 Hz, C_5-H), 5.8—5.1 (2H, broad m, exchangeable with D_2O), 4.06 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 3.90 (4H, broad), 1.20 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$).

Oxidation of 5-(Benzimidazol-1H-1-yl)-5-deoxy-D-ribofuranose (37)——A solution of **37** (6.0 g) and NaOH (3.4 g) in H_2O (1.2 liters) and Amberlite IR-120 (wet 100 ml) were treated in the manner described in the general procedure. The solution of resulting residue in EtOH was treated with Norite and followed by evaporation to give a mixture of 3.5 g. This foams (580 mg) was esterified with satd. EtOH–HCl and worked up in the same manner described above. The crude products were chromatographed on silica gel. The first part of elution with 5% EtOH–$CHCl_3$ gave 76 mg (9.4% from **37**) of ethyl (benzimidazol-1H-1-yl)-acetate (**44**) as liquid. IR ν_{max}^{Liquid} cm^{-1}: 1730 (C=O), 1610, 1200 (C–O). NMR ($CDCl_3$) δ: 7.81 (1H, s, C_2-H), 7.75 (1H, m), 7.20 (3H, m), 4.78 (2H, s, $-CH_2-$), 4.15 (2H, q, J=7 Hz, O–$C\underline{H}_2-CH_3$), 1.20 (3H, t, J=7 Hz, $-CH_2C\underline{H}_3$). Mass Spectrum *m/e*: 204 (M^+), 132 (M^+-72), 131 (M^+-73). **44** was hydrolyzed to give acid, mp 231—233° (decomp.). The second part of elution with 5% EtOH–$CHCl_3$ gave 116 mg (12.5% from **37**) of ethyl 3-(benzimidazol-1H-1-yl)-2(*R*)-hydroxypropionate (**45**) as liquid. IR ν_{max}^{Liquid} cm^{-1}: 3300—3050 (–OH), 1720 (C=O), 1610, 1200 (C–O). NMR ($CDCl_3$) δ: 7.15—6.9 (5H, m), 4.6—3.9 (6H, m), 1.64 (3H, t, J=7 Hz, $-O-CH_2-C\underline{H}_3$). Mass Spectrum *m/e*: 234 (M^+), 161 (M^+-73), 132 (M^+-102), 131 (M^+-103). **45** was hydrolyzed to give acid, mp 203—204° (decomp.). Elution with 10% EtOH–$CHCl_3$ gave 160 mg (15.2% from **37**) of ethyl 4-(benzimidazol-1H-1-yl)-2(*R*),3(*R*)-dihydroxybutyrate (**46**). Recrystallization from EtOH-isopropyl ether afforded an analytical sample of **46** as colorless needles: mp 158—160°. IR ν_{max}^{Nujol} cm^{-1}: 3300—3100 (–OH), 1734 (C=O), 1610, 1200 (C–O). UV λ_{max}^{EtOH} mμ (ε): 248 (6700), 254 (6700), 266 (4000), 275 (4550), 282 (4770). NMR (DMSO-d_6) δ: 8.35 (1H, broad), 7.85 (2H, broad m), 7.50 (2H, broad m), 6.15 (1H,

m, exchangeable with D_2O, –OH), 5.75 (1H, m, exchangeable with D_2O, –OH), 4.7—4.0 (4H, m), 4.29 (2H, q, J=7 Hz, $-OC\underline{H}_2CH_3$), 1.40 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$).

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