Partial Protection of Carbohydrate Derivatives. Part 3.[1] Regioselective 2'-*O*-Deacylation of Fully Acylated Purine and Pyrimidine Ribonucleosides with Hydrazine Hydrate

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In 1 : 4 (v/v) glacial acetic acid–pyridine, partial *O*-deacylation of fully acylated purine and pyrimidine ribonucleosides upon hydrazinolysis was found to be induced regioselectively in respect to the three ester functions at the 2'-position to give the corresponding 2'-OH derivatives in good yields; *e.g.* 3',5'-di-*O*-benzoyladenosine (70% yield), N^2,3',5'-tribenzoylguanosine (63% yield), 3',5'-di-*O*-benzoylinosine (52% yield), N^2-benzoyl-3',5'-di-*O*-acetylguanosine (42% yield), and 3',5'-di-*O*-benzoyluridine (39% yield) were isolated. Moreover, 5'-*O*-acylribonucleosides were prepared in quantitative yields by use of an excess of hydrazine hydrate in 1 : 1 (v/v) chloroform–methanol and in pyridine. Hydrazinolysis of 3',5'-di-*O*-acetyl-2'-deoxyribonucleosides in pyridine was found to give both 5', and 3'-*O*-acetyl-2'-deoxyribonucleosides in comparable amounts (80—90% total yields).

Furthermore, hydrazinolysis of N^6,2',5'-triacetyl-3'-*O*-methyladenosine and N^6,3',5'-triacetyl-2'-*O*-methyladenosine demonstrated that the 2'-*O*-acetyl group is far more labile toward the nucleophile than the 3'-*O*-acetyl group.

The possible factors involved in the regioselectivity of hydrazinolysis are discussed.

THERE has been significant progress in the synthetic study of 2'-deoxyribonucleotide oligomers or polymers in connection with the study of DNA.[2] In contrast, the synthetic study of ribonucleotide oligomers or polymers has been less well developed on account of the difficulty in differentiating chemically between the 2'- and 3'-hydroxy-groups on the β-D-ribofuranosyl moiety of ribonucleosides, although various attempts have been made at the partial protection of the hydroxy-groups of ribonucleosides by acetylation,[3] tosylation,[4] benzylation,[5] silylation,[6] tritylation,[7] 3'-benzoylpropionylation,[8] partial hydrolysis of their 2',3'-orthoacetates,[9] and partial methanolysis,[10] *etc.* In some cases, mixtures of several protected ribonucleosides were obtained which required chromatographic separation; such were the difficulties associated with the synthesis of ribonucleoside oligomers. These problems prompted us to develop a new method for potentially regiospecific protection of the ribonucleoside hydroxy-groups, since we have been involved in the study of specific *N*-debenzoylation of fully benzoylated adenosine and cytidine.[11] We now report in full the results that we have recently communicated as a novel procedure for regioselective 2'-*O*-deacylation of fully acylated purine and pyrimidine ribonucleosides with hydrazine hydrate.[12]

The unusual acidity of the 2'-hydroxy-group of ribonucleosides has been suggested by partial 2'-*O*-benzylation of uridine and cytidine,[5] partial methylation of adenosine with diazomethane,[13] and chromatographic separation of the resulting mixture from the latter on a column of strongly basic ion-exchange resin,[14] which gave the 2'-*O*-methyl derivative as the first fraction and the 3'-*O*-methyl one as the second fraction. Moreover, *X*-ray crystal structural analysis of a series of purine ribonucleosides[15] showed that the C(2')–O(2') bond is the shortest among the three alcoholic functions at the 2', 3', and 5' positions. These facts suggested the possibility that the 2'-*O*-acyl groups of fully acylated ribonucleosides might behave as the most active of the three ester functions towards an appropriate nucleophile such as hydrazine hydrate (1), which has commonly been used for the preparation of hydrazides from alkyl esters of the corresponding carboxylic acids,[16] and for the specific *N*-debenzoylation of fully benzoylated 2'-deoxy-adenosine and -cytidine.[17]

Consequently, we attempted a partial *O*-debenzoylation of N^6,N^6,2',3',5'-pentabenzoyladenosine (2) with (1) (3.3 molar equivalents) in 1 : 4 v/v glacial acetic acid–pyridine. The conditions used here were directly from those which have been used for the specific *N*-debenzoylation by Letsinger *et al.*;[17] the present reaction at room temperature for 8 days, followed by quenching with acetone, evaporation, and separation on a column of silica gel, gave 2',3',5'-tri-*O*-benzoyladenosine (3) (10% yield), 3',5'-di-*O*-benzoyladenosine (4) (63% yield), and 5'-*O*-benzoyladenosine (5) (25% yield). An attempt at the partial *O*-debenzoylation with benzohydrazide, in place of (1), resulted, under the same reaction conditions, in a quantitative recovery of (2). A reaction using benzohydrazide in pyridine under reflux gave (3) (55% yield), N^6,2',3',5'-tetrabenzoyladenosine (33% yield), and *NN'*-dibenzoylhydrazine (35% yield). Such a promising result with (1) in this solvent system prompted us to make a detailed investigation of the conditions for potentially regiospecific 2'-*O*-deacylation of fully acylated ribonucleosides, by use of (3) as the model compound, the latter being readily prepared upon treatment of (2) with phenols or alcohols.[11] All reactions were performed by use of a solution of (3) (0.1 mmol) in a solvent (3 ml), which was treated with a solution of (1) (1.0 mmol ml^{-1}) under the conditions described in each Table. Material balances of each reaction were monitored by means of high performance l.l.c. under the conditions described in the Experimental section; (3), (4), and (5) respectively were detected as peaks with different retention times.

The effect of the amount of (1) on the selectivity in the formation of the di-*O*-benzoate (4) was first examined by

TABLE 1

Effect of the proportion of hydrazine hydrate (1) on partial deprotection of 2',3',5'-tri-*O*-benzoyladenosine (3) [a]

(1)/(3)	Conditions: Temp. (°C)	Conditions: Period (day [b])	Yield of products (%): (4)	Yield of products (%): (5)	Recovery of (3) (%)
2	RT *	4	9		91
4	RT	4	50		50
6	RT	4	57	<1	42
8	RT	1	65	5	30
12	RT	1	61	18	21
16	RT	1	59	30	11
20	RT	1	54	41	5
6	60—65	6 h	46	<1	53
6	70—75	6 h	50	<1	49
6	80—85	6 h	61	<1	38

[a] All reactions were performed by use of (3) (0.1 mmol) in glacial acetic acid–pyridine (1 : 4, v/v) (3 ml). [b] Unless otherwise stated.

* RT = Room temperature.

treating a solution of (3) in 1 : 4 (v/v) glacial acetic acid–pyridine; the results thus obtained are summarized in Table 1. As seen from the table, it was found that the regioselective *O*-deacylation could be performed by treating (3) with 4—6 molar equivalents of (1) at room temperature for 4 days. An elevated temperature was found to facilitate the reaction without any undesirable effect on the selectivity. However, we decided to perform the *O*-deacylation at room temperature in view of the period for equilibration between 3',5'- and 2',5'-di-*O*-acetyluridine; *i.e.*, 24 days at room temperature and 2.5 h at 60 °C in pyridine, respectively, as reported by Reese and Trentham.[18] The solvent effect was next examined with respect to the reaction of (3); the results obtained are summarized in Table 2. The requirement, that the solvent should be able to dissolve both water-soluble (1) and -insoluble (3), and be inert toward (1), prompted us to use pyridine, *NN*-dimethylformamide (DMF), ethanol, chloroform–methanol (1 : 1, v/v), and 1,4-dioxan; all reactions were performed by use of (1) (2—4 molar equivalents) at room temperature for 2 days. Hexane, benzene, 1,2-dimethoxyethane, carbonyl compounds, and esters such as ethyl acetate were thus inadequate for this purpose. As seen from the Table, the reactions with 4 molar equivalents of (1) in DMF, ethanol, and chloroform–methanol (1 : 1, v/v) unexpectedly afforded free adenosine. However, reactions with 2 molar equivalents of (1) gave (4) and (5) together with recovery of (3) in the yields shown in the Table. The selectivity observed for these reactions was inferior to that in the reaction in glacial acetic acid–pyridine (1 : 4, v/v). Alternatively, the reactions in chloroform–methanol (1 : 1, v/v) and in pyridine suggested their promising application to the preparative synthesis of 5'-*O*-acylribonucleosides which are described later. Moreover, these experiments may indicate that the entity giving such regioselectivity in glacial acetic acid–pyridine (1 : 4, v/v) is hydrazine, either inactivated by the acetic acid involved in the solvent system, or buffered by acetic acid. From these considerations, the effect of varying the proportion of acetic acid to pyridine was examined by treating (3) with (1) in solvents with a series of different compositions; the results thus obtained are

TABLE 2

Examination of solvent effect on the partial deprotection of (3) [a]

Solvent	(1)/(3)	Yield of product (%): (4)	Yield of product (%): (5)	Recovery of (3) (%)
Pyridine [b]	2	38	15	47
Pyridine [b]	4	18	81	1
DMF	2	10	42	48
DMF [c]	4			
EtOH	2	26	43	31
EtOH [c]	4			
1 : 1 $CHCl_3$–MeOH	2	10	78	12
1 : 1 $CHCl_3$–MeOH [c]	4			
Dioxan	2	22		78
Dioxan	4	40	22	38

[a] All reactions were performed at room temperature for 2 days. [b] 10% Methanol was added to effect complete solution of (1). [c] T.l.c. of these reactions showed the formation of free adenosine.

summarized in Table 3. As seen from the Table, when the concentration of acetic acid was below 1%, the selectivity of the reaction to give (5) in high yield was low whilst, when the concentration was above 40%, the reaction was found to be much delayed and gave (4) (22% yield) with recovery of (3) (78% yield). It was thus concluded that the most advantageous concentration of glacial acetic acid in pyridine was in the

TABLE 3

Effect of the proportion of glacial acetic acid to pyridine on the partial deprotection of (3) [a]

Glacial acetic acid: v/v %	Glacial acetic acid: mmol [b]	Yield of products (%): (4)	Yield of products (%): (5)	Recovery of (3) (%)
0	0	15	85	
1	0.5	58	21	21
5	2.5	60	8	32
10	5.0	63		37
20	10	58		42
40	20	22		78

[a] All reactions were performed by use of (3) (0.1 mmol) and (1) (0.4 mmol) at room temperature for 4 days. [b] mmolar equivalent of glacial acetic acid in the solvent system (3 ml).

range 5—20%; within such a range of the concentration differences in the yield of (4) were small. Subsequently, we scrutinized the effect of the proportion of glacial acetic acid to (1) in the partial *O*-deacylation, by treating (3) with 4 molar equivalents of (1) in glacial acetic acid–pyridine (1 : 4, v/v) (increasing the volume from 1, 2, 3, 5, and then up to 10 ml, in turn) at room temperature for 4 days. The results thus obtained are summarized in Table 4. These results led us to conclude that the regioselectivity which led to (4) in the partial *O*-deacylation was satisfactory provided we used 5—25 molar equivalents of glacial acetic acid to (1).

On the basis of the above results, we performed partial *O*-deacylation of fully acylated purine and pyrimidine ribonucleosides; the conditions used and the results thus obtained are summarized in Table 5. Compound (3), N^2,2',3',5'-tetrabenzoylguanosine (6), 2',3',5'-tri-*O*-benzoylinosine (7), 2',3',5'-tri-*O*-acetyladenosine (8), N^2-acetyl-(9), and N^2-benzoyl-2',3',5'tri-*O*-acetylguanosine

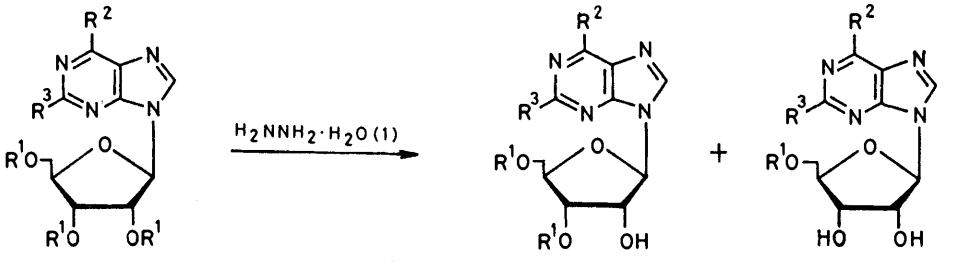
(10), 2',3',5'-tri-*O*-acetylinosine (11), 2',3',5'-tri-*O*-benzoyl- (12), and -acetyluridine (13), N^4,2',3',5'-tetrabenzoyl- (14), and -acetylcytidine (15) were respectively subjected to the reaction with (1) as shown in the 12 entries. Entries 1, 3, 5, 7, 8, 9, 10, and 12 show successful partial *O*-deacylation, followed by the same work-up as described above, to give mixtures of the corresponding 3',5'- and 2',5'-di-*O*-acylribonucleosides, and their subsequent crystallization afforded the 3',5'-di-*O*-acyl derivatives in satisfactory yields, except in the case of (11), exceptionally, which gave the 2',5'-di-*O*-acetyl derivative; the 3',5'-di-*O*-acetylinosine is different from the others in being syrupy. The corresponding 5'-*O*-acyl derivatives were obtained in low yield as seen from entries 1, 3, 4, 5, 10, 11, and 12. Entries 2, 4, and 6 also demonstrate successful trials to shorten the reaction period by performing the reactions at an elevated temperature. On the other hand, the reactions of fully acylated pyrimidine ribonucleosides showed lower regioselectivity than that observed in the series of those with the fully acylated purine ribonucleosides. Compounds (12) and (13) gave the corresponding 3',5'-di-*O*-acyl derivatives (39% and 46% yields, respectively) together with the

TABLE 4

Effect of the proportion of glacial acetic acid to (1) on the partial deprotection of (3) [a]

Glacial acetic acid–pyridine (1 : 4, v/v) Volume (ml)	mmol of AcOH [b]	Yield of products (%) (4)	(5)	Recovery of (3) (%)
1	3.5	65	5	30
2	7	68		32
3	10.5	60		40
5	17.5	26		74
10	35	24		76

[a] All reactions were performed by use of (3) (0.1 mmol) and (1) (0.4 mmol) at room temperature for 4 days. [b] Total amount of glacial acetic acid in the solvent system.



	R¹	R²	R³
(3)	Bz	NH_2	H
(6)	Bz	OH	NHBz
(7)	Bz	OH	H
(8)	Ac	NH_2	H
(9)	Ac	OH	NHBz
(10)	Ac	OH	NHBz
(11)	Ac	OH	H

SCHEME 1

TABLE 5

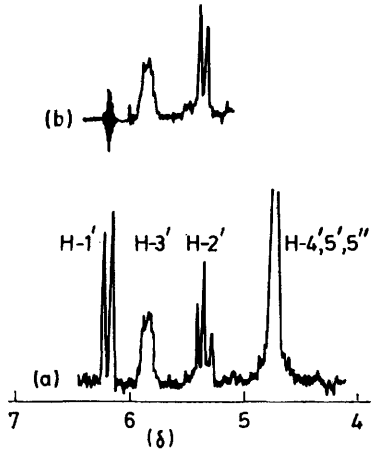
Partial deprotection of fully acylated purine and pyrimidine ribonucleosides with hydrazine hydrate [a]

Entry	Acylated nucleosides (Ns) R¹	R²	R³		Reactant ratio (1):Ns	Temp. (°C) *	Period (days [b])	Yield of nucleoside acylate: Mixtures of diacylates [c]	3',5'-Diacylates	2',5'-Diacylates	5'-Acylates
1	Bz	NH_2	H	(3)	6	RT	2	81 (100 : 0)	(4) 64		(5) 9
2	Bz	NH_2	H	(3)	4	70—75	15 h	80 (100 : 0)	(4) 70		
3	Bz	OH	NHBz	(6)	4	RT	1	82 (90 : 10)	(6a) 63		(6c) 11
4	Bz	OH	NHBz	(6)	2	70—75	10 h	77 (90 : 10)	(6a) 55		(6c) 9
5	Bz	OH	H	(7)	2	RT	2	74 (90 : 10)	(7a) 51		(7c) 10
6	Bz	OH	H	(7)	1.2	70—75	3 h	80 (90 : 10)	(7a) 52		
7	Ac	NH_2	H	(8)	1.2	RT	1	76 (80—75 : 20—25)	(8a) 53		
8	Ac	OH	NHAc	(9)	1.2	RT	2	69 (100 : 0)	(9a) 52		
9	Ac	OH	NHBz	(10)	1.2	RT	1		(10a) 42 [d]		
10	Ac	OH	H	(11)	1.2	RT	2	85 (80—75 : 20—25)		(11b) 30	(11c) 10
11	Tri-*O*-benzoyluridine			(12)	1.2	RT	4	65 (67 : 33)	(12a) 39		(12c) 28
12	Tri-*O*-acetyluridine			(13)	1.2	RT	3.5 h	76 (67 : 33)	(13a) 46		(13c) 11

[a] All reactions were performed in 1 : 4 v/v glacial acetic acid–pyridine. [b] Unless otherwise noticed after the numbers. [c] All the ratios in parentheses were the proportions of 3',5'- and 2',5'-di-*O*-acrylribonucleosides determined by ^{1}H n.m.r. spectroscopy in terms of the area ratios of the corresponding H-1' signals. [d] This yield was of the product obtained by direct crystallization of the concentrate prior to the silica gel chromatography.

* RT = Room temperature.

corresponding 5′-*O*-acyl derivatives (28% and 11% yields, respectively). Compound (14), in contrast with the others, gave 4-isopropylidenehydrazino-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyrimidin-2(1*H*)-one (16) (22% yield) [19] and 2′,3′,5′-tri-*O*-benzoylcytidine (47% yield) in addition to a mixture of the di-*O*-benzoyl derivatives (*ca.* 25% yield), both of which were syrupy and could not be separated from each other. Compound (15) also failed to give crystalline diacetates, but instead gave a syrupy mixture of the corresponding 3′,5′- and 2′,5′-diacetate (60% yield) * containing 44% of the latter, together with 2′,3′,5′-tri-*O*-acetyl- (11% yield), and 5′-*O*-acetylcytidine (14% yield). The structures of all the products were confirmed by ^{1}H n.m.r. spectroscopy with the double resonance technique as has been reported by Fromageot *et al.*[20] In order to check if the isolated yields of the diacylates reflected, by and large,



(a) 90-MHz ^{1}H n.m.r. spectrum (δ 4—7) of 3′,5′-di-*O*-benzoyladenosine (4) in $(CD_3)_2SO$–D_2O. (b) That in which H-1′ was irradiated.

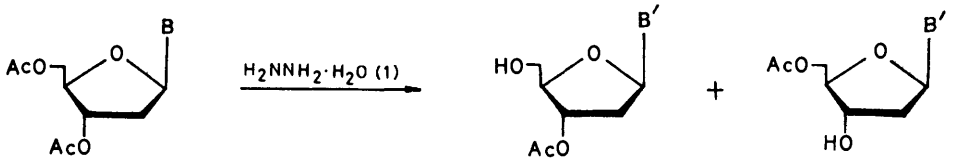
the amount of them actually formed in the reactions, the resulting diacylate mixtures were, prior to crystallization, subjected to the ^{1}H n.m.r. spectroscopic determination. The proportions of the 3′,5′- and 2′,5′-diacylates obtained by comparing the area-ratios of the corresponding H-1′ signals are shown in the 6th column of Table 5. Incidentally, N^2,3′,5′-tribenzoylguanosine was quantitatively converted into N^2,2′,5′-tribenzoylguanosine on dissolution in methanol under reflux and crystallization three times; this is, presumably, a result of the latter, being much more easier to crystallize from alcohols than the former. Any correlation between the isolated yields and the proportions of products formed should therefore be estimated, consideration of acyl migration being taken into account. It is further of interest to notice that the partial *O*-deacylation has been induced at the 2′-position almost regiospecifically in the cases of compounds (2), (3), and (9), judging from the pattern of the anomeric region of the ^{1}H n.m.r. spectra of their resulting mixtures. Almost the same regioselectivity in the partial *O*-deacylation at 70—75 °C (entries 2, 4, and 6) is also of interest in comparing the equilibration time for the foregoing di-*O*-acetyluridine in pyridine; [18] the present results may, therefore, reflect certain effects of unforeseen factors.† The diacylates obtained from (9) and (10) have recently been shown to be useful intermediates for oligonucleotide synthesis in connection with the ' Cap ' structure; [21] they can replace 3′-*O*-acetyl-N^2,5′-dibenzoylguanosine [22] synthesized from N^2,5′-dibenzoylguanosine 2′,3′-methylorthoacetate by partial hydrolysis, followed by chromatographic separation of the resultant 1 : 1 mixture of 2′- and 3′-*O*-acetyl-N^2,5′-dibenzoylguanosine. Gregoire and Neilson [23] have recently proved the utility of the present procedure in the field of nucleic acid chemistry.

With the evidence of the practical utility of the partial *O*-deacylation procedure, we subsequently undertook an investigation of the preparative procedure for 5′-*O*-acylribonucleosides by use of (2) and (12). The 5′-acetates have usually been prepared *via* 2′,3′-*O*-isopropylideneribonucleosides, which undergo 5′-*O*-acylation, followed by *O*-deisopropylidenation.[24] Moreover, partial *O*-deacylation with methanolic ammonia [25] and with morpholine [26] have been reported only with respect to synthesis of 5′-*O*-acetyladenosine. In the light of the study of the solvent effect (see Table 2), we prepared compound (5) and 5′-*O*-benzoyluridine, the conditions and the results thus obtained being summarized in Table 6. The desired products were obtained in quantitative yields, as we expected.

Following this, we were further interested in the behaviour of fully acylated 2′-deoxyribonucleosides toward (1), since they are devoid of the 2′-hydroxy-

* Trials of crystallization of the both products were all unsuccessful.

† The chromatographic separation involved in this procedure using the silica gel of Wakogel C–300 has recently been proved to be crucial to give such regioselectivity (Y. Ishido, N. Sakairi, and I. Hirao, 6th Symposium on Nucleic Acid Chemistry, Nagoya, Japan, October 25—26, 1978).



(17) B = N^6-acetyladenin-9-yl
(18) B = guanin-9-yl
(19) B = N^4-acetylcytosin-1-yl
(20) B = thymin-1-yl

B′ = adenin-9-yl
B′ = guanin-9-yl
B′ = cytosin-1-yl
B′ = thymin-1-yl

SCHEME 2

TABLE 6

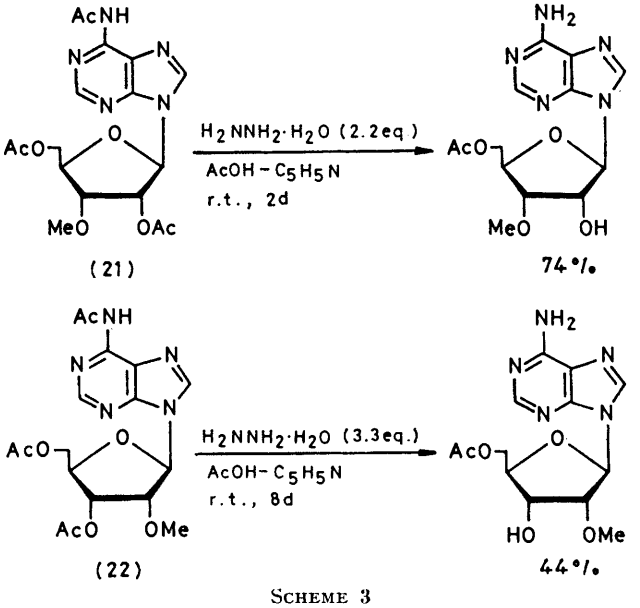
Preparations of 5′-*O*-benzoyladenosine (5) and uridine (12c) by hydrazinolysis [a]

Entry	Fully acylated ribonucleosides (Ns)	Reaction conditions (1)/Ns	Solvent [b]	Period (day)	Yield of product (%)
1	(2)	6	*A*	2	99
2	(2)	6	*B*	3	98
3	(12)	3	*A*	2	87

[a] All reactions were performed at room temperature. [b] *A* 1 : 1 v/v $CHCl_3$–MeOH, and *B* pyridine

group. We chose N^6,3′,5′-triacetyl-2′-deoxyadenosine (17), 3′,5′-di-*O*-acetyl-2′-deoxyguadenosine (18), N^4,3′,-5′-triacetyl-2′-deoxycytidine (19), and 3′,5′-di-*O*-acetylthymidine (20) as the substrates for the partial *O*-deacylation; the acetates were used here because the corresponding benzoates were less reactive than the acetates towards (1). The conditions and the results thus obtained are summarized in Table 7. Compounds (17), (18), (19), and (20) were not susceptible to hydrazinolysis in glacial acetic acid–pyridine (1 : 4, v/v), but in pyridine gave the corresponding 3′- and 5′-*O*-acetyl derivatives; the yields are shown in the table. In contrast, partial *O*-deacylation was unsuccessful in chloroform–methanol (1 : 1, v/v), free 2′-deoxyribonucleosides being given as the main product. According to Andersen *et al.*[27] partial ammonolysis of (17) with methanolic ammonia gave the 3′-acetate (19% yield) and 5′-acetate (29% yield).

Surveying the results obtained here, we further performed partial *O*-deacylation of N^6,2′,5′-triacetyl-3′-*O*-methyl-(21) and N^6,3′,5′-triacetyl-2′-*O*-methyladenosine (22) in order to correlate the activity of the *O*-acetyl groups toward (1); the conditions and the results thus obtained are summarized in Table 8. A striking



SCHEME 3

TABLE 8

Examination of correlative activity of 2′-*O*-acetyl group of (21) and 3′-*O*-acetyl group of (22) toward (1) [a]

N^6,2′ (or 3′), 5′-Triacetyladenosine	Period (day)	Yield of product (%) 2′ (or 3′)-*O*-Methyl-5′-acetate	Diacetate
3′-*O*-Methyl- (21)	2 [b]	(21a) 74	(21b) 14
2′-*O*-Methyl- (22)	8 [c]	(22a) 44	(22b) 54

[a] Both reactions were performed in glacial acetic acid–pyridine (1 : 4, v/v). [b] This reaction was performed by use of (1) (2.2 molar equivalents) at room temperature. [c] This reaction was performed by use of (1) (3.3 molar equivalents) at room temperature.

difference was found between the *O*-acetyl groups in (21) and (22); namely, the 2′-*O*-acetyl group in (21) was much more easily removed than the 3′-*O*-acetyl in (22). The latter was barely removed by use of an excess of (1) even with a reaction period 4 times that used for the deacylation of compound (21). Such a remarkable difference may be rationalized as follows: (i) the *O*-acyl groups at the 2′-position of fully acylated ribonucleosides should be removed first in the partial *O*-deacylation in glacial acetic acid–pyridine; (ii) the resulting 2′-hydroxy-group may hydrogen-bond with the carbonyl oxygen of the 3′-*O*-acyl groups to make the carbonyl carbon more positively charged, the nucleophilic attack of (1) on the carbon in pyridine then being facilitated to give the 5′-acylates. It is of interest to find that the present results are consistent with the neighbouring-group effect for *O*-acyl groups under solvolytic conditions reported by Zachau and Karau.[28,*] In the 2′-deoxynucleosides, the 2′-hydroxy-group is lacking, and thus the comparative stability of the 3′-

* A similar investigation has been performed with respect to cyclopentanediol system by Bruice and Fife (T. C. Bruice and T. H. Fife, *J. Amer. Chem. Soc.*, 1962, **84**, 1973) in the light of those by Henbest and Lovell (H. B. Henbest and B. J. Lovell, *J. Chem. Soc.*, 1957, 1965), on solvolysis of the 3-acetoxy-5-hydroxy-system involved in cholestane and coprostane derivatives, and by Kupchan *et al.* (S. M. Kupchan, W. S. Johnson, and S. Rajagopalam, *Tetrahedron*, 1959, **7**, 47), on solvolysis of germine and cevine derivatives.

TABLE 7

Partial deprotection of fully acetylated 2′-deoxyribonucleosides with hydrazine hydrate [a]

Entry	Nucleoside acetates (Ns)	Conditions (1) : Ns	Period (day)	Yield (%) of 3′-*O*-Acetate	5′-*O*-Acetate
1	N^6,3′,5′-Triacetyl-2′-deoxyadenosine (17)	3	1	(17a) 18	(17b) 65
2	3′,5′-Di-*O*-acetyl-2′-deoxyguanosine (18)	2	1	(18a) 32	(18b) 56
3	N^4,3′,5′-Triacetyl-2′-deoxycytidine (19)	2	2	(19a) 18	(19b) 38
4	3′,5′-Di-*O*-acetylthymidine (20)	2	2	(20a) 32	(20b) 60

[a] All reactions were performed at room temperature in pyridine.

and 5′-*O*-acyl groups towards (1) can be explained in terms of (ii) above; the *O*-acyl groups in contrast with those of the corresponding ribonucleoside derivatives, whose 3′-*O*-acyl groups are more labile than the 5′-*O*-acyl groups, give 5′-*O*-acylates quantitatively under the conditions used (*cf.* Tables 6 and 7). Furthermore, on the basis of these results the concomitant formation of the 3′,5′- and 2′,5′-di-*O*-acylribonucleosides in the partial *O*-deacylation procedure arises, conceivably, as a result of *O*-acyl migration and/or equilibration between the diacylates after removal of the 2′-*O*-acyl groups. In this connection, it is indeed of interest to consider why the reactions at an elevated temperature (see entries 2, 4, and 6 in Table 5) still resulted in marked regioselectivity to give the corresponding 3′,5′-dibenzoates in excellent yields,* and why the 2′-*O*-acyl groups of 2′,5′-diacylates resulting from the acyl migration and/or equilibration can survive under these conditions.† The unusual lability of the 2′-*O*-acyl group of fully acylated ribonucleosides can be assumed to be due to a stronger electron-withdrawing effect of their heterocyclic moieties than the 1-*O*-methyl group of fully acylated methyl β-D-ribofuranosides, which gave the corresponding 2,5-di-*O*-acylates, *i.e.* the 3-OH derivatives, preferentially.†

EXPERIMENTAL

Melting points are uncorrected. U.v. spectra were recorded with a Hitachi EPS-3T spectrometer for solution in ethanol. Specific rotational values were determined with a Hitachi PO-B or Carl Zeiss LEP A-1 polarimeter. ^{1}H N.m.r. spectra were recorded with a Varian EM-390 or T-60 instruments for solutions in $(CD_3)_2SO$ ($SiMe_4$ as internal standard). ^{13}C N.m.r. spectra were recorded with a Varian CFT-20 instrument for the same solutions by Mr. K. Kushida and his staff, ANELVA Corporation. T.l.c. was performed on Merck silica gel 60 F_{254} precoated plates (thickness 0.25 mm) employing benzene–methanol (9 : 1, v/v) or chloroform–methanol (9 : 1, v/v) as eluant. Column chromatography was performed on Wakogel C-300 employing chloroform–methanol as eluant. Liquid–liquid chromatography (l.l.c.) was performed with a Varian LC-8520 apparatus [column of MicroPak CN-10 (15 cm × 2 mm); mobile phase hexane (Silvent A) and 20% propan-2-ol in dichloromethane (Solvent B); solvent composition 25—60% B with a slope of 4% min^{-1}; flow rate 100 ml h^{-1}; detection by u.v. at 260 nm (Variscan apparatus). Elemental analyses were performed by the members of Laboratory of Organic Analysis, Tokyo Institute of Technology.

Pyridine used here was pretreated with 5% aqueous potassium permanganate solution at 50—60 °C before distillation, and redistille from barium oxide.

General Procedure for Examination of Reaction Conditions.—All reactions were performed by use of a solution of (3) [11] (0.1 mmol) in a solvent (3 ml), which was treated with a solution of (1) (1.0 mmol ml^{-1}) under the conditions described in each Table. As for the reactions in pyridine, 10% methanol was added to effect complete dissolution of (1). The resulting solutions were respectively quenched with acetone and then diluted with chloroform to a volume of 10 ml, each of which was subjected to the l.l.c. analysis under the conditions described above in this section. Under the l.l.c. condition, (3), (4) and (5) were detected as peaks with retention times of *ca.* 4, 6, and 10 min.

Partial Debenzoylation of (2) *with* (1).—A solution of (2) [29] (790 mg, 1 mmol) in glacial acetic acid–pyridine (1 : 4, v/v) (10 ml) was treated with (1) (0.16 ml, 3.1 mmol) with stirring at room temperature for 8 days. The resulting mixture was quenched with acetone (5 ml) with stirring at room temperature for several hours, and then evaporated below 50 °C (bath temperature) to give a syrup. Chromatography of the syrup was performed on the silica gel; elution with chloroform gave (3) (55 mg, 10% recovery yield), that with methanol–chloroform (3 : 97, v/v) gave (4) (300 mg, 63% yield; syrup), and that with methanol–chloroform (5 : 95, v/v) gave (5) (93 mg, 25% yield) as well as isopropylidenebenzohydrazide [390 mg, 68% yield based on (1); m.p. 143 °C (from acetone), lit.[30] m.p. 143 °C (from acetone)], which was eluted between the fractions of (2) and (3) as a broad fraction; thus a small amount of the hydrazide still remained inseparable from the bulk of (3).

Attempted Debenzoylation of (2) *with Benzohydrazide.*—Treatment of (2) (1 580 mg, 2 mmol) with benzohydrazide (844 mg, 6.2 mmol) in glacial acetic acid–pyridine (1 : 4, v/v) (20 ml) at room temperature resulted in a quantitative recovery of (2); reaction in pyridine (20 ml) under reflux for 9 h and a similar work-up as has been described above to give (3) (634 mg, 55% yield), N^6,2′,3′,5′-tetrabenoyladenosine [11] (451 mg, 33% yield), and *NN*′-dibenzoylhydrazine (533 mg, 35% yield) [m.p. 243.5 °C (from ethanol); lit.[30] 236 °C (from ethanol)].

Partial O-*Debenzoylation of* (3) *with* (1).—A solution of (3) [11] (10 g, 17.2 mmol) in glacial acetic acid–pyridine (1 : 4, v/v) (150 ml) was treated with (1) (3.35 ml, 68.8 mmol) with stirring at room temperature for 1 day, after which further (1) (1.67 ml, 34.4 mmol) was added, and the mixture was stirred for a second day. The resulting mixture was quenched with acetone (50 ml) and worked up to give (3) (0.5 g, 5% recovery yield), di-*O*-benzoyladenosine (6.6 g, 81% yield), and (5) (0.57 g, 9% yield, after crystallization from methanol). Crystallization of the second fraction gave (4) (5.23 g, 64% yield). The reaction at 70—75 °C for 15 h, followed by work-up, gave (4) (70% yield) by crystallization of the resulting syrupy dibenzoate (80% yield) as well as (3) (13% recovery).

Compound (4) had m.p. 193—194 °C (from methanol or chloroform), $[\alpha]_D^{22}$ −55° (*c* 1.3 in Me_2NCHO), $\lambda_{max.}$ (EtOH) 246 nm (ε 13 400); δ_H[$(CD_3)_2SO$–$SiMe_4$] *ca.* 5.7 (3 H, m, H-4′, 5′, and 5″), 5.80 (1 H, m, H-3′), 5.28 (1 H, q, $J_{2',3'}$ 6.0 Hz, H-2′), 6.13 (1 H, d, $J_{2',2'\text{-OH}}$ 6.0 Hz, 2′-OH), 6.16 (1 H, d, $J_{1',2'}$ 6.0 Hz, H-1′), 7.36br (2 H, s, NH_2), 8.15 (1 H, s, H-8), and 8.43 (1 H, s, H-2); δ_C[$(CD_3)_2SO$–$SiMe_4$] 64.1 (C-5′), 71.3 (C-3′), 73.3 (C-2′), 79.5 (C-4′), 88.3 (C-1′), 119.6 (C-5), 140.3 (C-8), 149.6 (C-4), 152.9 (C-2), and 156.3 (C-6) (Found: C, 60.4; H, 4.45; N, 14.55. $C_{24}H_{21}N_5O_6$ requires C, 60.6; H, 4.45; N, 14.75%).

Compound (5) had m.p. 126—129 °C followed by liquefaction at 158 °C (from methanol) (lit.,[31] m.p. 106—108 °C, dihydrate); $[\alpha]_D^{18}$ −35.6° (*c* 1.5 in Me_2NCHO), $\lambda_{max.}$ (EtOH)

* An investigation in connection with this problem is now in progress in terms of spectroscopic techniques.

† Y. Ishido, M. Sekiya, and N. Nakazaki, unpublished results; presented at 2nd Joint Meeting of Canad. Chem. Inst. and Amer. Chem. Soc., Montreal, May 29—June 2, 1977; Abstract, CARB 28; in addition to the electronic effect of the aglycone moiety, conformational factors are conceivable to be involved in affording the excellent regioselectivity, and are under investigation.

259 (ε 15 900) and 231 nm (ε 14 700); $\lambda_{min.}$ (EtOH) 243.5 nm (ε 11 600); δ_H[$(CD_3)_2SO$–$SiMe_4$] 4.33 (1 H, q, $J_{3',4'}$ 3.5 Hz, H-4'), *ca.* 4.5 (3 H, m, H-3', 5', and 5''), 4.85 (1 H, m, $J_{2',3'}$ 3.5 Hz, H-2'), 5.46 and 5.65 (2 H, $J_{2',2'\text{-OH}}$ 5.5 Hz and $J_{3'3'\text{-OH}}$ 5.5 Hz, 2'- and 3'-OH), 6.02 (1 H, d, $J_{1'.2'}$ 3.5 Hz, H-1'), 7.31br (2 H, s, NH_2), 8.16 (1 H, s, H-8), and 8.33 (1 H, s, H-2); δ_C[$(CD_3)_2SO$–$SiMe_4$] 64.4 (C-5'), 70.3 (C-3'), 73.0 (C-2'), 81.6 (C-4'), 88.3 (C-1'), 119.4 (C-5), 140.1 (C-8), 149.1 (C-8), 149.4 (C-4), 152.8 (C-2), and 156.2 (C-6) (Found: C, 52.55; H, 4.8; N, 17.9. $C_{17}H_{17}N_5O_5 \cdot H_2O$ requires C, 52.45; H, 4.9; N, 18.0%).

Partial O-Debenzoylation of (6) *with* (1).—A solution of (6) [32] (3.5 g, 5 mmol) in glacial acetic acid–pyridine (1 : 4, v/v) (100 ml) was treated with (1) (0.97 ml, 20 mmol) at room temperature for 1 day. The same work-up as described above after the reaction gave N^2,3',5'-tribenzoylguanosine (6a) (1.87 g, 63% yield), by crystallization of the resulting syrup (2.83 g, 82% yield), and N^2,5'-dibenzoylguanosine (6c) (0.27 g, 11% yield) together with the recovery of (6) (0.21 g, 6% yield). The reaction at 70—75 °C for 10 h by use of (6) (3.5 g, 5 mmol) and (1) (0.49 ml, 10 mmol), followed by the same work-up, gave (6a) (1.66 g, 55% yield), by crystallization of the resulting syrup (77% yield), and (6c) (9% yield) as well as (6) (13% recovery yield).

Compound (6a) had m.p. 230—231.5° (from methanol), $[\alpha]_D^{18}$ −11.6° (c 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 297 (ε 13 800), 284 (ε 15 200), 257 (ε 15 300), and 232 nm (ε 36 700); $\lambda_{max.}$ (EtOH) 290 (ε 13 500), 273 (ε 12 200), 261 (ε 15 000), and 253.5 nm (ε 15 200); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 4.6—4.8 (3 H, m, H-4', 5', and 5''), 5.6—5.8 (1 H, m, H-3'), 5.0—5.3 (1 H, m, $J_{1'.2'}$ 7.5 Hz, H-2'), 6.03 (1 H, d, H-1'), and 8.27 (1 H, s, H-8); δ_C[$(CD_3)_2SO$–$SiMe_4$] 64.3 (C-5'), 71.3 (C-3'), 73.5 (C-2'), 79.7 (C-4'), 87.2 (C-1)', 121.0 (C-5), 138.1 (C-8), 148.2 (C-4), 148.9 (C-2), and 155.0 (C-6) (Found: C, 60.85; H, 4.3; N, 11.3. $C_{31}H_{25}N_5O_8 \cdot H_2O$ requires C, 60.7; H, 4.45; N, 11.4%).

Compound (6c) had m.p. 235—236 °C (from methanol) (lit.,[33] m.p. 231—232°), $[\alpha]_D^{18}$ −2.0° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 231 (ε 24 500) and 296 nm (ε 13 500); $\lambda_{shoulder}$ (EtOH) 253—265 nm (ε 12 900); $\lambda_{min.}$ (EtOH) 273 nm (ε 10 900); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 5.99 (1 H, d, $J_{1',2'}$ 4.8 Hz, H-1') and 8.24 (1 H, s, H-8); δ_C[$(CD_3)_2SO$–$SiMe_4$] 64.5 (C-5'), 70.2 (C-3'), 73.2 (C-2'), 81.7 (C-4'), 87.3 (C-1'), 121.0 (C-5), 138.1 (C-8), 148.1 (C-2), and 155.0 (C-6) (Found: C, 56.25; H, 4.2; H, 13.75. $C_{24}H_{21}N_5O_7 \cdot 1/2H_2O$ requires C, 57.6; H, 4.45; N, 14.0%).

A Quantitative Conversion of (6a) *into* (6b).—Compound (6a) (200 mg) was dissolved in methanol (20 ml) under reflux, and the resulting solution was allowed to cool to room temperature; this procedure was further repeated twice, giving (6c) (185 mg, 93% yield).

Compound (6b) had m.p. 145—146° (from methanol) (lit.,[33] m.p. 146—147 °C); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 4.9—5.1 (1 H, m, H-3'), 5.93 (1 H, dd, $J_{1'.2'}$ 4.0 Hz and $J_{2'.3'}$ 3.0 Hz, H-2'), 6.35 (1 H, d, H-1'), and 8.30 (1 H, s, H-8).

Partial O-*Debenzoylation of* (7).—A solution of (7) [34] (5.97 g, 10.3 mmol) in glacial acetic acid–pyridine (1 : 4, v/v) (60 ml) was treated with (1) (1.0 ml, 21 mmol) at room temperature for 2 days, and the resulting solution was worked up as above described to give 3',5'-di-*O*-benzoylinosine (7a) (2.49 g, 51% yield) by crystallization of the resulting syrup (3.6 g, 74% yield), and 5'-*O*-benzoylinosine (7c) (0.38 g, 10% yield) together with recovery of (7) (0.58 g, 10% yield). The reaction of (7) (2.9 g, 5 mmol) in the solvent (30 ml) at 70—75 °C, followed by the same work-up, gave (7a) (1.24 g, 52% yield) by crystallization of the syrup (1.9 g, 80% yield), and the recovery of (7) (0.46 g, 16% yield).

Compound (7a) had m.p. 167—168 °C (from methanol), $[\alpha]_D^{22}$ −60° (*c* 1.0 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 230.5 nm (ε 25 700), $\lambda_{shoulder}$ (EtOH) 251 (ε 11 300), 273 (ε 5 900), and 281.5 nm (ε 4 000); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 5.85 (1 H, m, $J_{2',3'}$ 7.0 Hz, H-3'), 5.26 (1 H, t, $J_{1',2'}$ 7.0 Hz, H-2'), 6.20 (1 H, d, H-1'), 8.03 (1 H, s, H-8), and 8.40 (1 H, s, H-2); δ_C[$(CD_3)_2SO$–$SiMe_4$] 64.1 (C-5'), 71.8 (C-3'), 73.2 (C-2'), 79.7 (C-4'), 88.3 (C-1'), 125.1 (C-5), 139.5 (C-8), 146.1 (C-2), 148.5 (C-4), and 156.7 (C-6) (On drying over P_2O_5 under 0.6 mmHg at 110 °C for 6 h, Found: C, 60.5; H, 4.25; N, 11.75. $C_{24}H_{20}N_4O_7$ requires C, 60.5; H, 4.25; N, 11.8%).

The 2',5'-dibenzoate in the residual syrup had δ_H[$(CD_3)_2$-SO–$SiMe_4$; D_2O was added] 6.46 (1 H, d, $J_{1',2'}$ 4.5 Hz, H-1').

Compound (7c) had m.p. 169 °C (from methanol), $[\alpha]_D^{18}$ −55.5° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 232 nm (ε 16 000). $\lambda_{shoulder}$ (EtOH) 259 (ε 10 400) and 273 nm (ε 4 600) δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 4.3—4.7 (3 H, m, H-4', 5', and 5''; 4.57 (1 H, q, $J_{3',4'}$ 9.0 Hz, $J_{2',3'}$ 4.5 Hz, and $J_{3',3'\text{-OH}}$ 6.0 Hz, H-3'), 4.82 (1 H, t, $J_{1',2'}$ 4.5 Hz and $J_{2',2'\text{-OH}}$ 6.0 Hz, H-2') [5.52 (1 H, d, 3'-OH) and 5.72 (1 H, d, 2'-OH) were observed prior to addition of D_2O], 6.05 (1 H, d, H-1'), 8.10 (1 H, s, H-8), and 8.33 (1 H, s, H-2); δ_C[$(CD_3)_2SO$–$SiMe_4$] 64.6 (C-5'), 70.5 (C-3'), 73.7 (C-2'), 82.2 (C-4'), 88.7 (C-1'), 125.1 (C-5), 139.7 (C-8), 146.3 (C-2), 148.7 (C-4), and 157.2 (C-6) (Found: C, 53.8; H, 4.35; N, 14.8. $C_{17}H_{16}N_4O_6 \cdot 1/2H_2O$ requires C, 53.55; H, 4.5; N, 14.7%).

Partial O-*Deacetylation of* (8).—A solution of (8) [35] (1.97 g, 5 mmol) in the solvent (50 ml) was treated with (1) (0.29 ml, 6 mmol) at room temperature for 1 day, and the resulting solution was worked up as described above to give 3',5'-di-*O*-acetyladenosine (8a) (0.93 g, 53% yield) by crystallization of the resulting syrup (1.34 g, 76% yield), and (8) (0.19 g, 10% recovery yield).

Compound (8a) had m.p. 172—173 °C (from methanol) (lit.,[9] m.p. 175—176 °C), $[\alpha]_D^{18}$ −50.6° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 259 nm (ε 13 600); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.05 (3 H, s, OAc), 2.15 (3 H, s, OAc), *ca.* 4.3 (3 H, m, H-4', 5', and 5''), 5.2—5.4 (1 H, m, H-3'), 5.05 (1 H, t, $J_{1',2'}$ 6.0 Hz and $J_{2'.3'}$ 6.0 Hz, H-2'), 5.93 (1 H, d, H-1'), 8.18 (1 H, s, H-8), and 8.37 (1 H, s, H-2) (Found: C, 47.9; H, 4.9; N, 20.2. $C_{14}H_{17}N_5O_6$ requires C, 47.85; H, 4.9; N, 19.95%).

Partial O-*Deacetylation of* (9).—A solution of (9) [35] (5.66 g, 12.5 mmol) in the solvent (100 ml) was treated with (1) (0.73 ml, 15 mmol) at room temperature for 2 days, and worked up as described above to give N^2,3',5'-triacetylguanosine (9a) (2.67 g, 52% yield) by crystallization of the resulting syrupy mixture (3.54 g, 69% yield), and (9) (0.53 g, 9% recovery yield).

Compound (9a) had m.p. 131—132 °C (from methanol), $[\alpha]_D^{18}$ −36° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 280 (ε 11 600), 259 (ε 15 700), and 254 nm (ε 15 700); $\lambda_{min.}$ (EtOH) 271 (ε 11 600) and 257 nm (ε 15 600); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.03 (3 H, s, OAc), 2.06 (3 H, s, OAc), 2.20 (3 H, s, NAc), 5.2—5.4 (1 H, m, $J_{2'.3'}$ 6.0 Hz, H-3'), 4.80 (1 H, t, $J_{1'.2'}$ 6.0 Hz, H-2'), 5.90 (1 H, d, H-1'), and 8.00 (1 H, s, H-8) (Found: C, 43.25; H, 4.95; N, 15.85. $C_{16}H_{19}N_5O_8 \cdot 2H_2O$ requires C, 43.15; H, 5.2; N, 15.75%).

N^2-*Benzoylation of* 2′,3′,5′-*Tri*-O-*acetylguanosine*.—A suspension of 2′,3′,5′-tri-*O*-acetylguanosine [35] (15 g) in pyridine (100 ml) was treated with benzoyl chloride (12 ml) at 50—60 °C for h with stirring. The resulting mixture was poured into ice–water, and the mixture was extracted with chloroform. The organic layer was then washed successively with 1M-hydrochloric acid, aqueous sodium hydrogen carbonate solution, and water, and was then dried (Na_2SO_4). The organic layer was, after filtering off the desiccant, evaporated to dryness, and the residue chromatographed on a column of silica gel by use of chloroform–methanol to give 2′,3′,5′-tri-*O*-acetyl-N^2-benzoylguanosine (10) (16.6 g, 87% yield; syrup), which was identified with an authentic specimen [23] by ^{1}H n.m.r. spectroscopy.

Partial O-*Deacetylation of* (10).—A solution of (10) (7.87 g, 15.3 mmol) in the solvent (50 ml) was treated with (1) (0.89 ml, 18.4 mmol) at room temperature for 1 day, and the resulting mixture was evaporated to a syrup; crystallization of the syrup gave 3′,5′-di-*O*-acetyl-N^2-benzoylguanosine (10a) (3.03 g, 42% yield).

Compound (10a) had m.p. 127—128 °C (from methanol) (lit.,[23] m.p. 131—133 °C), $[\alpha]_D^{18}$ −21° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 269 (ε 14 300), 264 (ε 13 700), 257 (ε 13 900), and 237.5 nm (ε 16 300); $\lambda_{min.}$ (EtOH) 273 (ε 10 200), 262 (ε 13 600), and 252.5 nm (ε 13 700); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.10 (3 H, s, OAc), 2.18 (3 H, s, OAc), 5.3—5.5 (1 H, m, $J_{2',3'}$ 6.0 Hz, H-3′), 5.00 (1 H, t, $J_{1',2'}$ 6.0 Hz, H-2′), 6.03 (1 H, d, H-1′), and 8.33 (1 H, s, H-8) (Found: C, 51.25; H, 4.75; N, 14.2. $C_{21}H_{21}N_5O_8 \cdot H_2O$ requires C, 51.55; H, 4.75; N, 14.3%).

Partial O-*Deacetylation of* (11).—A solution of (11) [35] (1.18 g, 3 mmol) in solvent (20 ml) was treated with (1) (0.16 ml, 0.33 mmol) at room temperature for 2 days, and the resulting mixture was worked up as described above to give 2′,5′-di-*O*-acetylinosine (11b) (0.32 g, 30% yield) by crystallization of the resulting syrup (0.90 g, 85% yield) at room temperature for 2 weeks, and 5′-*O*-acetylinosine (11c) (0.1 g, 10% yield).

Compound (11b) had m.p. 210—211 °C (from methanol), $[\alpha]_D^{22}$ −53° (*c* 0.8 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 244 nm (ε 10 800); $\lambda_{shoulder}$ (EtOH) 250 (ε 9 800) and 274 nm (ε 2 800); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.00 (3 H, s, OAc), 2.07 (3 H, s, OAc), 4.0—4.4 (3 H, m, H-4′, 5′, and 5″), 4.4—4.7 (1 H, m, $J_{2',3'}$ 4.5 Hz, H-3′), 5.61 (1 H, t, $J_{1',2'}$ 4.5 Hz, H-2′), 6.12 (1 H, d, H-1′), 8.03 (1 H, s, H-8), and 8.23 (1 H, s, H-2) (after drying over P_2O_5 under 0.2 mmHg at 110 °C for 5 h, Found: C, 47.3; H, 4.65; N, 16.1. $C_{14}H_{16}N_4O_7$ requires C, 47.75; H, 4.6; N, 15.9%).

Compound (11c) had m.p. 117—118 °C followed by liquefaction at 171 °C (from methanol), $[\alpha]_D^{18}$ −32.4° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 249 (ε 10 700) and 244 nm (ε 10 700); $\lambda_{min.}$ (EtOH) 247 nm (ε 10 500); $\lambda_{shoulder}$ (EtOH) 274 nm (ε 3 900); δ_C[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 4.0—4.4 (4 H, m, H-3′, 4′, 5′, and 5″), 4.55 (1 H, t, $J_{1',2'}$ 4.5 Hz and $J_{2',3'}$ 4.5 Hz, H-2′), 5.88 (1 H, d, H-1′), 8.05 (1 H, s, H-8), and 8.28 (1 H, s, H-2) (Found: C, 44.8; H, 4.65; N, 17.8. $C_{12}H_{14}N_4O_6 \cdot 1/2H_2O$ requires C, 45.15; H, 4.75; N, 17.55%).

Partial O-*Debenzoylation of* (12).—A solution of (12) [36] (1.11 g, 2 mmol) in solvent (30 ml) was treated with (1) (0.12 ml, 2.4 mmol) at room temperature for 4 days, and the resulting mixture was worked as described above to give 3′,5′-di-*O*-benzoyluridine (12a) (0.35 g, 39% yield) by crystallization of the resulting syrup (0.59 g, 65% yield), and 5′-*O*-benzoyluridine (12c) (0.1 g, 13% yield).

Compound (12a) had m.p. 199.5—200.5 °C (from methanol) (lit.,[24] m.p. 187—189 °C), $[\alpha]_D^{18}$ −35.5° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 258 (ε 11 000) and 230 nm (ε 24 400); $\lambda_{min.}$ (EtOH) 250 nm (ε 9 000); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 4.4—4.7 (4 H, m, H-2′, 4′, 5′, and 5″), 5.4—5.6 (1 H, m, H-3′), 5.62 (1 H, d, $J_{5,6}$ 8 Hz, H-5), and 5.88 (1 H, d, $J_{1',2'}$ 6 Hz, H-1′); δ_C[$(CD_3)_2SO$–$SiMe_4$] 64.0 (C-5′), 71.2 (C-3′), 72.6 (C-2′), 78.8 (C-4′), 89.7 (C-1′), 102.3 (C-5), 141.1 (C-6), 150.6 (C-2), and 163.1 (C-4) (Found: C, 60.7; H, 4.45; N, 6.05. $C_{23}H_{21}N_2O_7$ requires C, 61.05; H, 4.45; N, 6.2%).

The 2′,5′-dibenzoate in the residual syrup had δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 6.08 (1 H, d, $J_{1',2'}$ 3 Hz, H-1′).

Compound (12c) had m.p. 163—164 °C (from methanol) (lit.,[24] m.p. 169—170 °C), $[\alpha]_D^{18}$ −5.2° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 261 (ε 10 300) and 230 nm (ε 14 600; $\lambda_{min.}$ (EtOH) 249 nm (ε 7 300); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 4.1—4.4 (4 H, m, H-2′, 4′, 5′, and 5″), 4.5—4.7 (1 H, m, H-3′), 5.50 (1 H, d, $J_{5,6}$ 9 Hz, H-5), and 5.86 (1 H, d, $J_{1',2'}$ 2.3 Hz, H-1′); δ_C[$(CD_3)_2SO$–$SiMe_4$] 65.2 (C-5′), 70.8 (C-3′), 73.9 (C-2′), 82.1 (C-4′), 90.3 (C-1′), 103.0 (C-5), 141.8 (C-6), 151.6 (C-2), and 164.1 (C-4) (Found: C, 55.05; H, 4.6; N, 8.0. $C_{16}H_{16}N_2O_7$ requires C, 55.15; H, 4.65; N, 8.05%).

Partial O-*Deacetylation of* (13).—A solution of (13) [37] (1.11 g, 3 mmol) in solvent (30 ml) was treated with (1) (0.18 ml, 3.6 mmol) at room temperature for 3.5 h, and the resulting solution was worked up as described above to give 3′,5′-di-*O*-acetyluridine (13a) (0.45 g, 46% yield) by crystallization of the resulting syrup (0.74 g, 76% yield), and 5′-*O*-acetyluridine (13c) (0.10 g, 11% yield).

Compound (13a) had m.p. 150—152 °C (from methanol) (lit.,[9] m.p. 152—154 °C), $[\alpha]_D^{18}$ −6.4° (c 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 259 nm (ε 9 600); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.10 (6 H, s, OAc), *ca.* 4.4 (4 H, m, H-2′, 4′, 5′, and 5″), 5.00 (1 H, m, H-3′), 5.80 (1 H, d, $J_{5,6}$ 8.3 Hz, H-5), 5.90 (1 H, d, $J_{1',2'}$ 5.2 Hz, H-1′), and 7.60 (1 H, d, H-6) (Found: C, 47.7; H, 4.95; N, 8.61. $C_{13}H_{16}N_2O_8$ requires C, 47.6; H, 4.9; N, 8.55%).

Compound (13c) had m.p. 162—163 °C (from methanol) (lit.,[37] m.p. 163—164 °C), $[\alpha]_D^{18}$ −2.7° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 261 nm (ε 9 200); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.08 (3 H, s, OAc), 3.9—4.4 (5 H, m, H-2′, 3′, 4′, 5′, and 5″), 5.67 (1 H, d, $J_{5,6}$ 7.5 Hz, H-5), 5.73 (1 H, d, $J_{1',2'}$ 3.5 Hz, H-1′), and 7.57 (1 H, d, H-6) (Found: C, 46.15; H, 5.0; N, 9.85. $C_{11}H_{14}N_2O_7$ requires C, 46.15; H, 4.95; N, 9.8%).

Attempted Partial O-*Debenzoylation of* (14).—A solution of (14) [38] (1.29 g, 2 mmol) in solvent (30 ml) was similarly treated with (1) (0.3 ml, 6 mmol) at room temperature for 8 days, and the resulting solution was worked up as described above to give 4-isopropylidenehydrazino-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyrimidin-2(1*H*)-one (16) (0.27 g, 22% yield) and a mixture of 3′,5′- and 2′,5′-di-*O*-benzoylcytidine (0.22 g, 25% yield) together with 2′,3′,5′-tri-*O*-benzoylcytidine (0.51 g, 47% yield).

Compound (16) had m.p. 209.5—211 °C (from methanol), $[\alpha]_D^{22}$ −76° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 283 nm (ε 18 300); $\lambda_{min.}$ (EtOH) 254 nm (ε 11 300); δ_H[$(CD_3)_2SO$–$SiMe_4$] *ca.* 4.7 (3 H, m, H-4′, 5′, and 5″), 5.61 (1 H, d, $J_{5,6}$ 8.3 Hz, H-5), *ca.* 5.8 (2 H, m, H-2′, and 3′), 6.39 (1 H, d, $J_{1',2'}$ 6.0 Hz, H-1′), and 6.90 (1 H, d, H-6) (Found: C, 65.0; H, 5.0; N, 9.05. $C_{33}H_{30}N_4O_8$ requires C, 64.9; H, 4.95; N, 9.2%).

A mixture of 3,5- and 2,5-di-*O*-benzoylcytidine was syrupy and had δ_H[$(CD_3)_2SO$–$SiMe_4$] 5.87 (1 H, d, $J_{1'.2'}$ 3.8 Hz, H-1′ of the former) and 6.03 (1 H, d, $J_{1'.2'}$ 3.0 Hz, H-1′ of the latter) (Found: C, 61.3; H, 4.8; N, 9.5. $C_{23}H_{21}N_3O_7$ requires C, 61.2; H, 4.7; N, 9.3%).

2′,3′,5-Tri-*O*-benzoylcytidine (powder) had m.p. 183—184 °C (from ethanol) (lit.,[11] m.p. 183—184 °C).

Attempted Partial O-Deacetylation of (15).—A solution of (15) [39] (0.88 g, 2.1 mmol) in solvent (30 ml) was treated with (1) (0.23 ml, 4.6 mmol) at room temperature for 3 h, and the resulting solution was worked up as described above to give a mixture of 3′,5- and 2′,5′-di-*O*-acetylcytidine (0.42 g, 60% yield) and 5-*O*-acetylcytidine (15c) (0.08 g, 14% yield).

The mixture (syrup) had δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.03 (6 H, s, OAc of the diacetates), 5.02 (m, H-3′ of the former), 5.19 (dd, H-2′ of the latter), and 7.63 (1 H, d, $J_{5.6}$ 7.5 Hz, H-6 of the diacetates) (Found: C, 47.75; H, 5.35; N, 12.75. $C_{13}H_{17}N_3O_7$ requires C, 47.7; H, 5.25; N, 12.85%).

Compound (15c) [40] (syrup) had $[\alpha]_D^{18}$ +22° (*c* 0.8 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 270 nm (ε 8 200) [lit.,[40] $\lambda_{max.}$ (H_2O) 270 and 230 nm]: δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.06 (3 H, s, OAc), *ca.* 4.0 (3 H, m, H-4, 5, and 5″), *ca.* 4.3 (2 H, m, H-2′ and 3′), 5.93 (1 H, d, $J_{5.6}$ 8.0 Hz, H-5), (1 H, d, $J_{1'.2'}$ 3.0 Hz, H-1′), and 7.60 (1 H, d, H-6).

Compound (5) *from* (2).—A solution of (2) (1.58 g, 2 mmol) in pyridine (50 ml) was treated with (1) (0.58 ml, 12 mmol) at room temperature for 3 days, and worked up as described above to give (5) (0.74 g, 99% yield). The reaction in chloroform–methanol (1 : 1, v/v) (50 ml) with (1) at room temperature for 2 days, followed by quenching with acetone, evaporation, dilution with chloroform, removal of insoluble material by filtration, and crystallization from methanol, gave (5) (0.63 g, 98% yield).

Compound (12c) *from* (12).—A solution of (12) (1.11 g, 2 mmol) in chloroform–methanol (1 : 1, v/v) (30 ml) was treated with (1) (0.29 ml, 6 mmol) at room temperature for 2 days, followed by the column chromatographic separation and crystallization from ethanol, gave (12c) (0.61 g, 87% yield).

Partial O-Deacetylation of (17).—A solution of (17) [27] (667 mg, 2 mmol) in pyridine (20 ml) was treated with (1) (0.3 ml, 6 mmol) at room temperature for 1 day, and worked up in the same way as described for compound (3) to give 3′-*O*-acetyl-2′-deoxyadenosine (17a) (110 mg, 18% yield) and 5′-*O*-acetyl-2′-deoxyadenosine (17b) (379 mg, 65% yield) together with 3′,5′-di-*O*-acetyl-2′-deoxyadenosine (90 mg, 13% yield).

3′,5′-di-*O*-acetyl-2′-deoxyadenosine (syrup) had δ_H[$(CD_3)_2SO$–$SiMe_4$] 2.00 (3 H, s, OAc), 2.05 (3 H, s, OAc), 2.50 (1 H, ddd, $J_{1'.2'}$ 6.0 Hz, $J_{2'.2''}$ 13.5 Hz, and $J_{2'.3'}$ 2.5 Hz, H-2′), 2.97 (1 H, ddd, $J_{1'.2''}$ 7.0 Hz and $J_{2''.3'}$ 7.5 Hz, H-2″), *ca.* 4.3 (3 H, m, H-4′, 5′, and 5″), 5.26—5.50 (1 H, m, H-3′), 6.35 (1 H, dd, H-1′), 8.00 (1 H, s, H-8), and 8.23 (1 H, s, H-2).

Compound (17a) had m.p. 218.0—219.0 °C (from ethyl acetate) (lit.,[27] m.p. 211—212.5 °C), $[\alpha]_D^{18}$ −32.8° (*c* 1.35 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 260 nm (ε 14 500); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added) 2.10 (3 H, s, OAc), 2.50 (1 H, ddd, $J_{1'.2'}$ 6.0 Hz, $J_{2'.2''}$ 14.0 Hz, and $J_{2'.3'}$ *ca.* 1.5 Hz, H-2′), 2.65 (1 H, ddd, $J_{1'.2''}$ 7.5 Hz, and $J_{2''.3'}$ 7.5 Hz, H-2″), 3.6—3.8 (2 H, m, H-5′ and 5″), 4.1—4.2 (1 H, m, H-4′), 5.35—5.6 (1 H, m, H-3′), 6.40 (1 H, dd, H-1′), 8.17 (1 H, s, H-8), and 8.32 (1 H, s, H-2) (Found: C, 48.9; H, 5.15; N, 24.1. $C_{12}H_{15}N_5O_4$ requires C, 49.15; H, 5.16; N, 23.9%).

Compound (17b) (syrup) had $[\alpha]_D^{18}$ −7.6° (*c* 1.65 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 260 nm (ε 15 000) [lit.,[27] m.p. 140—141 °C; $\lambda_{max.}$ (EtOH) 260 nm (ε 14 400]; δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.00 (3 H, s, OAc), 2.36 (1 H, ddd, $J_{1'.2'}$ 6.0 Hz, $J_{2'.2''}$ 14.0 Hz, and $J_{2'.3'}$ 4.5 Hz, H-2′), 2.90 (1 H, dt, $J_{1'.2''}$ 6.0 Hz and $J_{2''.3'}$ 6.0 Hz, H-2″), 3.9—4.1 (1 H, m, H-4′), 4.2—4.4 (2 H, m, H-5′ and 5″), 4.4—4.6 (1 H, m, H-3′), 6.40 (1 H, t, H-1′), 8.20 (1 H, s, H-8), and 8.33 (1 H, s, H-2) (Found: C, 49.15; H, 5.2; N, 23.6. $C_{12}H_{15}N_5O_4$ requires C, 49.15; H, 5.15; N, 23.9%).

Partial O-Deacetylation of (18).—A solution of (18) [41] (550 mg, 1.5 mmol) in pyridine (10 ml) was treated with (1) (0.15 ml, 3 mmol) at room temperature for 1 day, followed by work-up, to give 3′-*O*-acetyl-2′-deoxyguanosine (18a) (150 mg, 32% yield) and 5′-*O*-acetyl-2′-deoxyguanosine (18b) (260 mg, 56% yield); (18) (40 mg, 8% yield) was recovered unchanged.

Compound (18a) had m.p. >250 °C (from methanol) (lit.,[41] m.p. >240 °C), $[\alpha]_D^{18}$ −13.3° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 254 nm (ε 13 800); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.07 (3 H, s, OAc), 2.40 (1 H, ddd, $J_{1'.2'}$ 6.0 Hz, $J_{2'.2''}$ 13.5 Hz, and $J_{2'.3'}$ 6.0 Hz, H-2′), 2.80 (1 H, dd, $J_{1'.2''}$ 9.0 Hz, H-2″), 3.5—3.7 (2 H, m, H-5′ and 5″), 3.9—4.1 (1 H, m, H-4′), 5.35—5.4 (1 H, m, H-3′), 6.13 (1 H, dd, H-1′), and 7.95 (1 H, s, H-8) (Found: C, 45.25; H, 4.75; N, 21.8. $C_{12}H_{15}N_5O_5 \cdot 1/2H_2O$ requires C, 45.3; H, 5.05; N, 22.0%).

Compound (18b) had m.p. 166—168 °C (decomp.) (from aqueous ethanol) [lit.,[41] m.p. 170 °C (decomp.)], $[\alpha]_D^{18}$ −31.0° (*c* 1.65 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 260 nm (ε 10 000); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.03 (3 H, s, OAc), 2.30 (1 H, ddd, $J_{1'.2'}$ 7.0 Hz, $J_{2'.2''}$ 13.5 Hz, and $J_{2'.3'}$ 4.5 Hz, H-2′), 2.72 (1 H, ddd, $J_{1'.2''}$ 7.0 Hz and $J_{2''.3'}$ *ca.* 1 Hz, H-2″), 3.8—4.1 (1 H, m, H-4′), 4.1—4.3 (2 H, m, H-5′ and 5″), 4.3—4.5 (1 H, m, H-3′), 6.15 (1 H, t, H-1′), and 7.87 (1 H, s, H-8) (Found: C, 43.95; H, 5.15; N, 21.1. $C_{12}H_{15}N_5O_5 \cdot H_2O$ requires C, 44.05; H, 5.25; N, 21.2%).

N⁴,3′,5′-*Triacetyl-2′-deoxycytidine* (19).—To a solution of 2′-deoxycytidine (3 g) in anhydrous pyridine (30 ml) was added acetic anhydride (10 ml) with ice cooling; the resulting mixture was set aside overnight at room temperature and was then treated with methanol with ice cooling and evaporated to dryness. The residue was chromatographed to give syrupy (19) (4.0 g, 86% yield); this was confirmed as pure enough in terms of t.l.c. [R_F 0.46 chloroform–methanol (9 : 1, v/v)] for subsequent use.

Compound (19) had δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.06 (6 H, s, OAc), 2.27 (3 H, s, NAc), 2.6—3.0 (2 H, m, $J_{1'.2'}$ 6.0 Hz and $J_{1'.2''}$ 8.0 Hz, H-2′ and H-2″), 4.2—4.4 (3 H, m, H-4′, 5′, and 5″), 5.1—5.3 (1 H, m, H-3′), 6.20 (1 H, dd, H-1′), 7.50 (1 H, d, $J_{5.6}$ 8 Hz, H-5), and 8.03 (1 H, d, H-6)

Partial Deacetylation of (19).—A solution of (19) (1.29 g, 3.6 mmol) in pyridine (50 ml) was treated with (1) (0.4 ml, 8 mmol) at room temperature for 1 day, and the resulting mixture was worked up as described above to give 3′,5′-di-*O*-acetyl-2′-deoxycytidine (290 mg, 25% yield), 3′-*O*-acetyl-2′-deoxycytidine (19a) (130 mg, 13% yield), and 5′-*O*-acetyl-2′-deoxycytidine (19b) (380 mg, 38% yield).

3′,5′-Di-*O*-acetyl-2′-deoxycytidine (syrup) had δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.06 (6 H, s, OAc), 2.6—3.0 (2 H, m, $J_{1'.2'}$ 6.0 Hz and $J_{1'.2''}$ 6.0 Hz, H-2′ and 2″), 4.15—4.45 (3 H, m, H-4′, 5′, and 5″), 5.10—5.35 (1 H, m, H-3′), 5.80 (1 H, d, $J_{5.6}$ 7.0 Hz, H-5), 6.20 (1 H, t, H-1′), and 7.60 (1 H, d, H-6).

Compound (19a) (syrup) had $\lambda_{max.}$ (EtOH) 273 nm (ε 8 400); δ_H[$(CD_3)_2SO$; $SiMe_4$; D_2O was added] 2.05 (3 H, s, OAc), 2.00—2.3 (2 H, m, $J_{1'.2'}$ 6.0 Hz and $J_{1'.2''}$ 6.0 Hz, H-2′ and 2″), 3.95—4.3 (3 H, m, H-4′, 5′, and 5″), 5.1—5.3 (1 H, m, H-3′), 5.80 (1 H, d, $J_{5.6}$ 7.0 Hz, H-5), 6.16 (1 H, t, H-1′), and 7.85 (1 H, d, H-6); picrate had m.p. 174.0—175.0 °C (decomp.) (from water) [lit.,[42] m.p. 173 °C (decomp.)], $[\alpha]_D^{18}$ +35.2° (*c* 1.0 in Me_2NCHO) (Found: C, 41.1; H, 3.65; N, 17.4. $C_{11}H_{15}N_3O_5 \cdot C_6H_3N_3O_7$ requires C, 41.0; H, 3.65; N, 16.9%).

Compound (19b) had m.p. 185.0—186.0 °C (from ethanol), $[\alpha]_D^{18}$ +43.1° (*c* 1.0 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 273 nm (ε 7 900); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.03 (3 H, s, OAc), 2.0—2.3 (2 H, m, $J_{1'.2'}$ 6.5 Hz and $J_{1'.2''}$ 6.5 Hz, H-2′ and 2″), 3.8—4.1 (1 H, m, H-4′), 4.1—4.4 (3 H, m, H-3′, 5′, and 5″), 5.80 (1 H, d, $J_{5.6}$ 7.0 Hz, H-5), 6.20 (1 H, t, H-1′), and 7.58 (1 H, d, H-6) (Found: C, 48.9; H, 5.65; N, 15.7. $C_{11}H_{15}N_3O_5$ requires C, 49.05; H, 5.6; N, 15.6%).

Partial O-Deacetylation of (20).—A solution of (20)[43] (1.9 g, 6 mmol) in pyridine (50 ml) was treated with (1) (0.6 ml, 12 mmol) at room temperature for 1 day, and the resulting solution was worked up as described above to give 3′-*O*-acetylthymidine (20a) (365 mg, 21% yield), 5′-*O*-acetylthymidine (20b) (920 mg, 56% yield); (20) (190 mg, 10% yield) was recovered unchanged.

Compound (20b) had m.p. 151.5—152° (from acetone–cyclohexane) (lit.,[43] m.p. 146 °C), $[\alpha]_D^{18}$ −7.1° (*c* 1.05 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 266 nm (ε 10 500); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 1.80 (3 H, s, Me-5), 2.03 (3 H, s, OAc), 2.0—2.3 (2 H, m, $J_{1'.2'}$ 7.5 Hz and $J_{1'.2''}$ 7.5 Hz, H-2′ and 2″), 3.8—4.0 (1 H, m, H-3′), 4.1—4.3 (3 H, m, H-4′, 5′, and 5″), 6.16 (1 H, t, H-1′), and 7.43 (1 H, s,H-6) (Found: C, 50.8; H, 5.60; N, 10.05. $C_{12}H_{16}N_2O_6$ requires C, 50.7; H, 5.65; N, 9.85%).

Compound (20a) had m.p. 174.5—176.0° (from acetone–cyclohexane) (lit.,[43] m.p. 176°) $[\alpha]_{546}^{18}$ +2.0° and $[\alpha]_D^{18}$ 0° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 265 nm (ε 9 500); δ_H-[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 1.80 (3 H, s, Me-5), 2.06 (3 H, s, OAc), 2.2—2.4 (2 H, m, $J_{1'.2'}$ 7.5 Hz and $J_{1'.2''}$ 7.5 Hz, H-2′ and 2″), 3.55—3.7 (2 H, m, H-5′ and 5″), 3.9—4.1 (1 H, m, H-4′), 5.1—5.3 (1 H, m, H-3′), 6.20 (1 H, t, H-1′), and 7.75 (1 H, s, H-6) (Found: C, 50.65; H, 5.65; N, 10.15. $C_{12}H_{16}N_2O_6$ requires C, 50.7; H, 5.65; N, 9.85%).

Acetylation of 3′-O-*Methyladenosine*.—3′-*O*-Methyladenosine[44] (7.5 g, 26.7 mmol) was treated in acetic anhydride (100 ml) in the presence of anhydrous sodium acetate (1.0 g) at 80° for 5 h, and the resulting mixture was then evaporated to dryness. The residue was chromatographed on a column of silica gel with ethanol–chloroform as eluant to give (21) (8.29 g, 85% yield); which was chromatographically confirmed to be pure enough for subsequent use [R_F 0.24 benzene–methanol) (9 : 1, v/v)].

Compound (21) had δ_H($CDCl_3$–$SiMe_4$) 2.06 (3 H, s, OAc), 2.16 (3 H, s, OAc), 2.62 (3 H, s, NAc), 3.42 (3 H, s, OMe), *ca.* 4.5 (4 H, m, H-3′, 4′, 5′, and 5″), 5.95 (1 H, m, $J_{1'.2'}$ 3.0 Hz, H-2′), 6.25 (1 H, d, H-1′), 8.39 (1 H, s, H-8), 8.69 (1 H, s, H-2), and 9.95br (1 H, s, NH).

Acetylation of 2′-*O-Methyladenosine*.—In a similar way to the above acetylation, 2′-*O*-methyladenosine[44] (7.5 g, 26.7 mmol) was worked up with acetic anhydride in the presence of anhydrous sodium acetate to give (22) (8.5 g, 87% yield; syrup); which was also confirmed chromatographically to be pure enough for subsequent use [R_F 0.24 benzene–methanol) (9 : 1, v/v)].

Compound (22) had δ_H($CDCl_3$–$SiMe_4$) 2.13 (3 H, s, OAc), 2.20 (3 H, s, OAc), 2.59 (3 H, s, NAc), 3.54 (3 H, s, OMe), 4.4—4.6 (3 H, m, H-4′, 5′, and 5″), 5.4—5.6 (1 H, m, H-3′), 4.79 (1 H, t, $J_{1'.2'}$ 5.0 Hz and $J_{2'.3'}$ 5.0 Hz, H-2′), 6.19 (1 H, d, H-1′), 8.40 (1 H, s, H-8), and 8.70 (1 H, s, H-2).

Partial O-Deacetylation of (21).—A solution of (21) (5 g, 12.3 mmol) in glacial acetic acid–pyridine (1 : 4, v/v) (150 ml) was treated with (1) (1.32 ml, 27.1 mmol) at room temperature for 2 days, and the resulting mixture was worked up as described in the partial *O*-debenzoylation of (3), to give 2′,5′-di-*O*-acetyl-3′-*O*-methyladenosine (21b) (0.63 g, 14% yield) and 5′-*O*-acetyl-3′-*O*-methyladenosine (21a) (2.83 g, 74% yield).

Compound (21b) had m.p. 198—200 °C (from methanol), $[\alpha]_D^{18}$ −27° (*c* 1.0 in $CHCl_3$); $\lambda_{max.}$ (EtOH) 260 nm (ε 14 300); δ_H($CDCl_3$–$SiMe_4$) 2.05 (3 H, s, OAc), 2.13 (3 H, s, OAc), 3.42 (3 H, s, OMe), 4.3—4.6 (4 H, m, H-3′, 4′, 5′, and 5″), *ca.* 6.0 (3 H, m, H-2′ and NH_2), 6.13 (1 H, d, $J_{1'.2'}$ 4.5 Hz, H-1′), 7.94 (1 H, s, H-8), and 8.35 (1 H, s, H-2) (Found: C, 49.5; H, 5.25; N, 19.35. $C_{15}H_{19}N_5O_6$ requires C, 49.3; H, 5.25; N, 19.15%).

Compound (21a) had m.p. 198.5 °C (from methanol), $[\alpha]_D^{18}$ −42.4° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 259 nm (ε 13 400), δ_H[$(CD_3)_2SO$–$SiMe_4$] 2.03 (3 H, s, OAc), 3.43 (3 H, s, OMe), 4.00 (1 H, t, $J_{3'.4'}$ 5.3 Hz and $J_{2'.3'}$ 5.3 Hz, H-3′), 4.1—4.5 (3 H, m, H-4′, 5′, and 5″), 4.88 (1 H, m, $J_{1'.2'}$ 5.3 Hz and $J_{2'.2'\text{-OH}}$ 6.0 Hz, H-2′), 5.94 (1 H, d, H-1′), 7.3br (2 H, s, NH_2), 8.00 (1 H, s, H-8), and 8.33 (1 H, s, H-2) (Found: C, 47.8; H, 5.3; N, 21.55. $C_{13}H_{17}N_5O_5$ requires C, 48.3; H, 5.2; N, 21.65%).

Partial O-Deacetylation of (22).—A solution of (22) (0.92 g, 2.3 mmol) in solvent (30 ml) was treated with (1) (0.36 ml, 7.6 mmol) at room temperature for 8 days, and the resulting mixture was worked up as described above to give 3′,5′-di-*O*-acetyl-2′-*O*-methyladenosine (22b) (0.45 g, 54% yield) and 5′-*O*-acetyl-2′-*O*-methyladenosine (22a) (0.33 g, 44% yield).

Compound (22b) had m.p. 133—134 °C (from methanol); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.09 (3 H, s, OAc), 2.19 (3 H, s, OAc), 3.30 (3 H, s, OMe), 4.3—4.5 (3 H, m, H-4′, 5′, and 5″), 5.5—5.7 (1 H, m, $J_{2'.3'}$ 6.0 Hz, H-3′), 4.93 (1 H, t, $J_{1'.2'}$ 6.0 Hz, H-2′), 6.09 (1 H, d, H-1′), 8.20 (1 H, s, H-8), and 8.40 (1 H, s, H-2) (Found: C, 49.2; H, 5.2; N, 18.85. $C_{15}H_{19}N_5O_6$ requires C, 49.3; H, 5.25; N, 19.15%).

Compound (22a) had m.p. 138.5—139.5 °C (from methanol); $[\alpha]_D^{18}$ −25.8° (*c* 1.5 in Me_2NCHO); $\lambda_{max.}$ (EtOH) 260 nm (ε 14 100); δ_H[$(CD_3)_2SO$–$SiMe_4$; D_2O was added] 2.03 (3 H, s, OAc), 3.45 (3 H, s, OMe), 4.0—4.2 (1 H, m, H-3′), *ca.* 4.3 (3 H, m, H-4′, 5′, and 5″), *ca.* 4.5 (1 H, m, $J_{1'.2'}$ 4.0 Hz, H-2′), 6.10 (1 H, d, H-1′), 8.23 (1 H, s, H-8), and 8 39 (1 H, s, H-2) (Found: C, 48.15; H, 5.25; N, 21.6. $C_{13}H_{17}N_5O_5$ requires C, 48.3; H, 5.3; N, 21.65%).

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