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BIS(TRIBUTYLTIN) OXIDE–PHENYL ISOCYANATE SYSTEM FOR REGIOSELECTIVE (PHENYLCARBAMOYL)ATION OF PURINE AND PYRIMIDINE RIBONUCLEOSIDES*†

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ABSTRACT

On benzylaminolysis, 5′-*O*-benzoyl-N^6-benzyladenosine 2′,3′-carbonate gave a 3:1 mixture of the corresponding 3′- and 2′-benzylcarbamate (67% total yield); hydrazinolysis and hydroxaminolysis were, however, unsuccessful. An alternative approach to regioselective carbamoylation of ribonucleosides, by use of bis(tributyltin) oxide–phenyl isocyanate, was examined, because it is a much simpler procedure. Procedure A, involving two-stage treatment of ribonucleosides, first with bis(tributyltin) oxide in toluene under reflux, and then with phenyl isocyanate, was found to give the corresponding 5′-phenylcarbamate, but was, however, feasible only for N^6-benzyladenosine. Procedure B, involving a one-stage treatment of ribonucleosides with bis(tributyltin) oxide–phenyl isocyanate in a solvent, was found to give the corresponding 3′- or 2′-phenylcarbamate regioselectively on suitably changing the polarity (or composition) of the solvent system used, and was useful for a variety of ribonucleosides. The reaction of 2′-deoxyribonucleosides by Procedure **B** was of interest, as it gave the corresponding 5′-phenylcarbamates regiospecifically. The factors possibly involved in the regioselectivity of these reactions are discussed.

INTRODUCTION

Regioselective *O*-deacylation of fully acylated ribonucleosides with hydrazine hydrate in 1:4 acetic acid–pyridine[2] and with hydroxylaminium acetate in pyridine[3], and of fully acylated glycoside derivatives with hydrazine hydrate in pyridine[4], was successfully used to give, in good yield, the corresponding derivatives bearing a free hydroxyl group at C-2′ or C-2. As an extension of these procedures, we have examined the behavior of 5′-*O*-benzoyl-N^6-benzyladenosine 2′,3′-carbonate (**2**), as a model ribonucleoside cyclic carbonate derivative, toward nucleophilic amines, assuming

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*Partial Protection of Carbohydrate Derivatives. Part 8. For Part 7, see ref. 1.

†Dedicated to Professor Sumio Umezawa on the occasion of his 73rd birthday and the 25th anniversary of the Microbial Chemistry Research Foundation.

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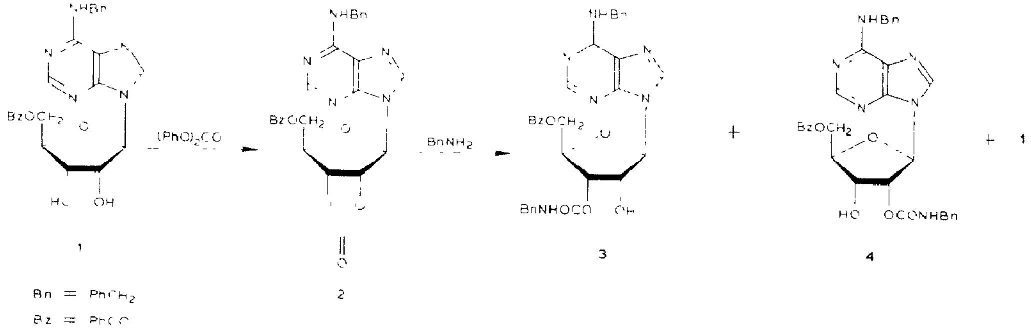
that **2** should be susceptible to regioselective cleavage at the 2′-ester linkage under similar conditions. Incidentally, the carbamoyl group is not so susceptible to migration as acetyl and benzoyl groups, but requires rather drastic conditions for its removal, *e.g.*, refluxing in an alcoholic alkoxide solution. Should the regioselectivity be excellent, however, the protecting group can be used as a temporary one, similar to the triphenylmethyl group (widely employed in the field of carbohydrate chemistry). An alternative approach to regioselective carbamoylation of ribonucleosides having free hydroxyl groups was achieved through use of the bis(tributyltin) oxide–phenyl isocyanate system[5], as the aforementioned procedure was tedious to perform as regards preparation of the starting material for the aminolysis; the reagent system proved useful for regioselective protection of ribonucleosides, as has been briefly communicated[6]. We now describe, in full, the results thus obtained.

RESULTS AND DISCUSSION

The aminolysis reactions of compound* **2** were respectively performed by use of hydroxylaminium acetate in pyridine, hydrazine hydrate in 1:4 acetic acid–pyridine, and benzylamine in 1:1 chloroform–methanol. Hydroxylaminolysis of **2**, followed by chromatographic separation on a column of silica gel, gave 5′-*O*-benzoyl-*N*^{6}-benzyladenosine (**1**) (26% yield) and **2** (72% recovery). The recovery of **2** might have arisen from recyclization, catalyzed by silica gel, of the resulting hydroxamates during the column-chromatographic separation, although t.l.c. of the resulting mixture gave two new spots that might correspond to the hydroxamates, and proved complete consumption of **2**. Hydrazinolysis of **2** was also unfruitful, as it gave an inseparable mixture of the corresponding carbamates, in addition to **2** (17% recovery) and **1** (19% yield). Benzylaminolysis of **2** was, however, successful, giving 5′-*O*-benzoyl-*N*^{6}-benzyladenosine 3′- (**3**) and 2′-benzylcarbamate (**4**) as a 3:1



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*Compound **2** was prepared from inosine through 5 reaction-steps, *i.e.*, *O*-benzoylation with benzoyl chloride in pyridine, chlorination with the Vilsmeier reagent (prepared from thionyl chloride and DMF, in methanol–dichloromethane), amination with benzylamine in benzene under reflux, removal of the benzoyl groups at O-2′ and O-3′ by hydrazinolysis, and carbonylation with diphenyl carbonate–sodium hydrogencarbonate in DMF (see Experimental section).

TABLE I

EXAMINATION OF FORMATION OF N^6-BENZYLADENOSINE TRIBUTYLTIN ALKOXIDE FROM **5** AND BIS(TRIBUTYLTIN) OXIDE[a]

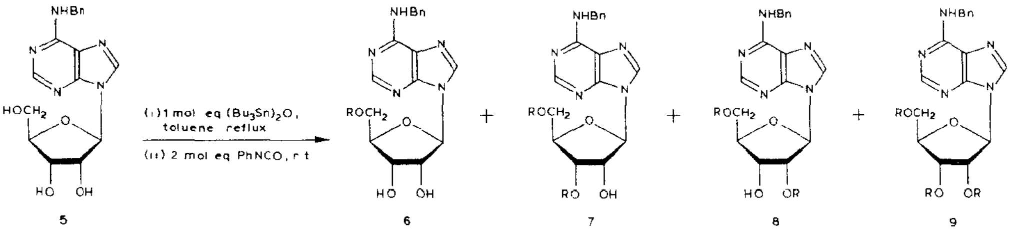
Entry	**5** (*x mmol*)	$(Bu_3Sn)_2O$ (*y mmol*)	*Apparatus used (desiccant)*	*Reaction time (h)*	*Recovered* **5** (*z mmol*)	$2y/(x-z)$
1	0.60	0.20	A	1	0.33	1.5
2	6.00	1.00	A	2	4.73	1.6
3	6.00	1.01	A	2	4.71	1.6
4	6.00	1.01	B (molecular sieves 3 A)	2	4.36	1.2
5	2.98	0.50	B	4	2.06	1.1
6	2.99	0.51	B	4	2.14	1.2

[a] All reactions were performed in boiling toluene under reflux in a nitrogen atmosphere.

mixture (67% total yield), in addition to **1** (27% yield). Pure samples of **3** and **4** were obtained by re-chromatography.

We were also interested in carbamoylation through use of the bis(tributyltin) oxide–isocyanate system reported by Davies[5], as an alternative approach to partial carbamoylation of the hydroxyl groups of ribonucleosides. First, the two-stage treatment of ribonucleosides involving preparation of the corresponding tin alkoxide and its addition reaction to an isocyanate (Procedure A) was examined by use of N^6-benzyladenosine (**5**) as a model compound, as all of the possible carbamates are readily differentiated in liquid chromatography (l.c.) as clearly separated peaks if phenyl isocyanate is used for carbamoylation. The first stage of the tin alkoxide formation was examined by treating **5** with bis(tributyltin) oxide in toluene under reflux according to the method[7–9] traditionally used in the field of carbohydrate chemistry. The resulting tin alkoxide was examined in terms of the value of $2y/(x-z)$, derived by weighing the unchanged **5** (z mmol) isolated by filtration of the mixture resulting from the reaction of **5** (x mmol) with bis(tributyltin) oxide (y mmol; $y < x/2$) in toluene under reflux (nitrogen), in the way reported by Crowe and Smith[8]. The results thus obtained are summarized in Table I. Entries 1–3 are those obtained by use of a Dean–Stark apparatus (Apparatus A)[10,11], showing values ranging from 1.5 to 1.6, which apparently deviated from the integer 1, or 2, whereas Entries 4–6 are those obtained by use of Apparatus B, equipped with a Soxhlet extractor or a dropping funnel containing a desiccant[12], showing values that ranged from 1.1 to 1.2; these are close to the theoretical value of 1, and may indicate that a hydroxyl group of **5** was converted into the tin alkoxide. The deviation observed in Entries 1–3 might have arisen from incomplete removal of water (which would undesirably interfere with the alkoxide formation). Although anhydrous magnesium sulfate was also useful as a desiccant, molecular sieves 3A were used in Apparatus B in the following experiments.

The conditions for the carbamoylation of the resulting alkoxide by use of phenyl isocyanate were next examined. The alkoxide, prepared from **5** (2 mmol) and bis(tributyltin) oxide (2 mmol) as already described, was treated with phenyl isocyanate (4 mmol) in solution for 15 h at room temperature, giving the 5′- (**6**) (25% yield), 3′,5′- bis- (**7**) (33% yield), 2′,5′-bis- (**8**) (5% yield), and 2′,3′,5′-tris-(phenylcarbamate) (**9**) (17% yield); the structures of these products were readily confirmed by ^{1}H-n.m.r. spectroscopy. Consequently, we examined the conditions for obtaining better regioselectivity in the reaction; the results thus obtained, and the conditions used, are summarized in Table II. Use of 1 molar equivalent of phenyl isocyanate (Entries 1 and 2) was found to be sufficiently regioselective to give **6**, and an excess of phenyl isocyanate (2 and 3 mol. equiv.; Entries 3 and 4) produced **9** (13 and 39% yield, respectively), in addition to **6**, **7**, and **8**; this is suggestive in considering the reaction mechanism involved in Procedure A, as discussed later. Reaction on a larger scale, using **5** (1 mmol), bis(tributyltin) oxide (0.5 mmol) in



R = CONHPh

TABLE II

(PHENYLCARBAMOYL)ATION OF 5 INVOLVING THE REACTION OF ITS TRIBUTYLTIN ALKOXIDE WITH PHENYL ISOCYANATE (PROCEDURE A)[a]

Entry	*Procedure A*			*Yield (%) of*				*Recovery (%) of*
	1st stage $(Bu_3Sn)_2O$ *(mmol)*	*2nd stage PhNCO (mmol)*	*Time (h)*	6	7	8	9	5
1	0.05	0.1	1	83	trace	trace	trace	13
2	0.06	0.1	1	59	trace	trace	trace	21
3	0.05	0.2	2	46	22	6	13	0
4	0.06	0.3	3	22	23	8	39	0

[a] All reactions were performed by use of **5** (0.1 mmol); the 1st stages were conducted in boiling toluene (4–5 mL) under reflux (nitrogen atmosphere) for 4 h, and the 2nd stages at room temperature. Each resulting mixture was diluted to 10 mL with methanol and chloroform, and all of the products, as well as the unchanged **5**, were determined by the l.c. technique (see Experimental section).

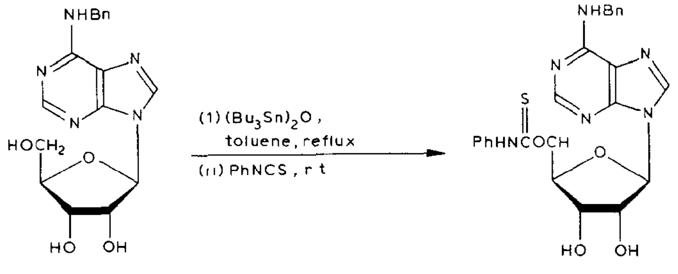
TABLE III

(PHENYLTHIOCARBAMOYL)ATION OF **5** INVOLVING THE REACTION OF ITS TRIBUTYLTIN ALKOXIDE WITH PHENYL ISOTHIOCYANATE (PROCEDURE A)[a]

Entry	**5** *(mmol)*	*1st stage*		*2nd stage*		*Yield (%) of* **10**	*Recovery (%) of* **5**
		$(Bu_3Sn)_2O$ (mmol)	*Toluene (mL)*	*PhNCS (mmol)*	*Reaction time (h)*		
1	1.0	0.55	15	1	20	13	77
2	0.5	0.28	1	5	19	76 (64[b])	19
3	1.0	1.00	5	4	40	70 (68[b])	trace
4	1.0	1.00	3	4	19	75 (69[b])	trace
5	1.0	0.75	3	4	22	68	trace

[a] All reactions were performed as described in Table II. [b] The yields are those of the phenylcarbamate obtained by crystallization from chloroform.

toluene (30 mL) under reflux (nitrogen) for 4 h and then with phenyl isocyanate (1 mmol) for 45 min at room temperature, gave **6** (70% isolated yield). Similarly, (phenylthiocarbamoyl)ation of **5** was performed by use of phenyl isothiocyanate instead of phenyl isocyanate; the results thus obtained are summarized in Table III. The reaction gave N^6-benzyladenosine 5′-(phenylthio)carbamate (**10**) in good yield (see Entries 2, 3, and 4), provided that an excess of the reagent and a much longer time were used.



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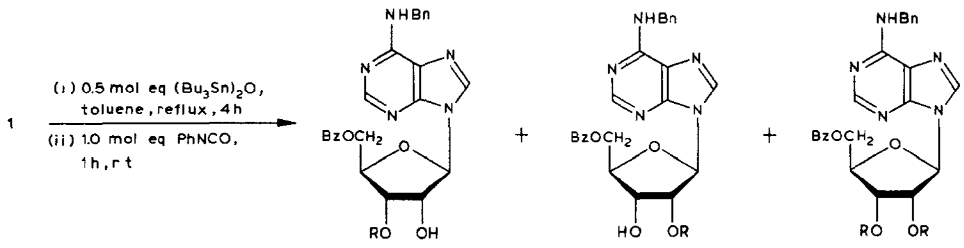

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12

13

R = CONHPh

TABLE IV

(PHENYLCARBAMOYL)ATION OF **1** BY PROCEDURE A[a]

Entry	*1st stage*		*2nd stage*	*Yield (%) of*			*Recovery (%) of*
	$(Bu_3Sn)_2O$ (mmol)	*Reaction time (h)*	*Reaction temp.*	**11**	**12**	**13**	**1**
1	0.05	4	room temp.	34	14	10	40
2	0.05	3	80°	28	16	13	43
3	0.05	4	0°	16	9	3	62
4	0.1	8	room temp.	31	16	9	39

[a] All reactions were performed by use of **1** (0.1 mmol) and phenyl isocyanate (0.1 mmol), and the 2nd stages were conducted for 1 h. L.c. determination of the species involved in each resulting mixture was performed as described in footnote to Table II; for the conditions used, see Experimental section.

We were next interested in the effect of introduction of a protecting group (*e.g.*, benzoyl) at O-5′ prior to (phenylcarbamoyl)ation. Treatment of 5′-*O*-benzoyl-*N*⁶-benzyladenosine (**1**) with bis(tributyltin) oxide (0.5 mmol) in toluene (15 mL) for 4 h under reflux, and then with phenyl isocyanate (1 mmol) for 1 h at room temperature, gave 5′-*O*-benzoyl-*N*⁶-benzyladenosine 3′- (**11**) (26% yield), 2′- (**12**) (16% yield), and 2′,3′-bis-(phenylcarbamate) (**13**) (27% yield), together with **1** (25% recovery). Attempts to improve the regioselectivity by changing the conditions were unfruitful, as may be seen from Table IV.

On the basis of the foregoing results, attempts were made to extend Procedure A to other ribonucleosides, but these were unsuccessful; *e.g.*, *N*⁶-benzoyladenosine (**14**) is insoluble in toluene on utilization of 0.5 mol. equiv. of bis(tributyltin) oxide, and dissolves in toluene on using 1 mol. equiv. of the oxide, but, on reaction with phenyl isocyanate, the resultant tin alkoxide gave a complex** mixture (thin-layer chromatography).

Confronted with the situation that Procedure A was impractical for **5**, we examined the possibility of using bis(tributyltin) oxide as the catalyst for regioselective (phenylcarbamoyl)ation. The reaction of **1** was first examined as the regioselectivity of Procedure A was insufficient, the desired product being accompanied by **13** and recovery of **1** (see Table IV). The results thus obtained and the conditions used are summarized in Table V. A solution of **1** in 1:1 toluene–DMF gave **1** (94% recovery) on treatment with phenyl isocyanate (1 mol. equiv.) in the absence of the catalyst (Entry 1), and in the presence of 0.5 mol. equiv. thereof (Entry 2). An increase in phenyl isocyanate from 1 to 2 mol. equiv. gave **11** (28% yield) and **12** (20% yield) (but no **13**), together with **1** (51% recovery) (Entry 3). Replacement of the atmosphere with nitrogen brought about no substantial difference in the yields and regioselectivity

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**Similar results were obtained in attempts to use inosine and thymidine.

TABLE V

REGIOSELECTIVE (PHENYLCARBAMOYL)ATION OF **1** THROUGH ONE-STAGE TREATMENT (PROCEDURE B)[a]

Entry	*$(Bu_3Sn)_2O$ (mmol)*	*PhNCO (mmol)*	*Reaction conditions*			*Yield (%) of*			*Recovery (%) of* **1**
			Solvent system	*Temp.*	*Time (h)*	**11**	**12**	**13**	
1[b]	0	0.1	toluene–DMF (27:1, v/v; 3.1 mL)	room temp.	0	0	0	0	94
2[b]	0.05	0.1			1	trace	trace	0	97
3[b]	0.05	0.2			1	28	20	0	51
4	0.05	0.2			1	25	17	0	62
5	0.05	0.2	toluene–DMF (3:1, v/v; 4.0 mL)		2	32	28	0	38
6	0.05	0.2		0°	1	47	48	0	0
7	0.05	0.2		−18 to 0°	1	47	52	0	<7
8	0.05	excess		−78°	1	7	12	0	72
9	0.05	excess		−78 → −45°	49	40	60	trace	0
10	0.05	0.2	toluene–DMF (10:1, v/v; 3.3 mL)	0°	1	47	36	0	19
11	0.05	0.2		0°	100	62	34	0	0
12	0.05	0.2	acetone–DMF (6:1, v/v; 3.5 mL)	0°	1	51	53	0	0
13	0.05	0.2	CH_3CN–DMF (7:1, v/v; 2.3 mL)	0°	1	46	53	0	0
14[c]	0.05	0.2	toluene–DMF (13:1, v/v; 4.3 mL)	0°	2	40	25	0	17

[a] All reactions were performed by use of **1** (0.1 mmol), and l.c. determinations were conducted as described in Table IV. [b] Other than these reactions, all reactions were performed under nitrogen atmosphere. [c] This reaction was performed by use of the 5′-phenylcarbamate (**6**) of **5**, instead of **1**.

TABLE VI

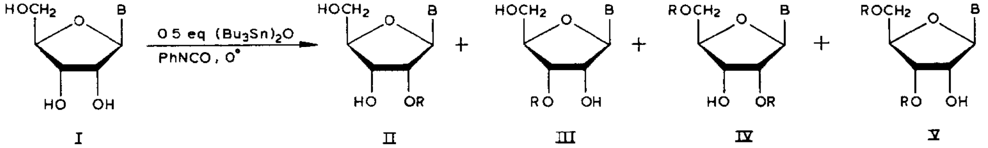
REGIOSELECTIVE (PHENYLCARBAMOYL)ATION OF **5** THROUGH ONE-STAGE TREATMENT (PROCEDURE B)[a]

Entry	*$(Bu_3Sn)_2O$ (mmol)*	*PhNCO (mmol)*	*Reaction conditions*			*Yield (%) of*		*Recovery (%) of* **5**
			Solvent system	*Temp. (°C)*	*Time (h)*	**15**	**16**	
1	0.05	0.2	toluene–DMF (10:1, v/v; 3.3 mL)	25	13	41	trace	23
2	0.05	0.2		0	2	73	10	0
3	0.05	0.05		0	2	8	trace	70
4	0.05	0.1		0	2	23	4	59
5	0.05	0.15		0	2	53	8	27
6	0.016	0.15		0	2	80	10	10
7	0.036	0.17		0	2	78	16	trace
8	0.05	0.18	DMF (0.8 mL)	0	2	52	46	0
9	0.05	0.18	toluene–DMF (1:1, v/v; 1.0 mL)	0	2	55	43	0
10	0.05	0.20	acetone–DMF (4:1, v/v; 2.5 mL)	0	2	48	50	0
11	0.05	0.20	CH_3CN–DMF (7:1, v/v; 2.3 mL)	0	2	45	51	0
12	0.05	0.18	toluene–DMF (10:1, v/v; 3.3 mL)	0	2	49	13	13
13	0.05	0.23		0	2	76	24	0

[a] All reactions were performed by use of **5** (0.1 mmol), and l.c. determination was conducted as described in Table IV. In these cases, the corresponding 3′,5′- and 2′,5′-bis(phenylcarbamate) were proved by the l.c. to be produced in traces.

(Entry 4). Some improvement in the yields of **11** and **12** was attained by changing the solvent ratio from 1:1 to 3:1, and prolonging the time from 1 to 2 h (Entry 5). The effect of the temperature on the reaction was next examined (see Entries 6–9); the yield was improved by conducting the reaction at 0 to −18°, instead of at room temperature, and this may reflect the exothermic character of this reaction. The reaction at 0° was found appropriate for practical use, based on the yields of **11** and **12**, although the reaction at −78 → −45° was more regioselective, giving **12** in preference to **11**. Change of the solvent ratio from 3:1 to 10:1 (Entries 10 and 11) interestingly gave reversed regioselectivity (**11** in preference to **12**; *cf.*, Entry 9). Other solvent systems (Entries 12 and 13) gave substantially the same regioselectivity as that obtained in Entry 6. These results indicate that the regioselectivity, as between O-2′ and O-3′ of **1**, is low, provided that O-5′ is protected with a benzoyl group, except in a few cases. Compound **6**, protected with a phenylcarbamoyl group at O-5′, gave a little better regioselectivity, although some **6** was recovered, despite use of a doubled reaction-time.

On the basis of the foregoing results, we next examined the behavior of **5** in the (phenylcarbamoyl)ation reaction catalyzed by bis(tributyltin) oxide; the conditions used, and the results obtained, are summarized in Table VI. As with the reaction of **1**, it was found better to perform this reaction at 0° than at room temperature (compare Entry 1 with Entry 2). Compared with the foregoing reaction, the regioselectivity was greatly improved, as may be seen from Entries 1–7, giving a preponderance of the 3′- (**15**) over the 2′-*O*-(phenylcarbamoyl) derivative (**16**) of N^6-benzyladenosine. The use of 1 mol. equiv. of bis(tributyltin) oxide and of phenyl isocyanate (Entry 4), and of less of the latter reagent (Entry 3), resulted in the recovery of **5** (59 and 70% yield, respectively); these results may furnish some clue regarding the mode of catalysis by bis(tributyltin) oxide in the partial (phenylcarbamoyl)ation. Satisfactory yields and regioselectivity were, however, obtained, by use of a sufficient excess of phenyl isocyanate over that of bis(tributyltin) oxide (Entries 2, 6, and 7). Comparison of the results shown in Entries 8–13 proved that less-polar solvent-systems should be used in order to obtain excellent regioselectivity in Procedure B.



R = CONHPh

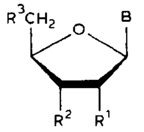
The excellent regioselectivity thus attained prompted performance of a series of partial (phenylcarbamoyl)ations of other ribonucleosides bearing three free hydroxyl groups; the results thus obtained are summarized in Table VII. The reaction in Entry 1 was performed because of an interest in introducing two phenylcarbamoyl

TABLE VII

REGIOSELECTIVE (PHENYLCARBAMOYL)ATION OF SOME RIBONUCLEOSIDES THROUGH PROCEDURE B[a] (SCHEME 5)

Entry	*B of [I]*	*PhNCO (mol. equiv.)*	*Reaction conditions*		*Yield (%) of phenylcarbamate*[b]				*Recovery (%) of [I]*
			Solvent system	*Time (h)*	*2′- [II]*	*3′- [III]*	*2′,5′- [IV]*	*3′,5′- [V]*	
1	Ad^{Bn}	3	toluene–DMF (3:1, v/v)	47	7	32		53	0
2	Ad^{Bn}	2	(5:1, v/v)	1.2	20	48	trace	trace	31
3	Ad^{Bn}	2	(6:1, v/v)	5	17	60	trace	trace	15
4	Ad	2	toluene–DMF–Me_2SO (15:2:1, v/v/v)	2	12[c]	70[c]	14		0
					(—	55[d])			
5	Ad	2.3	toluene–Me_2SO (1:1, v/v)	2	16[c]	56[c]	23		0
6	Ad	2.7	(3:1, v/v)	5	0	0	24	63	0
7	Hx	2	(7:1, v/v)	2	31	67	0	0	0
8	Ur	2	toluene–DMF (10:1, v/v)	2	12	35	16	33	0
9	Ur	2	(6:1, v/v)	1.5	15	55	29		0
10	Ur	1.8	(7:1, v/v)	1.5	18	50	9	12	trace
11	Ur	3.5	(5:1, v/v)	6	0	0	30	59	0
12	Cy	2.1	toluene–Me_2SO (2.5:1, v/v)	3.5	0	0	24	63	0

[a] All reactions were performed by use of 0.5 equiv. of bis(tributyltin) oxide at 0° under a nitrogen atmosphere. [b] All yields were of isolated products, unless noted otherwise. [c] These yields were obtained by calculation in terms of area-ratios of proton signals [H-2′ of 2′-phenylcarbamates at δ 5.69 (t) and H-3′ of 3′-phenylcarbamates at δ 5.23–5.43 (m)], and the weight of their mixtures. [d] This yield is of the product isolated by crystallization.



	B	R^1	R^2	R^3		B	R^1	R^2	R^3
14	Ad^{Bz}	OH	OH	OH	28	Hx	OR	OH	OH
15	Ad^{Bn}	OH	OR	OH	29	Ur	OH	OR	OH
16	Ad^{Bn}	OR	OH	OH	30	Ur	OR	OH	OH
17	Ad	OH	OH	OH	31	Ur	OH	OR	OR
18	Hx	OH	OH	OH	32	Ur	OR	OH	OR
19	Ur	OH	OH	OH	33	Cy	OH	OR	OR
20	Cy	OH	OH	OH	34	Cy	OR	OH	OR
21	Ad^{Bz}	OH	OR	OH	35	Ur	H	OH	OH
22	Ad^{Bz}	OR	OH	OH	36	Th	H	OH	OH
23	Ad	OH	OR	OH	37	Ad	H	OH	OH
24	Ad	OR	OH	OH	38	Ur	H	OH	OR
25	Ad	OH	OR	OR	39	Th	H	OH	OR
26	Ad	OR	OH	OR	40	Ad	H	OH	OR
27	Hx	OH	OR	OH					

R = CONHPh

groups into **5** by use of phenyl isocyanate (3 mol. equiv.); this regioselectively gave the corresponding 3′,5′-bis- (**7**) over the 2′,5′-bis-(phenylcarbamate) (**8**), the latter being obtained as an inseparable mixture with **15**.

Excellent regioselectivity was also observed on introducing one phenylcarbamoyl group into other ribonucleosides. Reactions of **14** (Entries 2 and 3), adenosine (**17**) (Entries 4 and 5), and inosine (**18**) (Entry 7) respectively showed excellent regioselectivity in the favored formation of the corresponding 3′- (**21**, **23**,

TABLE VIII

REGIOSELECTIVE (PHENYLCARBAMOYL)ATION OF SOME 2′-DEOXYRIBONUCLEOSIDES BY PROCEDURE B[a]

Entry	*Heterocyclic moiety*	*PhNCO (mol. equiv.)*	*Reaction conditions Solvent system*	*Time (h)*	*Yield (%)[b] of the corresponding 5′-phenylcarbamate*
1	Ur (**35**)	2.1	toluene–DMF (2.5:1, v/v)	2	(**38**) 99 (97[c])
2	Th (**36**)	1.8	toluene–DMF (3:1, v/v)	0.5	(**39**) 93 (84[c])
3	Ad (**37**)	5.5	toluene–DMF (1.5:1, v/v)	121	(**40**) 67 (57[c])

[a] All reactions were performed by use of bis(tributyltin) oxide (0.5 mol. equiv. for each 2′-deoxyribonucleoside) at 0°. [b] The yields are of isolated products. [c] These are the yields of the products isolated by crystallization.

and **27**) over the 2′-phenylcarbamates (**22**, **24**, and **28**, respectively). The reactions of **14** were comparatively slower than those of the others, and some **14** was recovered, and those of **17** were enough to give the corresponding 3′,5′- (**25**) and 2′,5′-bis-(phenylcarbamate) (**26**).

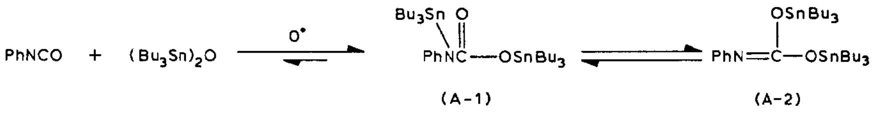
The ready formation of **25** and **26** prompted us to perform the reaction by use of an excess (2.7 mol. equiv.) of phenyl isocyanate, by making the polarity of the solvent system lower, and by prolonging the reaction time (Entry 6), and the desired compounds were obtained in satisfactory yields and with regioselectivity. The same tendency was found in the reactions of uridine (**19**) and cytidine (**20**); for the former (Entries 8, 9, and 10), the corresponding 3′- (**29**) was obtained in preference to the 2′-phenylcarbamate (**30**), although it was accompanied by the corresponding 3′,5′- (**31**) and 2′,5′-bis(phenylcarbamate) (**32**). Performance of the reaction of **19** and of **20** with an excess of phenyl isocyanate (3.5 and 2.1 mol. equiv., respectively) gave the corresponding 3′,5′- (**31** and **33**, respectively) and 2′,5′-bis(phenylcarbamate) (**32** and **34**, respectively) in good yields and with good regioselectivity (Entries 11 and 12).

We next performed (phenylcarbamoyl)ation of 2′-deoxyribonucleosides, of interest because of being devoid of a 2′-hydroxyl group; the results thus obtained and the conditions used are summarized in Table VIII. The reaction of 2′-deoxyuridine (**35**) and thymidine (**36**) proceeded effectively, to give the corresponding 5′-phenylcarbamates (**38** and **39**, respectively) almost regiospecifically (99 and 93% yield, respectively). However, the reaction of 2′-deoxyadenosine (**37**) (Entry 3) contrasts with those reactions, proceeding very slowly (reaction time: 121 h) to give the corresponding 5′-phenylcarbamate (**40**) in only 67% yield. The formation of a single product in these cases may be ascribable to lack of a 2′-hydroxyl group. The striking difference in reaction time between the pyrimidine and purine 2′-deoxyribonucleosides, compared with the similar trend observed in the 5′-phenylcarbamoylation of ribonucleosides (*cf.*, Table VII), is also interesting.

Finally, the potential mode of behavior of bis(tributyltin) oxide in the reactions performed, in terms of Procedures A and B, will be discussed on the basis of the results already described, as well as of some additional evidence obtained (described later).

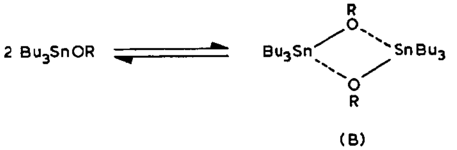
In Procedure A, the reaction can be explained by the mechanism proposed by Davies[5], *i.e.*, addition of the tributyltin alkoxide to phenyl isocyanate. The resulting adduct might, at equilibrium, be inclined toward the tin 3′-alkoxide and partially toward 2′-alkoxide, judging from the order of stability, N-SnBu$_3$ < O-SnBu$_3$ which is readily deducible from the basicity order[13] of N-SnBu$_3$ > O-SnBu$_3$. On using an excess of phenyl isocyanate, formation of either the 3′,5′- or the 2′,5′-bis(phenylcarbamate), or the 2′,3′,5′-tris(phenylcarbamate) might be explained on the same assumption.

In Procedure B, on the other hand, the one-stage treatment gave none of the corresponding 5′-phenylcarbamates, but afforded the 3′- and 2′-phenylcarbamates regioselectively in the case of ribonucleosides. Moreover, the importance of the 2′-hydroxyl group was interestingly shown by the reactions of 2′-deoxyribonucleosides,



Scheme 1

which give the corresponding 5′-phenylcarbamates regiospecifically. These results led us to an alternative concept to explain the mechanism involved. According to Bloodworth and Davies[14–16], bis(tributyltin) oxide adds to isocyanates exothermically, to give the corresponding tributyltin *N*-(tributylstannyl)carbamates (A-1), which should be capable of equilibration with (A-2) (see Scheme 1). The exothermic character of the addition reaction may well correspond to the reaction through Procedure B, which was induced more effectively at 0° than at room temperature (see Table V). Moreover, it was reported that the *N*-$SnBu_3$ function in (A-1) was readily transferred to the oxygen atom of methanol or ethanol, to give the corresponding tin alkoxides, which gave the corresponding carbamates on adding isocyanates. However, such an explanation seems unlikely for the reaction by Procedure B, as the formation of 2′,3′-bis- and 2′,3′,5′-tris-(phenylcarbamate)s is hard to detect unless an excess of phenyl isocyanate is used and the reaction is continued for a much longer time. It is, therefore, not possible to explain the reaction by the mechanism involving the alkoxide species as the intermediate (assumed for explaining the mechanism of Procedure A).



Scheme 2

On the other hand, Davies *et al.*[17] demonstrated that intermolecular exchange of the alkoxide moieties of the tributyltin alkoxides occurred through the four-centered, dimeric intermediate (B) (see Scheme 2), in which intermolecular exchange became more difficult as the alkyl groups got bulkier, *i.e.*, in the sequence Me, Et, $PhCH_2$, Me_3CCH, and Ph_2CH. Judging from this aspect**, such an exchange reaction between the adduct (A-1) and ribonucleosides might thus be difficult. The difference observed between ribonucleosides and 2′-deoxyribonucleosides in the reaction is not yet explicable, but it may be concluded that the 2′-hydroxyl group of ribonucleosides is crucially concerned, as the reaction gives the corresponding 3′-

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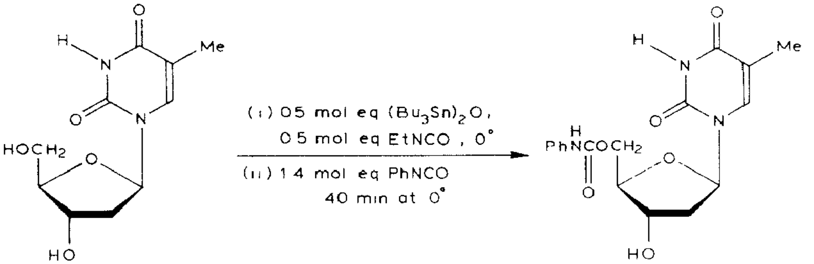
**In contrast with this, the *N*-$SnBu_3$ function formed in Procedure A can be readily transferred to adjacent hydroxyl groups, due to the advantage arising from their intramolecular relationship, which may facilitate the transfer in terms of the entropy effect.

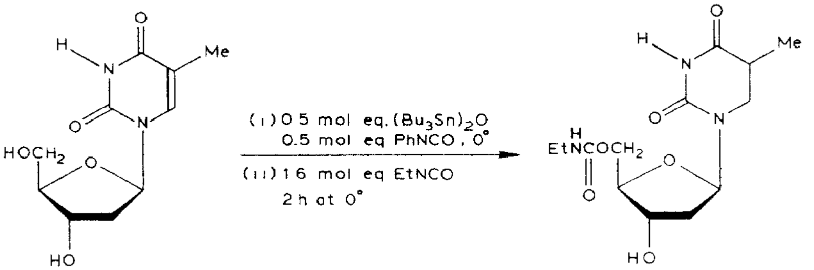
phenylcarbamates regioselectively for ribonucleosides if a less-polar solvent-system is used; alternatively, its lack brings about formation of 5′-phenylcarbamates of 2′-deoxyribonucleosides.

Subsequently, we examined the behavior of bis(tributyltin) oxide in the (phenylcarbamoyl)ation of thymidine as a model substrate. Treatment thereof with a solution containing a species prepared by reaction of bis(tributyltin) oxide (0.5 mol. equiv.) with ethyl isocyanate (0.5 mol. equiv.) in 5:1 toluene–DMF, followed by treatment with phenyl isocyanate (1.4 mol. equiv.) for 40 min at 0°, gave the corresponding 5′-phenylcarbamate **39** (74% yield). On the other hand, initial treatment with a species prepared from the tin oxide (0.5 mol. equiv.) and phenyl isocyanate (0.5 mol. equiv.), followed by ethyl isocyanate (1.6 mol. equiv.) for 2 h at 0°, gave the corresponding 5′-ethylcarbamate **41** (85% yield) (see Schemes 3 and 4). These results clearly demonstrated that the adduct formed from the tin oxide and an isocyanate should be unable to exchange its *N*-$SnBu_3$ function with any hydroxyl group on the D-ribofuranosyl or 2′-deoxy-D-*erythro*-pentofuranosyl moieties, and should at least activate the hydroxyl group so as to attack the isocyanate function to give the corresponding carbamates.



36 39

Scheme 3



36 41

Scheme 4

It should be emphasized that the mechanism (Scheme 1) discussed according to the concept proposed by Davies *et al.*[5,14] is infeasible for the reaction through Procedure B. Furthermore, the possibility of migration of the phenylcarbamoyl group during the reaction was examined by treating **11** and **12**, respectively, with a solution of phenyl isocyanate (0.5 mol. equiv.) and bis(tributyltin) oxide (0.5 mol. equiv.) in 10:1 toluene–DMF for 100 h at 0°. Quantitative analysis of each resulting mixture by l.c. proved that the former afforded a mixture of **11** (96% recovery) and **13** (2% yield), containing no **12** at all, and that the latter gave a mixture of **11** (2% yield) and **12** (106% yield), containing no **13** at all. Therefore, the proportions of the products in all of the reaction mixtures herein discussed can be assumed to reflect the actual regioselectivity obtained.

EXPERIMENTAL

General methods. — Melting points are uncorrected. U.v. spectra were recorded with a Shimadzu double-beam spectrophotometer UV-200 for solutions in ethanol (predistilled from potassium hydroxide). Specific rotations were determined with a JASCO DIP-4 apparatus. ^{1}H-N.m.r. spectra were recorded with a Varian T-60, EM-360, or EM-390 instrument for solutions in $CDCl_3$, $(CD_3)_2SO$, or $CDCl_3$ to which $(CD_3)_2SO$ was added until a sample dissolved (Me_4Si as the internal standard). T.l.c. was performed on plates precoated with Merck silica gel 60 F_{254} (thickness 0.25 mm), employing 9:1 or 19:1 chloroform–ethanol as the eluant, unless noted otherwise.

Column chromatography was performed on Wakogel C-300, employing various chloroform–methanol systems as the eluant. Liquid chromatography (l.c.) was performed with a Varian LC-8520 apparatus having a column of either MicroPak Si-10 (25 cm × 2.2 mm) or MicroPak Si-5 (30 cm × 4 mm), the mobile phase being hexane (Solvent *A*) or 2:3 isopropyl alcohol–dichloromethane (the solvent composition being described for each experiment); flow rate 100 mL/h; detection by u.v. at 270 nm (Variscan apparatus). Elemental analyses were performed by use of a Perkin–Elmer 240-002 apparatus.

Toluene was distilled from metallic sodium after being refluxed therewith for a few days, and was stored over molecular sieves. *N*,*N*-Dimethylformamide (DMF) was pretreated with phosphorus pentaoxide for a few days at room temperature, and the supernatant liquor was decanted onto potassium hydroxide; after a few hours, it was distilled, and the distillate stored over molecular sieves. Dimethyl sulfoxide was pretreated with calcium hydride, distilled, and stored over molecular sieves. Bis(tributyltin) oxide was purchased from Tokyo Kasei Co., Ltd., and distilled under diminished pressure prior to use. Phenyl isocyanate and isothiocyanate (also purchased from Tokyo Kasei Co., Ltd.) were distilled under diminished pressure (b.p. 50°/13 mmHg and 91°/13 mmHg, respectively), and stored in sealed vessels. Chloroform containing ethanol (0.5%, v/v) was purchased commercially, and used as such.

*5′-O-Benzoyl-*N^6*-benzyladenosine 2′,3′-carbonate* (**2**). — To a solution of 2′,3′,5′-tri-*O*-benzoyl-*N*^{6}-benzyladenosine[18] (6.7 g, 10 mmol) in 1:1 chloroform–methanol (125 mL) was added hydrazine hydrate (1.93 mL, 40 mmol), and the mixture was stirred for 2 days at room temperature. The reaction was quenched with acetone (125 mL), and, after a few hours, the mixture was evaporated to dryness. The residue was crystallized by triturating with chloroform (50 mL), and the crystals were filtered off, and recrystallized, giving 5′-*O*-benzoyl-*N*^{6}-benzyladenosine (**1**) (3.6 g, 73% yield); m.p. 180–181° (from methanol).

Anal. Calc. for $C_{24}H_{23}N_5O_5$: C, 62.46; H, 5.02; N, 15.18. Found: C, 62.40; H, 5.02; N, 15.06.

A mixture of **1** (3.5 g, 7.5 mmol), diphenyl carbonate (3.1 g, 14.5 mmol), and sodium hydrogencarbonate (0.1 g) in DMF (20 mL) was stirred for 4.5 h at 78°, cooled, and evaporated to a syrup, which crystallized to give **2** (2.8 g, 78% yield); m.p. 87° (from ethanol), $[\alpha]_D^{22}$ $-32.3°$ (*c* 1, DMF); λ_{max}^{EtOH} 267 (ε_{mM} 19.20) and λ_{min}^{EtOH} 246 nm (8.40); n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; Varian EM-390]: δ 4.30–4.84 (m, 5 H, H-4′,5′,5″, and CH_2-Ph), 5.74 (dd, 1 H, $J_{2',3'}$ 7.5, $J_{3',4'}$ 3.0 Hz, H-3′), 6.16 (dd, 1-H, $J_{1',2'}$ 2.0 Hz, H-2′), 6.44 (d, 1 H, H-1′), and 7.14–8.27 (m, 12 H, H-2,8 and 2 C_6H_5).

Anal. Calc. for $C_{25}H_{21}N_5O_6$: C, 61.60; H, 4.34; N, 14.37. Found: C, 61.30; H, 4.41; N, 14.25.

Benzylaminolysis of **2**. — To a solution of **2** (980 mg, 2 mmol) in 1:1 methanol–chloroform (20 mL) was added benzylamine (0.22 mL, 2 mmol), and the mixture was stirred for 1 day at room temperature. The mixture was treated with a small amount of acetic acid, stirred for a few hours, and evaporated to a glass which was chromatographed on a column of silica gel by use of 1:49 methanol–chloroform, to give a mixture of 5′-*O*-benzoyl-*N*^{6}-benzyl-3′-*O*- (**3**) and -2′-*O*-(benzylcarbamoyl)adenosine (**4**) (791 mg, 67% yield; **3**:**4** = 1:3, calculated in terms of the area-ratio of ^{1}H-n.m.r. signals of H-3′ of **3** and H-2′ of **4**) and **1** (245 mg, 27% yield). Pure samples of **3** and **4** were isolated from the mixture by rechromatography on a column of silica gel.

Compound **3** had m.p. 105–106° (from methanol), $[\alpha]_D^{22}$ $-51.2°$ (*c* 1, DMF); λ_{max}^{EtOH} 268 (ε_{mM} 20.90) and λ_{min}^{EtOH} 245 nm (9.10); n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si, Varian EM-390]: δ 4.19–5.19 (m, 6 H, H-2′,4′,5′,5″, and CH_2-Ph), 5.31–5.49 (m, 1 H, H-3′), 5.92 (bs, 1 H, O*H*-2′), 6.08 (d, 1 H, $J_{1',2'}$ 6.0 Hz, H-1′), and 6.76–8.33 (m, 19 H, H-2,8, 2 N*H* and 2 C_6H_5).

Anal. Calc. for $C_{32}H_{30}N_6O_6$: C, 64.63; H, 5.09; N, 14.14. Found: C, 64.35; H, 5.17; N, 14.00.

Compound **4** had m.p. 147–148° (from methanol); $[\alpha]_D^{22}$ $-44.9°$ (*c* 1, DMF); λ_{max}^{EtOH} 267 (ε_{mM} 21.50) and λ_{min}^{EtOH} 245 nm (9.00); n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; Varian EM-390]: δ 3.97–5.07 (m, 6 H, H-3′,4′,5′,5″, and CH_2-Ph), 5.31 (d, 1 H, $J_{3',3'-OH}$ 6.0 Hz, O*H*-3′), 5.74 (dd, 1 H, $J_{1',2'}$ 3.5, $J_{2',3'}$ 5.5 Hz, H-2′), 6.15 (d, 1 H, H-1′), and 6.77–8.32 (m, 19 H, H-2,8, 2 N*H*, and 3 C_6H_5).

Anal. Calc. for $C_{32}H_{30}N_6O_6$: C, 64.63; H, 5.09; N, 14.14. Found: C, 64.40; H, 5.09; N, 13.85.

Hydroxyaminolysis of **2**. — A solution of **2** (980 mg, 2 mmol) in anhydrous pyridine (20 mL) was stirred with hydroxylaminium acetate (182 mg, 2 mmol) for 24 h at room temperature, treated with acetone as before, stirred for a few hours, and evaporated to a glass, which was chromatographed on a column of silica gel to give **2** (708 mg, 72% recovery) and **1** (245 mg, 26% yield).

Hydrazinolysis of **2**. — A solution of **2** (983 mg, 2 mmol) in 1:4 acetic acid–pyridine (20 mL) was stirred with hydrazine hydrate (0.09 mL, 2 mmol) for 24 h at room temperature, and the mixture processed as before, to give **2** (168 mg, 17% recovery), a mixture of the corresponding carbamates (305 mg, inseparable), and **1** (174 mg, 19% yield).

(Phenylcarbamoyl)ation of **5** via *the corresponding tributyltin alkoxide (Procedure A).* — A mixture of **5** (714 mg, 2 mmol) and bis(tributyltin) oxide (1.0 mL, 2 mmol) in toluene (10 mL) was boiled under reflux (nitrogen atmosphere) for 2 h, the water formed concomitantly being removed azeotropically. To the resulting, clear solution was added phenyl isocyanate (0.44 mL, 4 mmol), the mixture was stirred overnight at room temperature, methanol (5 mL) was added, and the solution was evaporated to a syrup which was chromatographed on a column of silica gel, to give N^6-benzyl-5′-*O*-(phenylcarbamoyl)adenosine (**6**) (244 mg, 25% yield), -3′,5′-bis-*O*-(phenylcarbamoyl)adenosine (**7**) (317 mg, 33% yield), -2′,5′-bis-*O*-(phenylcarbamoyl)-adenosine (**8**) (51 mg, 5% yield), and -2′,3′,5′-tris-*O*-(phenylcarbamoyl)adenosine (**9**) (242 mg, 17% yield) (*cf.*, Table II).

Compound **6** had m.p. 202–203° (from methanol), $[\alpha]_D^{22}$ $-63.7°$ (c 1, DMF); λ_{max}^{EtOH} 267 (ε_{mM} 20.40) and 216 nm (20.40), and λ_{min}^{EtOH} 251 nm (ε_{mM} 11.90); n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; D_2O added; Varian EM-390] δ 4.18–4.97 (m, 6 H, H-3′,4′,5′,5″ and CH_2-Ph), 4.82 (q, 1 H, H-2′), 6.13 (d, 1 H, $J_{1',2'}$ 5.4 Hz, H-1′), and 6.92–8.42 (m, 12 H, H-2,8, and 2 C_6H_5).

Anal. Calc. for $C_{24}H_{24}N_6O_5$: C, 60.49; H, 5.08; N, 17.64. Found: C, 60.21; H, 4.94; N, 17.62.

Compound **7** had m.p. 170–171° (from ethyl acetate), $[\alpha]_D^{22}$ $-72°$ (c 1, DMF); λ_{max}^{EtOH} 269 (ε_{mM} 19.10) and 237 nm (33.00), and λ_{max}^{EtOH} 253 nm (ε_{mM} 12.70); n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; D_2O added; Varian EM-390] δ 4.23–4.95 (m, 5 H, H-4′,5′,5″, and CH_2-Ph), 5.05 (t, 1 H, H-2′), 5.30–5.52 (bd, 1 H, $J_{2',3'}$ 5.7 Hz, H-3′), 6.18 (d, 1 H, $J_{1',2'}$ 6.5 Hz, H-1′), and 6.98–8.35 (m, 17 H, H-2,8, and 3 C_6H_5).

Anal. Calc. for $C_{31}H_{29}N_7O_6$: C, 62.51; H, 4.91; N, 16.46. Found: C, 62.31; H, 4.92; N, 16.42.

Compound **8**, a glass, had n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; D_2O added; Varian T-60] δ 4.13–4.97 (m, 6 H, H-3′,4′,5′,5″, and CH_2-Ph), 5.65 (t, 1 H, H-2′), 6.22 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1′), 6.80–7.45 (m, 15 H, 3 C_6H_5), and 7.94 and 8.30 (each s, each 1 H, H-2 or 8).

Compound **9**, a glass, had n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; D_2O added; Varian EM0390] δ 4.13–4.80 (m, 5 H, H-4′,5′,5″, and CH_2-Ph), 5.71 (t, 1 H, H-3′), 5.87 (t, 1 H, H-2′), 6.23 (d, 1 H, $J_{1',2'}$ 5.8 Hz, H-1′), 6.77–7.47 (m, 20 H, 4 C_6H_5), and 8.00 and 8.33 (each s, each 1 H, H-2 or 8).

An examination of N^6*-benzyladenosine tributyltin alkoxide formation from* **5** *and bis(tributyltin) oxide.* — A mixture of **5** (x mmol, see Table I) and bis(tributyltin) oxide (y mmol, see Table I) in toluene (20–40 mL) was boiled under reflux for 1–4 h by use of Apparatus A or B, cooled, unchanged material quickly filtered off, and the residue washed with hexane (10 mL), dried over phosphorus pentaoxide under diminished pressure, and weighed, giving the amount of unchanged **5** (*z* mmol) (*cf.*, Table I).

Examination of conditions for the (phenylcarbamoyl)ation of **1** *or* **5** *through their tributyltin alkoxide.* — A mixture of **1** or **5** (0.1 mmol) and the amount of bis(tributyltin) oxide shown in Tables II–IV, in toluene (4–5 mL), was boiled under reflux (nitrogen atmosphere) for 4 h, with azeotropic removal of the water concomitantly produced, and then the amount of phenyl isocyanate shown in the Tables was respectively added to each cooled mixture. After the reaction time shown for each, 1 : 1 methanol–chloroform was added until the volume attained 10 mL. The resulting solutions were respectively subjected to l.c. analysis under the conditions described in the "general methods" section. Solvent composition for the resulting mixtures from **1**, 11–91.6% B: constant 11% up to 8 min, with a slope of 0.04%/min, of 10%/min up to 31 min, and finally, 91.6% constant to A; for the resulting mixture from **5**, 25–97% B: with a slope of 2%/min up to 6 min, of 10%/min up to 12 min, and finally, 97% constant to A.

N^6-*Benzyl-5'-O-(phenylcarbamoyl)adenosine* (**6**). — A mixture of **5** (371 mg, 1 mmol) and bis(tributyltin) oxide (309 mg, 0.5 mmol) in toluene (15 mL) was boiled under reflux (nitrogen atmosphere) for 4 h, with removal of the water concomitantly produced; then, phenyl isocyanate (0.12 mL, 1 mmol) was added, the mixture stirred for 1 h at room temperature, the reaction quenched with methanol (5 mL), the solution evaporated to dryness, and the residue chromatographed on a column of silica gel, to give **6** (407 mg, 82% yield); recrystallization gave a pure sample, m.p. 203° (348 mg, 70% yield).

N^6-*Benzyl-5'-O-(phenylthiocarbamoyl)adenosine* (**10**). — The mixture obtained by treating **5** (357 mg, 1 mmol) with bis(tributyltin) oxide (596 mg, 1 mmol) in toluene (4 mL) as just described was treated with phenyl isothiocyanate (0.47 mL, 4 mmol) for 19 h at room temperature, with stirring. The reaction was quenched with water–chloroform, methanol was added until the emulsion disappeared, and the organic layer was evaporated to dryness. The residue was extracted with chloroform–methanol, the extract was evaporated, and the residue was chromatographed on a column of silica gel, to give **10** (370 mg, 75% yield); recrystallization gave a pure sample (341 mg, 69% yield); m.p. 130° (from chloroform–ethanol), $[\alpha]_D^{22}$ −18.4° (*c* 1, DMF); λ_{max}^{EtOH} 273 nm (ε_{mM} 31.90); n.m.r. [$(CD_3)_2SO$–Me_4Si; D_2O added; Varian EM-360] δ 4.27–5.30 (m, 7 H, H-2',3',4',5',5'', and CH_2-Ph), 6.25 (d, 1 H, $J_{1',2'}$ 4.7 Hz, H-1'), and 7.20–8.67 (m, 12 H, H-2,8, and 2 C_6H_5); see Table III.

Anal. Calc. for $C_{24}H_{24}N_6O_4S$: C, 58.52; H, 4.91; N, 17.06; S, 6.51. Found: C, 58.30; H, 4.84; N, 16.76; S, 6.30.

*(Phenylcarbamoyl)ation of 5'-O-benzoyl-*N^6*-benzyladenosine* (**1**) via *the corresponding tributyltin alkoxide.* — A mixture of **1** (459 mg, 1 mmol) and bis(tributyltin) oxide (298 mg, 1 mmol) in toluene (15 mL) was boiled under reflux in the usual way for 4 h, cooled to room temperature, phenyl isocyanate (0.11 mL, 1 mmol) was

added, and the mixture stirred for 1 h. After quenching the reaction with methanol (5 mL), the solution was evaporated to a syrup, which was then chromatographed on a column of silica gel, followed by crystallization, to give 5′-*O*-benzoyl-*N*^{6}-benzyl-3′- (**11**) (154 mg, 26% yield), -2′-*O*- (**12**) (85 mg, 15% yield), and -2′,3′-bis-*O*-(phenylcarbamoyl)adenosine (**13**) (186 mg, 27% yield), in addition to **1** (113 mg, 25% recovery).

Compound **11** had m.p. 165–166° (from benzene); $\lambda_{\max}^{\mathrm{EtOH}}$ 269 ($\varepsilon_{\mathrm{mM}}$ 22.30) and 233 nm (32.10); $\lambda_{\min}^{\mathrm{EtOH}}$ 251 nm ($\varepsilon_{\mathrm{mM}}$ 13.80); n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; D_2O added; Varian T-60]: δ 4.40–5.93 (m, 5 H, H-4′,5′,5″, and CH_2-Ph), 5.08 (t, 1 H, H-2′), 5.43–5.64 (m, 1 H, H-3′), 6.12 (d, 1 H, $J_{1',2'}$ 5.8 Hz, H-1′), 6.94–7.64 (m, 15 H, 3 C_6H_5), and 7.94 and 8.24 (each s, each 1 H, H-2 or 8).

Anal. Calc. for $C_{31}H_{28}N_6O_6$: C, 64.13; H, 4.86; N, 14.47. Found: C, 64.11; H, 4.87; N, 14.30.

Compound **12** had m.p. 112–113° (from ethanol-free chloroform); n.m.r. ($CDCl_3$–Me_4Si; D_2O added; Varian T-60): δ 4.08–5.15 (m, 6 H, H-3′,4′,5′,5″, and CH_2-Ph), 5.73 (t, 1 H, H-2′), 6.18 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1′), and 6.82–8.28 (m, 17 H, H-2,8, and 3 C_6H_5).

Anal. Calc. for $C_{31}H_{28}N_6O_6$: C, 64.13; H, 4.86; N, 14.47. Found: C, 64.05; H, 4.82; N, 14.43.

Compound **13** had m.p. 112° (from chloroform–hexane), $[\alpha]_D^{22}$ −54° (*c* 1, DMF); $\lambda_{\max}^{\mathrm{EtOH}}$ 268 ($\varepsilon_{\mathrm{mM}}$ 21.50) and 233 nm (44.90), $\lambda_{\min}^{\mathrm{EtOH}}$ 252 nm ($\varepsilon_{\mathrm{mM}}$ 15.30); n.m.r. ($CDCl_3$–Me_4Si; D_2O added; Varian T-60): δ 4.37–4.90 (m, 5 H, H-4′,5′,5″, and CH_2-Ph), 5.69–6.14 (m, 2 H, H-2′,3′), 6.25 (d, 1 H, $J_{1',2'}$ 5.3 Hz, H-1′), and 6.83–8.37 (m, 22 H, H-2,8, and 4 C_6H_5); see Table IV.

Anal. Calc. for $C_{38}H_{33}N_7O_7$: C, 65.23; H, 4.75; N, 14.10. Found: C, 65.23; H, 4.74; N, 14.02.

(Phenylcarbamoyl)ation of **1** *or* **5** *through one-stage treatment (Procedure B). — Examination of conditions.* To a solution of **1** or **5** (0.1 mmol) and bis(tributyltin) oxide (for the amount: see Tables V and VI, respectively) in a solvent (for the volume: *ditto*) under nitrogen at room temperature was added phenyl isocyanate (for the amount: *ditto*); the resulting mixture was stirred at the chosen temperature for the chosen time. The reaction was now quenched with, and the total volume adjusted to 10 mL with, 1:1 methanol–chloroform. The resulting solution was subjected to quantitative l.c. analysis under the conditions already described. For details of the reaction conditions, see Tables V and VI, respectively.

N^6*-Benzyl-3′,5′-bis-*O*-(phenylcarbamoyl)adenosine* (**7**) *through (phenylcarbamoyl)ation by Procedure B.* — A solution of **5** (359 mg, 1 mmol) and bis(tributyltin) oxide (298 mg, 0.5 mmol) in DMF (1 mL) was mixed with toluene (3 mL); phenyl isocyanate (0.11 mL, 1 mmol) was added under nitrogen with stirring, the temperature being kept at ~0° with ice-water. The mixture was stirred for a further 1 h, phenyl isocyanate (0.22 nL, 2 mmol) was added dropwise during 46 h, and the reaction was quenched with water–methanol–chloroform, with stirring. The organic layer was extracted with chloroform, the extract dried (anhydrous magnesium sulfate), and evaporated to dryness, and the residue chromatographed on a column of silica gel, to give **7** (315 mg, 53% yield), a mixture of **8** with the 3′-phenylcarbamate (**15**) (193 mg, 32%), and the 2′-phenylcarbamate **16** (35 mg, 7% yield).

N^6-*Benzyl-3′*-O- (**15**) *and -2′*-O-*(phenylcarbamoyl)adenosine* (**16**) *through (phenylcarbamoyl)ation of* **5** *by Procedure B.* — To a solution of **5** (1.07 g, 3.0 mmol) and bis(tributyltin) oxide (894 mg, 1.5 mmol) in DMF (1.5 mL) was added acetonitrile (10.5 mL), and the mixture was treated with phenyl isocyanate (0.67 mL, 6 mmol) for 1 h at 0° under a nitrogen atmosphere, with stirring. After quenching the reaction with methanol (5 mL), the mixture was evaporated to a syrup, which was then chromatographed on a column of silica gel, to give **15** (786 mg, 55% yield) and **16** (357 mg, 25% yield).

Compound **15** had m.p. 123–125° (from chloroform–methanol–hexane), $[\alpha]_D^{22}$ $-68.6°$ (*c* 1, DMF); λ_{max}^{EtOH} 269 (ε_{mM} 18.60) and 237 nm (17.10), λ_{min}^{EtOH} 251 nm (ε_{mM} 10.70); n.m.r. [$(CD_3)_2SO$–Me_4Si; D_2O added; Varian EM-390]: δ 3.57–4.97 (m, 5 H, H-4′,5′,5″, and CH_2-Ph), 5.00 (t, 1 H, H-2′), 5.39 (dd, 1 H, H-3′), 6.10 (d, 1 H, $J_{1',2'}$ 6.7 Hz, H-1′), 6.93–7.67 (m, 10 H, 2 C_6H_5), and 8.31 and 8.46 (each s, each 1 H, H-2 or 8).

Anal. Calc. for $C_{24}H_{24}N_6O_5$: C, 60.49; H, 5.08; N, 17.64. Found: C, 60.52; H, 4.99; N, 17.79.

Compound **16** was amorphous and had $[\alpha]_D^{22}$ $-74.2°$ (*c* 1, DMF); λ_{max}^{EtOH} 269 (ε_{mM} 19.50) and 237 nm (18.50), λ_{min}^{EtOH} 251 nm (ε_{mM} 11.20); n.m.r. [$(CD_3)_2SO$–Me_4Si, D_2O added; Varian EM-390]: δ 3.93–5.10 (m, 6 H, H-3′,4′,5′,5″, and CH_2-Ph), 5.73 (t, 1 H, H-2′), 6.28 (d, 1 H, $J_{1',2'}$ 6.2 Hz, H-1′), 6.87–7.67 (m, 10 H, 2 C_6H_5), and 8.29 and 8.48 (each s, each 1 H, H-2 or 8).

Anal. Calc. for $C_{24}H_{24}N_6O_5$: C, 60.49; H, 5.08; N, 17.64. Found: C, 60.38; H, 4.99; N, 17.80.

N^6-*Benzoyl-3′*-O- (**21**) *and -2′*-O-*(phenylcarbamoyl)adenosine* (**22**) *through (phenylcarbamoyl)ation of* N^6-*benzoyladenosine* (**14**) *by Procedure B.* — To a solution of[19] **14** (185 mg, 0.5 mmol) and bis(tributyltin) oxide (149 mg, 0.25 mmol) in DMF (2.3 mL) was added toluene (15 mL), and the solution was treated with phenyl isocyanate (0.11 mL, 1 mmol) under nitrogen for 5 h at 0°, with stirring. After the reaction had been quenched with methanol (5 mL), the solution was evaporated to dryness, and the residue was chromatographed on a column of silica gel, to give **21** (148 mg, 60% yield) and **22** (42 mg, 17% yield), in addition to **14** (28 mg, 15% recovery).

Compound **21** had m.p. 146–147° (from chloroform), $[\alpha]_D^{24}$ $-76.5°$ (*c* 1, DMF); λ_{max}^{EtOH} 280 (ε_{mM} 22.80) and 234 nm (30.30), λ_{min}^{EtOH} 253 nm (ε_{mM} 12.40); n.m.r. [$CDCl_3$–$(CD_3)_2SO$ (2:1, v/v–Me_4Si; D_2O added; Varian T-60]: δ 3.50–4.73 (m, 3 H, H-4′,5′,5″), 5.04 (t, 1 H, H-2′), 5.30–5.58 (m, 1 H, H-3′), 6.18 (d, 1 H, $J_{1',2'}$ 7.2 Hz, H-1′), 6.83–8.30 (m, 10 H, 2 C_6H_5), and 8.57 and 8.69 (each s, each 1 H, H-2 or 8).

Anal. Calc. for $C_{24}H_{22}N_6O_6$: C, 58.77; H, 4.52; N, 17.14. Found: C, 58.72; H, 4.60; N, 16.86.

Compound **22** had n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si: D_2O added; Varian T-60]: δ 3.53–4.83 (m, 4 H, H-3′,4′,5′,5″), 5.70 (t, 1 H, H-2′), 6.37 (d, 1 H, $J_{1',2'}$ 6.4 Hz, H-1′), and 6.57–8.67 (m, 12 H, H-2,8, and 2 C_6H_5).

3′-O- (**23**) *and 2′-O-(Phenylcarbamoyl)adenosine* (**24**) *through (phenylcarbamoyl)ation of adenosine* (**17**) *by Procedure B.* — To a solution of **17** (268 mg, 1 mmol) and bis(tributyltin) oxide (298 mg, 0.5 mmol) in 2:1 DMF–Me_2SO (3 mL) was added toluene (15 mL), and the resulting solution was treated with phenyl isocyanate (0.15 mL, 1.25 mmol) at 0° under nitrogen, with stirring; phenyl isocyanate (0.09 mL, 1.25 mmol) was then added dropwise during 2 h, with monitoring by t.l.c. of the spot of **17** until its disappearance. After the reaction had been quenched with methanol (5 mL), the solution was evaporated to dryness, and the residue was chromatographed on a column of silica gel, to give a mixture of **23** and **24** (319 mg, 82% yield; **23**:**24** = 6:1, according to the area-ratio of ^{1}H-n.m.r. proton signals of H-3′ of **23** and H-2′ of **24**), in addition to a mixture of 3′,5′- (**25**) and 2′,5′-bis-*O*-(phenylcarbamoyl)-adenosine (**26**) (69 mg, 14% yield). On fractional recrystallization, the former mixture gave a pure sample of **23** (214 mg, 55% yield).

Compound **23** had m.p. 183–184° (from ethanol), $[\alpha]_D^{24}$ −93.1° (*c* 1, DMF); λ_{max}^{EtOH} 260 (ε_{mM} 17.40) and 238 nm (22.00), λ_{min}^{EtOH} 252 nm (ε_{mM} 15.60); n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; D_2O added; Varian T-60]: δ 3.61–4.08 (m, 2 H, H-5′,5″), 4.22–4.43 (m, 1 H, H-4′), 4.96 (t, 1 H, H-2′), 5.23–5.43 (m, 1 H, H-3′), 6.03 (d, 1 H, $J_{1',2'}$ 7.0 Hz, H-1′), 6.77–7.91 (m, 5 H, C_6H_5), and 8.18 and 8.27 (each s, each 1 H, H-2 or 8).

Anal. Calc. for $C_{17}H_{18}N_6O_5$: C, 52.84; H, 4.70; N, 21.75. Found: C, 52.97; H, 4.64; N, 21.61.

Compound **24**, obtained as a mixture with **23**, had n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; D_2O added; Varian T-60]: δ 5.69 (t, 1 H, H-2′), and 6.28 (d, 1 H, $J_{1',2'}$ 6.0 Hz, H-1′).

3′,5′- (**25**) *and 2′,5′-Bis-O-(phenylcarbamoyl)adenosine* (**26**) *through (phenylcarbamoyl)ation of* **17** *by Procedure B.* — To a solution of **17** (531 mg, 2 mmol) and bis(tributyltin) oxide (593 mg, 1 mmol) in Me_2SO (3 mL) was added toluene (9 mL), and the mixture was treated with phenyl isocyanate (0.3 mL, 2.7 mmol) at 0° under nitrogen, with stirring; phenyl isocyanate (0.3 mL, 2.7 mmol) was now added dropwise (total time for the addition, 5 h). After the reaction had been quenched with methanol (5 mL), the mixture was processed in the usual way, and the material chromatographed, to give **25** (636 mg, 63% yield) and **26** (243 mg, 24% yield). The former was recrystallized from chloroform–ethanol–hexane, to give **25** (557 mg, 55% yield).

Compound **25** had m.p. 133–135° (from chloroform–ethanol–hexane), $[\alpha]_D^{24}$ −69.9° (*c* 1, DMF); λ_{max}^{EtOH} 259 (ε_{mM} 17.30) and 237 nm (39.00), λ_{min}^{EtOH} 253 nm (ε_{mM} 16.70); n.m.r. [$CDCl_3$–$(CD_3)_2SO$ (2:1, v/v)–Me_4Si; D_2O added; Varian T-60]: δ 4.17–4.73 (bs, 3 H, H-4′,5′,5″), 5.03 (t, 1 H, H-2′), 5.29–5.50 (m, 1 H, H-3′), 6.14 (d, 1 H, $J_{1',2'}$ 6.4 Hz, H-1′), 6.63–7.72 (m, 10 H, 2 C_6H_5), and 8.17 and 8.24 (each s, each 1 H, H-2 or 8).

Anal. Calc. for $C_{24}H_{23}N_7O_6$: C, 57.02; H, 4.59; N, 19.40. Found: C, 56.79; H, 4.71; N, 19.16.

Compound **26** was amorphous, and had $[\alpha]_D^{24}$ $-46°$ (*c* 1, DMF); λ_{max}^{EtOH} 258 (ε_{mM} 15.70) and 236 nm (35.00), λ_{min}^{EtOH} 253 nm (ε_{mM} 15.10); n.m.r. [$CDCl_3$-$(CD_3)_2SO$ (2:1, v/v)-Me_4Si; D_2O added, Varian T-60]: δ 4.15–4.59 (m, 3 H, H-4′,5′,5″), 4.63–4.89 (m, 1 H, H-3′), 5.62 (t, 1 H, H-2′), 6.30 (d, 1 H, $J_{1',2'}$ 5.2 Hz, H-1′), 6.70–7.70 (m, 10 H, 2 C_6H_5), and 8.20 and 8.25 (each s, each 1 H, H-2 or 8).

3′-O- (**27**) and *2′-O-(Phenylcarbamoyl)inosine* (**28**) *through (phenylcarbamoyl)-ation of inosine* (**18**) *by Procedure B.* — To a solution of **18** (268 mg, 1 mmol) and bis-(tributyltin) oxide (298 mg, 0.5 mmol) in Me_2SO (3 mL) was added toluene (20 mL), and the mixture was treated with phenyl isocyanate (0.22 mL, 2 mmol) under nitrogen, at 0°, for 2 h evaporated to dryness, and the residue subjected to chromatographic separation, to give **27** (260 mg, 67% yield) and **28** (122 mg, 31% yield).

Compound **27** had m.p. 165° (from methanol), $[\alpha]_D^{24}$ $-65°$ (*c* 1, DMF); λ_{max}^{EtOH} 238 nm (ε_{mM} 23.50); n.m.r. [$CDCl_3$-$(CD_3)_2SO$ (2:1, v/v)-Me_4Si; Varian T-60]: δ 3.50–4.47 (m, 3 H, H-4′,5′,5″), 4.90 (m, 1 H, H-2′), 5.23–5.47 (m, 1 H, H-3′), 6.04 (d, 1 H, $J_{1',2'}$ 6.6 Hz, H-1′), and 6.81–8.39 (m, 7 H, H-2,8, and C_6H_5).

Compond **28** was amorphous, and had n.m.r. [$CDCl_3$-$(CD_3)_2SO$-Me_4Si; D_2O added; Varian T-60]: δ 3.55–4.72 (m, 4 H, H-3′,4′,5′,5″), 5.59 (t, 1 H, H-2′), 6.23 (d, 1 H, $J_{1',2'}$ 5.5 Hz, H-1′), and 6.85–8.45 (m, 7 H, H-2,8, and C_6H_5).

3′-O- (**29**) *and 2′-O-(Phenylcarbamoyl)uridine* (**30**) *through (phenylcarbamoyl)-ation of uridine* (**19**) *by Procedure B.* — To a solution of **19** (246 mg, 1 mmol) and bis-(tributyltin) oxide (301 mg, 0.5 mmol) in DMF (5 mL) was added toluene (30 mL), and the solution was treated with phenyl isocyanate (0.22 mL, 2 mmol) under nitrogen for 1.5 h at 0°, with stirring. After quenching the reaction with methanol (5 mL), the solution was evaporated to dryness, and the residue was chromatographed on a column of silica gel, to give **29** (200 mg, 55% yield) and **30** (55 mg, 15% yield), in addition to a mixture of the corresponding 3′,5′- (**31**) and 2′,5′-bis-*O*-(phenylcarbamoyl)uridine (**32**) (152 mg, 29% yield).

Compound **29** had m.p. 177–178° (from chloroform–ethanol), $[\alpha]_D^{23}$ $-40.2°$ (*c* 1, DMF); λ_{max}^{EtOH} 262 (ε_{mM} 12.10) and 237 nm (20.10), λ_{min}^{EtOH} 253 nm (ε_{mM} 11.20); n.m.r. [$CDCl_3$-$(CD_3)_2SO$-Me_4Si; D_2O added; Varian T-60]: δ 3.50–4.40 (m, 3 H, H-4′,5′,5″), 4.46 (t, 1 H, H-2′), 5.13–5.33 (m, 1 H, H-3′), 5.75 (d, 1 H, $J_{5,6}$ 7.8 Hz, H-5), 6.07 (d, 1 H, $J_{1',2'}$ 6.6 Hz, H-1′), 6.79–7.80 (m, 5 H, C_6H_5), and 8.01 (d, 1 H, H-6).

Anal. Calc. for $C_{16}H_{17}N_3O_7$: C, 52.89; H, 4.72; N, 11.57. Found: C, 52.68; H, 4.70; N, 11.55.

Compound **30**, a glass, had n.m.r. [$CDCl_3$-$(CD_3)_2SO$-Me_4Si; D_2O added; Varian EM-390]: δ 3.24–3.90 (m, 3 H, H-4′,5′,5″), 4.00–4.30 (m, 1 H, H-3′), 5.23 (t, 1 H, H-2′), 5.71 (d, 1 H, $J_{5,6}$ 5.9 Hz, H-5), 6.19 (d, 1 H, $J_{1',2'}$ 6.2 Hz, H-1′), 6.87–7.80 (m, 5 H, C_6H_5), and 8.00 (d, 1 H, H-6).

3′,5′- (**31**) *and 2′,5′-Bis-O-(phenylcarbamoyl)uridine* (**32**) *through (phenylcarbamoyl)ation of* **19** *by Procedure B.* — To a solution of **19** (244 mg, 1 mmol) and bis(tributyltin) oxide (297 mg, 0.5 mmol) in DMF (1 mL) was added toluene (5 mL), and then phenyl isocyanate (0.3 mL, 2.8 mmol), at 0°, under nitrogen, and the mixture was stirred for 3 h. Further phenyl isocyanate (0.08 mL, 0.7 mmol) was added dropwise during 3 h, the reaction quenched with methanol (5 mL), and the material obtained by the usual processing was subjected to chromatographic separation on a column of silica gel, to give **31** (287 mg, 59% yield) and **32** (146 mg, 30% yield).

Compound **31** had m.p. 141–142° (from ethanol), $[\alpha]_D^{23}$ $-44°$ (*c* 1, DMF); λ_{max}^{EtOH} 262 (ε_{mM} 11.40) and 237 nm (36.30), λ_{min}^{EtOH} 254 nm (ε_{mM} 11.10); n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; D_2O added Varian T-60]: δ 3.40–4.77 (m, 4 H, H-2',4',5',5"), 5.10–5.40 (m, 1 H, H-3'), 5.68 (d, 1 H, $J_{5,6}$ 8.0 Hz, H-5), 6.08 (d, 1 H, $J_{1',2'}$ 6.6 Hz, H-1'), and 6.67–8.05 (m, 11 H, H-6, and 2 C_6H_5).

Anal. Calc. for $C_{23}H_{22}N_4O_8$: C, 57.26; H, 4.60; N, 11.61. Found: C, 57.54; H, 4.54; N, 11.70.

Compound **32** had m.p. 194–195° (from ethyl acetate), $[\alpha]_D^{23}$ $-6.2°$ (*c* 1, DMF); λ_{max}^{EtOH} 260 (ε_{mM} 10.80) and 237 nm (35.70), λ_{min}^{EtOH} 254 nm (ε_{mM} 10.60); n.m.r. [$CDCl_3$–$(CD_3)_2SO$ (2:1, v/v)–Me_4Si; D_2O added; Varian T-60]: δ 3.43–4.77 (m, 4 H, H-3',4',5',5"), 5.30 (t, 1 H, H-2'), 5.71 (d, 1 H, $J_{5,6}$ 8.2 Hz, H-5), 6.17 (d, 1 H, $J_{1',2'}$ 5.6 Hz, H-1'), and 6.75–7.82 (m, 11 H, H-6 and 2 C_6H_5).

Anal. Calc. for $C_{23}H_{22}N_4O_8$: C, 57.26; H, 4.60; N, 11.61. Found: C, 57.34; H, 4.61; N, 11.61.

3',5'- (**33**) *and 2',5'-Bis-O-(phenylcarbamoyl)cytidine* (**34**) *through (phenylcarbamoyl)ation of cytidine* (**20**) *by Procedure B.* — To a solution of **20** (486 mg, 2 mmol) and bis(tributyltin) oxide (596 mg, 1 mmol) was added toluene (5 mL), and the mixture was treated with phenyl isocyanate (0.45 mL, 4.1 mmol) for 3.5 h at 0°, under nitrogen, with stirring. After the reaction had been quenched with methanol (5 mL), the solution was evaporated to dryness, and the residue was chromatographed on a column of silica gel, to give **33** (611 mg, 63% yield) and **34** (227 mg, 24% yield)

Compound **33** had m.p. 143–145° (from chloroform), $[\alpha]_D^{24}$ $-38.2°$ (*c* 1, DMF); λ_{max}^{EtOH} 272 (ε_{mM} 9.30) and 237 nm (37.30), λ_{min}^{EtOH} 257 nm (ε_{mM} 8.30); n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; D_2O added; Varian T-60]: δ 5.15–5.71 (m, 4 H, H-2',4', 5',5"), 6.02–6.33 (m, 1 H, H-3'), 6.89 (d, 1 H, $J_{5,6}$ 7.3 Hz, H-5), 7.13 (d, 1 H, $J_{1',2'}$ 5.8 Hz, H-1'), and 7.65–8.71 (m, 11 H, H-6 and 2 C_6H_5).

Anal. Calc. for $C_{23}H_{23}N_5O_7$: C, 57.37; H, 4.82; N, 14.55. Found: C, 57.35; H, 4.93; N, 14.85.

Compound **34** had m.p. 195–196° (from ethyl acetate), $[\alpha]_D^{24}$ $-16.4°$ (*c* 1, DMF); λ_{max}^{EtOH} 271 (ε_{mM} 9.30) and 237 nm (38.40), λ_{min}^{EtOH} 258 nm (ε_{mM} 8.70); n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; D_2O added; Varian T-60]: δ 4.93–5.57 (m, 4 H, H-3',4', 5',5"), 6.20 (t, 1 H, H-2'), 6.86 (d, 1 H, $J_{5,6}$ 7.2 Hz, H-5), 7.09 (d, 1 H, $J_{1',2'}$ 4.8 Hz, H-1'), and 7.70–9.00 (m, 11 H, H-6 and 2 C_6H_5).

2'-Deoxy-5'-O-(phenylcarbamoyl)uridine (**38**) *through (phenylcarbamoyl)ation of 2'-deoxyuridine* (**35**) *by Procedure B.* — To a solution of **35** (230 mg, 1 mmol) and bis(tributyltin) oxide (295 mg, 0.5 mmol) in DMF (2 mL) was added toluene

(5 mL), and the mixture was treated with phenyl isocyanate (0.2 mL, 1.8 mmol) under nitrogen for 1 h at 0°, with stirring; more phenyl isocyanate (0.04 mL, 0.36 mmol) was then added dropwise during 1 h at the same temperature. The reaction was quenched with methanol (5 mL), the solution was processed as usual, and the product was chromatographed, to give the title compound (345 mg, 99% yield). Crystallization gave a pure sample (301 mg, 87% yield); m.p. 160–161° (from chloroform–hexane), $[\alpha]_D^{24}$ $-10.1°$ (c 1, DMF); λ_{max}^{EtOH} 262 (ε_{mM} 10.40) and 236 nm (19.50), λ_{min}^{EtOH} 252 nm (ε_{mM} 8.90); n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; D_2O added; Varian T-60]: δ 2.12–2.46 (m, 2 H, H-2′,2″), 3.97–4.61 (m, 4 H, H-3′,4′,5′,5″), 5.65 (d, 1 H, $J_{5,6}$ 8.1 Hz, H-5), 6.26 (t, 1 H, $J_{1',2'} = J_{1',2''} = 6.8$ Hz, H-1′), and 6.71–7.77 (m, 6 H, H-6 and C_6H_5).

Anal. Calc. for $C_{16}H_{17}N_3O_6$: C, 55.33; H, 4.93; N, 12.10. Found: C, 55.09; H, 4.84; N, 12.01.

5′-O-(Phenylcarbamoyl)thymidine (**39**) *through (phenylcarbamoyl)ation of thymidine* (**36**) *by Procedure B.* — To a solution of **36** (243 mg, 1 mmol) and bis(tributyltin) oxide (299 mg, 0.5 mmol) in DMF (1 mL) was added toluene (5 mL), and the solution was treated with phenyl isocyanate (0.2 mL, 1.8 mmol) for 0.5 h at 0° under nitrogen, with stirring. The reaction was quenched with methanol (5 mL), the solution evaporated, and the residue chromatographed on a column of silica gel, to give the title compound (335 mg, 93% yield); recrystallization gave a pure sample (302 mg, 84% yield); m.p. 210–211° (from methanol), $[\alpha]_D^{24}$ $-25.1°$ (c 1, DMF); λ_{max}^{EtOH} 267 (ε_{mM} 9.30) and 235 nm (18.10), λ_{min}^{EtOH} 252 nm (ε_{mM} 6.50); n.m.r. [$CDCl_3$–$(CD_3)_2SO$ (2:1, v/v); D_2O added; Varian T-60]: δ 1.79 (s, 3 H, 5 CH_3), 2.13–2.48 (m, 2 H, H-2′,2″), 3.98–4.60 (m, 4 H, H-3′,4′,5′,5″), 6.28 (t, 1 H, $J_{1',2'} = J_{1',2''} = 7.0$ Hz, H-1′), and 6.79–7.87 (m, 6 H, H-6 and C_6H_5).

Anal. Calc. for $C_{17}H_{19}N_3O_6$: C, 56.50; H, 5.30; N, 11.63. Found: C, 56.74; H, 5.24; N, 11.74.

2′-Deoxy-5′-O-(phenylcarbamoyl)adenosine (**40**) *through (phenylcarbamoyl)ation of 2′-deoxyadenosine* (**37**) *by Procedure B.* — To a solution of **37** (253 mg, 1 mmol) and bis(tributyltin) oxide (298 mg, 0.5 mmol) in DMF (6 mL) was added toluene (9 mL), and the solution was treated with phenyl isocyanate (0.6 mL, 5.5 mmol) at 0° under nitrogen, with stirring, the reagent being added dropwise during 121 h. The reaction was now quenched with methanol (5 mL), the solution was treated in the usual way, and the residue was chromatographed on a column of silica gel, to give the title compound (248 mg, 67% yield); recrystallization gave a pure sample (212 mg, 57% yield); m.p. 179–180° (from ethanol–hexane), $[\alpha]_D^{24}$ $-39.1°$ (c 1, DMF); λ_{max}^{EtOH} 261 (ε_{mM} 15.50) and 238 nm (20.50), λ_{min}^{EtOH} 251 nm (ε_{mM} 13.60); n.m.r. [$CDCl_3$–$(CD_3)_2SO$–Me_4Si; D_2O added; Varian T-60]: δ 2.20–3.25 (m, 2 H, H-2′,2″), 4.02–4.74 (m, 4 H, H-3′,4′,5′,5″), 6.77 (d, 1 H, $J_{1',2'}$ 6.6 Hz, H-1′), and 6.77–8.39 (m, 7 H, H-2,8, and C_6H_5).

Anal. Calc. for $C_{17}H_{18}N_6O_4$: C, 55.13; H, 4.90; N, 22.69. Found: C, 55.09; H, 4.87; N, 22.88.

Attempt at examination of potential migration of the phenylcarbamoyl group *under the reaction conditions used.* — A solution of **11** (29 mg, 0.05 mmol) and bis(tributyltin) oxide (15 mg, 25 μmol) in DMF (0.15 mL) was diluted with toluene (1.5 mL), and the solution was treated with phenyl isocyanate (2.7 μL, 25 μmol) for 100 h at 0°, with stirring. The reaction was quenched with methanol (3 mL), the volume was brought to 10 mL with chloroform, and the solution was subjected to l.c. analysis. Solvent composition, 9–13.8% of B; 9% for the initial 8 min, with a slope of 0.6%/min up to 16 min; finally, 13.8%.

Compound **12** was subjected to the same processing. The mixture resulting from **11** proved to be composed of **11** (96% recovery) and **13** (2% yield), containing no **12**. That from **12**, on the other hand, was composed of **11** (2% yield) and **12** (106% recovery), and contain no **13**.

For some of the new compounds described herein, no data for elemental analyses are given, due to their hygroscopic character.

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