B. In Methanol. A solution of **16** (315 mg) and mercuric acetate (477 mg) in methanol (20 ml) was stirred. Work-up gave **19** (455 mg): mp 132–134° (from MeOH); ir (KBr) 1740 cm^{-1}.

Anal. Calcd for $C_{12}H_{17}O_5HgCl$: C, 30.20; H, 3.59. Found: C, 30.18; H, 3.44.

C. In Acetic Acid. A solution of **16** (315 mg) and mercuric acetate (477 mg) in acetic acid (10 ml) was stirred. Work-up gave **20** (650 mg): mp 176–178° (from acetone); ir (KBr) 1745, 1720 cm^{-1}.

Anal. Calcd for $C_{13}H_{17}O_6HgCl$: C, 30.90; H, 3.39. Found: C, 30.80; H, 3.39.

Oxymercuration of 17. A. In Methanol. A solution of **17** (300 mg) and mercuric acetate (530 mg) in methanol (20 ml) was stirred. Work-up gave **17** in quantitative yield.

B. In Acetic Acid. A solution of **17** (300 mg) and mercuric acetate (530 mg) in acetic acid (10 ml) was stirred. Work-up gave **17** (280 mg).

Acknowledgment. We express our gratitude to Badishe Anilin Soda-Fabrick (BASF) AG for a generous gift of cyclooctatetraene.

Registry No.—**1,** 51447-09-7; **2,** 52730-88-8; **3,** 35211-83-7; **4a,** 52730-89-9; **4b,** 52730-90-2; **4c,** 52827-09-5; **5,** 52748-22-8; **6,** 52748-23-9; **7,** 52748-24-0; **8,** 52748-25-1; **9,** 52746-59-5; **10,** 944-41-2; **11,** 956-36-5; **12,** 52746-60-8; **13,** 52730-91-3; **14,** 52730-92-4; **15,** 129-64-6; **16,** 39589-98-5; **17,** 3753-88-1; **18,** 26097-22-3; **19,** 52730-93-5; **20,** 52730-94-6; mercuric acetate, 1600-27-7; diazomethane, 334-88-3; acetic anhydride, 108-24-7; *p*-nitrobenzoyl chloride, 122-04-3.

References and Notes

(1) For Paper XVI of this series, see T. Sasaki, K. Kanematsu, K. Hayakawa, and M. Sugiura, *J. Amer. Chem. Soc.*, in press.
(2) T. Sasaki, K. Kanematsu, and A. Kondo, *J. Org. Chem.*, **39,** 2246 (1974).
(3) Oxymercuration of some strained olefins was extensively investigated and well reviewed: (a) T. G. Traylor, *Accounts Chem. Res.*, **2,** 152 (1969); (b) A. Factor and T. G. Traylor, *J. Org. Chem.*, **33,** 2607, 2614 (1968); (c) N. C. Yang and J. Libman, *J. Amer. Chem. Soc.*, **94,** 9228 (1972).
(4) (a) E. C. Traylor, F. Kienzle, R. L. Robey, A. Mckillop, and J. D. Hunt, *J. Amer. Chem. Soc.*, **93,** 4845 (1971); (b) H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 227 (1959); (c) M. J. Abercombie, A. Rodgman, K. R. Bharucha, and G. F. Wright, *Can. J. Chem.*, **37,** 1328 (1959).
(5) This is not in conflict with the fact that oxymercuration of cyclobutene occurs at trans; see ref 3a.

Halo Sugar Nucleosides. IV.[1] Synthesis of Some 4′,5′-Unsaturated Pyrimidine Nucleosides

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Syntheses are described for the 1-(5-deoxypent-4-enofuranosyl) nucleosides derived from uridine, thymidine, cytidine, and 2′-deoxycytidine. These compounds were prepared *via* dehydrohalogenation of the appropriately acylated 5′-iodo-5′-deoxy nucleosides using either silver fluoride in pyridine or bases such as 1,5-diazabicyclo-[4.3.0]non-5-ene. The nucleoside diene 2-methylene-5-(*R*)-(thymin-1-yl)-2,5-dihydrofuran (**10**) could also be prepared either by treatment of 3′,5′-dideoxy-3′,5′-diiodothymidine with silver fluoride in pyridine or by base-catalyzed elimination of iodide from the 5′-iodo-2′,3′-unsaturated nucleoside **11b**. Catalytic reduction of N^4-acetyl-5′-deoxy-5′-iodo-2′,3′-*O*-isopropylidenecytidine followed by hydrolysis of the protecting groups gave the previously unknown 5′-deoxycytidine.

Previous work in this series has described the development of synthetic routes for the replacement of specific hydroxyl groups in both purine and pyrimidine nucleosides by iodo,[2] bromo,[1] or chloro[1] functions. In addition, other methods have been devised for the specific conversion of cis vicinal diols into vicinal chloro or bromo acetates.[3] The resulting halo sugar nucleosides are versatile starting materials for the preparation of unusual deoxy nucleosides,[2b,3b,3c] unsaturated nucleosides,[4] anhydro nucleosides,[3] etc.

Nucleosides containing unsaturated sugars have, in recent years, been the targets of considerable synthetic effort.[5] This is due both to the potential biological activity of these compounds, and to the possibility of using them as intermediates for the synthesis of other compounds, as in, *e.g.*, the synthesis of the antibiotic nucleocidin.[4a] We have been particularly interested in the synthesis of 4′,5′-unsaturated nucleosides since this structural feature is present in the nucleoside antibiotic Angustmycin A,[6] a compound that has been prepared both by modification of the antibiotic psicofuranine[7] and by total synthesis,[8] and in the products from treatment of coenzyme B_{12} with alkali.[9] In the present paper we describe the preparation of the 4′,5′-unsaturated nucleosides derived from the pyrimidine nucleosides uridine, thymidine, cytidine, and deoxycytidine. A part of this work has previously been briefly described.[10]

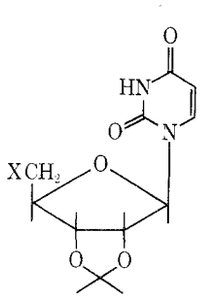
The early work of Helferich, *et al.*, has shown that 6-deoxyhex-5-enopyranosides can be prepared by treatment of the related 6-deoxy-6-halohexopyranose derivatives with silver fluoride in pyridine.[11] It was not until 1966, however, that this method was extended to the preparation of 5-deoxypent-4-enofuranose systems by Hough and Otter,[12] working with furanose sugars, and by our own preliminary work in the uridine series.[10]

The most readily available starting material for explorative studies on the dehydrohalogenation of 5′-halo-5′-deoxy nucleosides was 5′-deoxy-5′-iodo-2′,3′-*O*-isopropylideneuridine (**1a**),[2a] but, to our disappointment, we found that treatment of **1a** with a suspension of finely divided silver fluoride in pyridine at room temperature for several days led to three products, only a minor one being the desired 1-(5-deoxy-2,3-*O*-isopropylidene-β-D-*erythro*-pent-4-enofuranosyl)uracil (**2**). The major product, which was readily isolated owing to its solubility in water, was readily shown to be 2,5′-anhydro-2′,3′-*O*-isopropylideneuridine (**3**)[13] by comparison with an authentic sample.[2a] The organic solvent soluble products (20–35%) ran as a single spot upon tlc in a variety of systems, but examination of the nmr spectrum clearly showed this material to be a 3:1 mixture of 5′-deoxy-5′-fluoro-2′,3′-*O*-isopropylideneuridine (**1b**)[14] and the desired **2**. By subtraction of the resonances attributable to **2**, the characteristic spectrum of **1b** with large fluorine couplings ($J_{5'\text{-}F}$ = 46 Hz, $J_{4'\text{-}F}$ = 25 Hz) was readily apparent and was compared with that of an authentic sample.[14] The preferential formation of the cyclonucleoside (**3**) is presumably a consequence of the tendency of 2′,3′-*O*-iso-

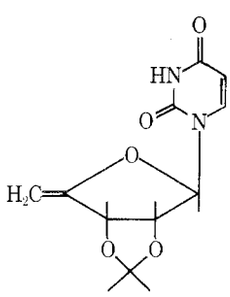
Table I
Nmr Chemical Shifts at 100 MHz

Compd	Solvent	$C_{1'}H$	$C_{2'a}H$	$C_{2'b}H$	$C_{3'}H$	$C_{4'}H$	$C_{5'a}H$	$C_{5'b}H$	C_5H	C_6H	Other
1b	C	5.88	4.90		4.90	4.41		4.68	5.79	7.32	1.38 and 1.60 (CMe_2)
2	C	5.68	5.03		5.32		4.42	4.61	5.75	7.21	1.40 and 1.53 (CMe_2)
6a	P	6.66	6.12		6.41		4.53	4.80	5.86	7.82	1.97 and 2.05 (OAc)
6b	D, D_2O	5.97	4.24		4.40		4.20	4.34	5.64	7.59	
8a	C	6.55	2.24	2.52	5.73		4.42	4.61		6.98	1.93 (C_5Me), 2.09 (3'-OAc)
8b	D	6.41	2.14	2.40	4.70		4.14	4.28		7.49	1.78 (C_5Me), 5.51 (3'-OH)
10	P	7.58	6.62		6.27		4.28	4.60		6.97	1.86 (C_5Me)
11a	D	6.83	6.39		5.90	4.77		3.62		7.66	1.75 (C_5Me)
11b	D	6.84	6.44		6.07	4.87		3.47		7.40	1.80 (C_5Me)
16a	P	6.40	5.20		5.20	4.63	3.98	4.14	7.55	8.49	1.34 and 1.58 (CMe_2),2.26 (NAc)
16b	P	6.11	5.43		5.18	4.58	3.57	3.86	7.60	8.12	1.32 and 1.54 (CMe_2), 2.28 (NAc)
16c	P	6.19	5.27		4.74	4.38		1.42	7.64	8.09	1.35 and 1.59 (CMe_2), 2.29 (NAc)
17a	D	5.85	4.17		3.85	3.85	3.51	3.63	7.23	8.09	2.11 (NAc), 5.31 and 5.51 (2'-and 3'-OH)
17b	C	6.10	5.44		5.24	4.16		3.52	7.49	7.99	2.06 and 2.09 (OAc), 2.26 (NAc)
18	P	6.82	4.78		5.05		4.66	4.78	6.04	7.57	
19	D, D_2O	5.64	4.06		3.61	3.92		1.30	6.18	7.85	
20b	F	6.30	2.33	2.52	4.34	4.07		3.58	7.41	8.27	7.55 and 8.12 (Ar)
20c	F	6.30	2.4		4.39	4.14		3.80	7.41	8.26	7.57 and 8.12 (Ar)
21a	P	6.90	2.55	2.80	5.12		4.54	4.72	7.63	7.94	7.50 and 8.17 (Ar)
21b	P, D_2O	6.85	2.38	2.72	5.10		4.58	4.63	6.13	7.36	

[a] Solvents are designated as C ($CDCl_3$), D (d_6-DMSO), F (d_7-DMF), P (d_5-pyridine).



1a, X = I
b, X = F



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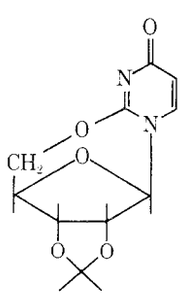

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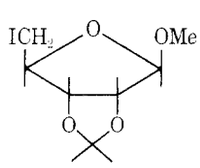


4

propylidene derivatives of pyrimidine nucleosides to undergo intramolecular cyclization reactions involving $C_{5'}$.[15] A previously described synthesis of **3** has indeed involved treatment of **1** with silver acetate.[13] The formation of the 5'-fluoro nucleoside (**1b**) in the above reaction is not surprising since Otter, et al.,[15] have mentioned, without any experimental details, that this compound arises from reaction of the cyclonucleoside (**3**) with silver fluoride.

The failure to convert the isopropylidene derivative (**1a**) to the desired olefin (**2**) is interesting in view of the fact that treatment of methyl 5-deoxy-5-iodo-2,3-*O*-isopropylidene-β-D-ribofuranoside (**4**) with silver fluoride in pyridine gives the ribofuranoside olefin equivalent to **2** in high yield.[12] It would appear that in the isopropylideneuridine series the reactive intermediate is almost totally trapped by reaction with the uracil ring giving **3**. It was, however, possible to prepare the isopropylidene olefin (**2**) in 84% yield by treatment of **1a** with potassium *tert*-butoxide in dimethyl sulfoxide. This same compound has also been prepared by Robins, *et al.*,[16] by treatment of 2',3'-*O*-isopropylidene-5'-*O*-*p*-toluenesulfonyluridine with potassium *tert*-butoxide and was obtained as a crystalline solvate with one half an equivalent of isopropyl alcohol. While we have not succeeded in obtaining **2** in crystalline form, its nmr spectrum (Tables I and II) is identical with that described by Robins, *et al.*[16]

Some preliminary studies were carried out to determine whether essentially neutral reagents other than silver fluoride in pyridine could be used for the dehydrohalogenation reaction. For this purpose, comparable reactions were carried out between **4**[17] and 1 molar equiv of silver fluoride, silver oxide, silver perchlorate, silver nitrate, silver acetate, and mercuric fluoride in pyridine and the products were examined by gas–liquid chromatography. As reported earlier, the reaction with silver fluoride readily gave methyl 5-deoxy-2,3-*O*-isopropylidene-β-D-*erythro*-pent-4-enofuranoside[12] while none of the other salts led to this product. The only salt which led to any significant reaction was silver acetate, which gave 40% conversion to methyl 5-*O*-acetyl-2,3-*O*-isopropylidene-β-D-ribofuranoside.[18]

Our own investigations on the acidic stability of **2**, and those of McCarthy, *et al.*,[19] in the related adenosine series, have shown that the exocyclic vinyl ether function is more sensitive to acid than is the isopropylidene group. Thus treatment of **2** with 80% acetic acid at room temperature

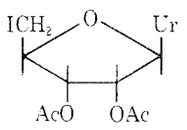
Table II
Coupling Constants (Hertz)

Compd	$J_{1',2'a}$	$J_{1',2'b}$	$J_{2'a,3'}$	$J_{2'b,3'}$	$J_{3',4'}$	$J_{3',5'a}$	$J_{3',5'b}$	$J_{4',5'a}$	$J_{4',5'b}$	$J_{5'a,5'b}$	$J_{5,6}$	Other
1b	1.5		<2		<2			<2	<2	0	7.5	$J_{5',F} = 46$, $J_{4',F} = 25$
2	0		6				1			3	7.5	
6a	4.5		6			1.5	1.5			2.5	8	
6b	5		5			<1	<1			1.5	8	
8a	7	6	7	2		0	0			2.5		$J_{2'a,2'b} = 14$, $J_{6,CH_3} = 1.5$
8b	6.5	6.5	3.5	6.5		<1	<1			1.5		$J_{2'a,2'b} = 14$, $J_{6,CH_3} = 1.5$
10	1.5		6			<1	1.5			2		$J_{1',3'} = 1.5$, $J_{6,CH_3} = 1.5$
11a	2		6		2	0	0	3	3	0		$J_{1',3'} = 2$, $J_{1',4'} = 2$, $J_{2',4'} = 1.5$
11b	1.5		6		2	0	0	5	5	0		$J_{1',3'} = 1.5$, $J_{1',4'} = 3.5$, $J_{2',4'} = 1.5$
16a	1		~1		<1	0	0	4	3.5	11.5	7.5	
16b	1		6.5		3.5	0	0	6	7.5	9.5	7.5	
16c	2		6		4	0	0	6.5	6.5	0	7.5	
17a	4		5		*a*	0	0	5	5	11	7.5	$J_{H,OH} = 5.5$
17b	5		6		5	0	0	4.5	4.5	0	7.5	
18	2.5		5			1	1			1	7.5	
19	3		5		6	0	0	6	6	0	7.5	
20b	6.5	6.5	6	6	3.5	0	0	6	6	0	7.5	$J_{2'a,2'b} = 12$
20c	6.5	6.5	6	6	3.5	0	0	5.5	5.5	0	7.5	
21a	6	5.5	6.5	6.5		<1	<1			1.5	7.5	$J_{2'a,2'b} = 12$
21b	6	6	6	6.5		1.5	<1			1.5	7.5	$J_{2'a,2'b} = 13$

[a] Non resolved.

for several hours, or at 100° for 5 min, leads to glycosidic cleavage (presumably *via* hydrolysis of the vinyl ether) and release of uracil. Since our ultimate objective was the preparation of the free, unblocked 4′,5′-unsaturated nucleosides, we attempted the direct reaction of 5′-deoxy-5′-iodouridine[2a] with silver fluoride in pyridine but were unable to isolate the desired olefin.

Since both the 2′,3′-*O*-isopropylidene derivative (**1a**) and the related 2′,3′-diol were not suitable starting materials, we turned to 2′,3′-di-*O*-acetyl-5′-deoxy-5′-iodouridine (**5**), a compound that we have previously prepared in 84% yield by iodination of 2′,3′-di-*O*-acetyluridine.[21] Preparation of the latter compound from uridine,[20] while simple, is not a high yield process and the overall yield of **5** from uridine



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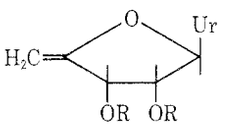
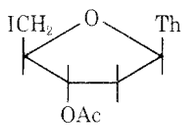


6a, R = Ac
b, R = H



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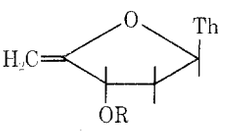
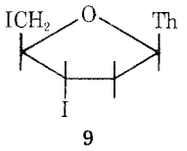


8a, R = Ac
b, R = H

was 40%. The preparation of **5** was more efficient *via* acidic hydrolysis of **1a** with 90% formic acid followed by acetylation, the overall yield of crystalline **5** being 88% from 2′,3′-*O*-isopropylideneuridine. Unlike the results obtained with **1a**, treatment of **5** with silver fluoride in pyridine at room temperature for 4 days gave, after purification by preparative tlc, the desired olefin (**6a**) in 85% yield. Deacetylation of **6** was readily achieved using methanolic ammonium hydroxide and gave crystalline 1-(5-deoxy-β-D-*erythro*-pent-4-enofuranosyl)uracil (**6b**) in 87% yield. It is interesting to note that a somewhat similar dependence of the reaction course upon the nature of protecting groups in the molecule has been observed by Kiss and Burkhardt.[21] These workers have shown that while 3-*O*-acetyl-5-deoxy-5-iodo-1,2-*O*-isopropylidene-D-xylofuranose is readily converted to the 5-deoxy-4-enofuranose derivative with silver fluoride in pyridine, the closely related 3-hydroxy- and 3-*O*-benzyloxy derivatives are inert.

The success of the above synthesis prompted us to investigate several base analogs of **6b**. Thus, treatment of 3′-*O*-acetyl-5′-deoxy-5′-iodothymidine (**7**)[21] with silver fluoride under the usual conditions gave the 4′,5′ olefin (**8a**) in 66% yield and subsequent deacetylation with methanolic ammonium hydroxide converted **8a** to crystalline 1-(2,5-dideoxy-β-D-*glycero*-pent-4-enofuranosyl)thymine (**8b**) in 85% yield.

Subsequent to our work, Kowollik, *et al.*,[22] have obtained **8b** in low yield by reaction of 5′-deoxy-5′-iodothymidine with potassium fluoride in hot dimethyl sulfoxide. The recorded melting point is, however, some 12° lower than we have observed. These same authors have also very recently prepared the 3′-fluoro analog of **8b** using the silver fluoride method. The reaction between the readily available 3′,5′-dideoxy-3′,5′-diiodothymidine (**9**)[2b] and silver



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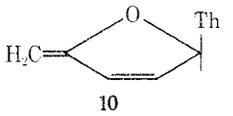

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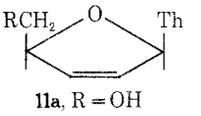
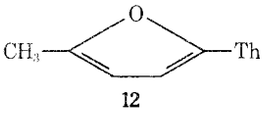


11a, R = OH
b, R = I



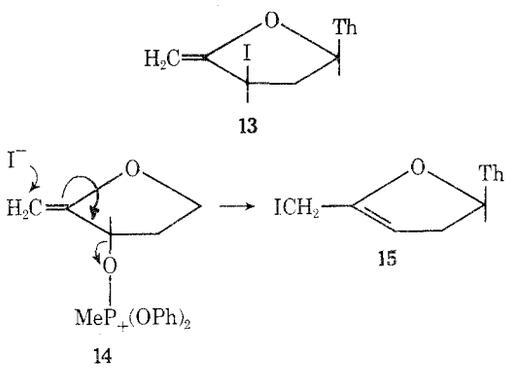
12

fluoride gave, somewhat to our surprise, the crystalline diene 2-methylene-5-(*R*)-(thymin-1-yl)-2,5-dihydrofuran

(**10**) in 41% yield. The latter compound could also be prepared by an alternate route.[23] Thus, iodination of the 2′,3′ olefin **11a**[24] with methyltriphenoxyphosphonium iodide in dimethylformamide[2] at room temperature for 3 min gave the crystalline allylic iodide (**11b**) in 82% yield. The nmr spectrum of **11b** was highly characteristic of 2′,3′-unsaturated nucleosides and showed, *inter alia*, the typical complex pattern for $C_{1'}$ H, which is coupled to $C_{2'}$ H, $C_{3'}$ H, and $C_{4'}$ H.[4b] Dehydrohalogenation of **11b** was readily accomplished by brief treatment with 1,5-diazabicyclo[4.3.0]-non-4-ene (DBN) in acetonitrile at 100°, this route giving optically active, crystalline **10** in a yield of 75%. We have not investigated the conversion of **11b** to **10** using the silver fluoride approach.

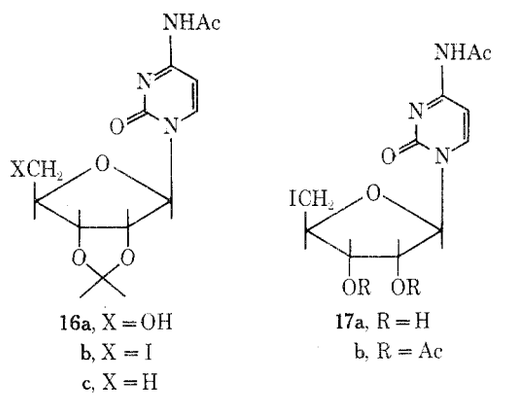
The nmr spectrum of **10** readily confirms the assigned structure. The $C_{1'}$, $C_{2'}$, and $C_{3'}$ protons appear as a typical, readily decoupled allylic system with $C_{3'}$ H showing further allylic coupling to $C_{5'}$ H_2. No signal for $C_{4'}$ H was apparent and the $C_{5'}$ protons were magnetically nonequivalent and appeared as well separated, narrow multiplets showing small (2 Hz) geminal coupling at 5.27 and 5.60 ppm. The appearance of the 5′ protons leaves no doubt as to their presence as a methylene group (compare with compounds **2**, **6**, **8**, **18**, and **21** in Tables I and II). It is interesting to note that Horwitz, *et al.*,[24a] have investigated the preparation of **10** by treatment of 3′,5′-di-*O*-methanesulfonylthymidine with potassium *tert*-butoxide in dimethyl sulfoxide. Under these conditions, however, the presumed **10** underwent isomerization to form the related 5-methylfuran nucleoside (**12**) which has a melting point essentially identical to that of **10**. The correctness of the structure of **12** is nevertheless apparent both from its reported nmr spectrum, which shows the $C_{5'}$ protons as a 3-proton singlet, and from its lack of optical activity.

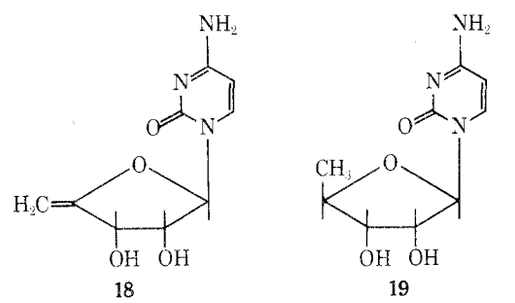
In a study somewhat related to our own work, Winkley[25] has reported that iodination of **8b**, prepared according to our preliminary communication,[10] using methyltriphenoxyphosphonium iodine in dimethylformamide, gave a crystalline product in 42% yield. Based upon some general rules that we have developed for assignment of configuration at $C_{3'}$ in 2′-deoxypyrimidine nucleosides,[2b,26] this product was assigned the structure **13**. This was unexpected to us since iodination of $C_{3'}$ OH in a variety of thymidine derivatives (although not in the presence of a 4′,5′ olefin) inevitably led to retention of configuration due to the intermediacy of an N^3,3′ cyclonucleoside.[2b] The reported nmr spectrum of **13** in d_6-DMSO appears to exhibit several inconsistencies. First of all, the $C_{5'}$-methylene protons are reported to be magnetically equivalent, appearing as a two-proton singlet at 4.10 ppm. In our experience, the 5′ protons in all the 4′,5′-unsaturated nucleosides we have examined are magnetically nonequivalent and appear as well separated one-proton signals showing a small (1–3 Hz) geminal coupling. Second, $C_{3'}$ H is reported as a multiplet at 5.30 ppm. The $C_{3'}$ proton in **8b**, however, appears as a multiplet at 4.70 ppm which sharpens upon addition of D_2O. It is generally accepted[27] that the replacement of a hydroxyl group by iodine leads to a roughly 0.7-ppm upfield shift of the carbinol CH and, hence, one would anticipate $C_{3'}$ H in **13** to appear at roughly 4.0 ppm rather than being deshielded relative to that in **8b**. We have made several unsuccessful attempts to isolate the crystalline product considered to be **13**.[28] The considerations above lead us to suggest that the iodination of **8b** leads, not to **13**, but rather to the isomer **15** arising by allylic attack of iodide on the intermediate **14**. The structure **15** would accommodate both the appearance of $C_{5'}$ H_2 as a singlet and the observed deshielding of $C_{3'}$ H relative to **8b**. The reported regeneration of **8b** upon sequential treatment with silver acetate and ammonia would then be a



consequence of yet another allylic rearrangement. Ultimate resolution of this problem will require a sample of the pure product (**13** or **15**) and, unfortunately, Dr. Winkley has informed us that one is no longer available.

For extension to the cytidine series, the logical starting material would be N^4,$O^{2'}$,$O^{3'}$-triacetyl-5′-deoxy-5′-iodocytidine (**17b**). The most convenient route to this compound proceeded *via* conversion of N^4-acetylcytidine[29] into its 2′,3′-*O*-isopropylidene derivative (**16a**) using perchloric acid as the catalyst.[30] Iodination of **16a** using methyltri-



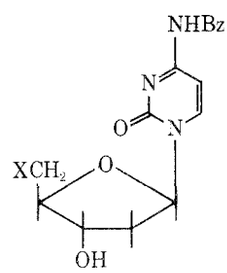


phenoxyphosphonium iodide gave crystalline **16b** in 91% yield and subsequent hydrolysis of the latter with 80% formic acid at room temperature led to N^4-acetyl-5′-deoxy-5′-iodocytidine (**17a**) in 78% yield. The use of formic acid for this hydrolysis was critical since treatment of **16b** with 80% acetic acid at 100°, one of the most commonly used methods for cleavage of nucleoside acetonides, led to extensive deamination to uridine derivatives. The desired intermediate (**17b**) was then readily available through acetylation with acetic anhydride. Following several model experiments, it was decided to use base-catalyzed dehydrohalogenation of **17b** rather than the silver fluoride method. Thus **17b** was treated with 2 equiv of DBN in dimethylformamide at room temperature. While the product of this reaction was indistinguishable from the starting material by tlc in several systems, the completeness of the reaction was checked at different times by sequential treatment with methanolic ammonium hydroxide and 80% acetic acid. Under these conditions, the desired vinyl ether was com-

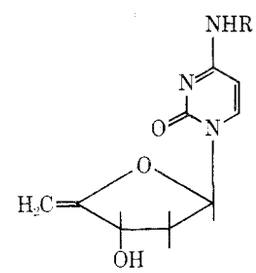
pletely degraded to cytosine while unreacted **17b** gave 5′-deoxy-5′-iodocytidine, the two compounds being readily separated by tlc. By this method it was shown that the dehydrohalogenation of **17b** was complete within 1 hr. Without purification, the crude product was deacetylated with ammonium hydroxide and purified by chromatography on a column of Bio Rad AG-1 × 2 (OH^-) resin using aqueous methanol.[31] By this technique homogeneous 1-(5-deoxy-β-D-*erythro*-pent-4-enofuranosyl)cytosine (**18**) was obtained in 63% yield. The only solvent from which **18** could be crystallized was pyridine, and under these conditions a tenacious pyridine solvate was obtained. The mole of pyridine could not be removed by drying *in vacuo* at 80° for 24 hr and, under more vigorous conditions, some decomposition resulted. The pyridine solvate was, of course, identical to the amorphous free compound by tlc and the lack of any covalent bonding of the pyridine was confirmed by nmr spectroscopy.

While many 5′-deoxy nucleosides, including 2′,5′-dideoxycytidine[32] and 1-(5-deoxy-β-D-arabinofuranosyl)cytosine,[33] have been previously described, 5′-deoxycytidine (**19**) itself does not appear to have been prepared. Accordingly, **16b** was subjected to palladium-catalyzed hydrogenation in the presence of sodium acetate to inhibit both reduction of the cytosine ring and possible acid-catalyzed deamination. The resulting crystalline deoxy nucleoside (**16c**, 83%) was then deblocked by sequential treatment with base and acid giving 5′-deoxycytidine (**19**) which was isolated as its crystalline hydrochloride in 50% overall yield.

Finally, we wished to prepare the 4′,5′ olefin derived from 2′-deoxycytidine. For this purpose, we examined the direct, selective iodination of the 5′-hydroxyl function of N^4-benzoyl-2′-deoxycytidine (**20a**).[34] The reaction of **20a**



20a, X = Bz
b, X = I
c, X = Br



21a, R = Bz
b, R = H

with methyltriphenoxyphosphonium iodide in dimethylformamide appeared to go satisfactorily at room temperature within 10 min according to tlc examination. Several attempts to purify the resulting product by preparative tlc led only to very low yields (14%) of the crystalline 5′-iodo compound (**20b**). Since the crude product looked reasonably clean by tlc, it is not clear why the isolated yield was so consistently low. The pure product has, however, very low solubility in most solvents and it is not impossible that the low yield is a consequence of difficulty in extracting the material from the silicic acid. Because of the low yield during synthesis of the iodo derivative (**20b**), we treated **20a** with triphenylphosphine and carbon tetrabromide in dimethylacetamide, a reaction that we have previously shown to be effective for the synthesis of bromo sugar nucleosides.[1] Using equimolar amounts of reagents, it was possible to isolate crystalline N^4-benzoyl-5′-bromo-2′,5′-dideoxycytidine (**20c**) in 57% yield. Attempted dehydrobromination of **20c** with DBN was accompanied by side reactions and better results were achieved using potassium *tert*-butoxide in dimethylformamide at room temperature. In this way the essentially pure 4′,5′ olefin (**21a**) was obtained in 72% yield by a simple precipitation work-up and could, if desired, be obtained in crystalline form. Deacylation of the crude product with methanolic ammonium hydroxide then gave pure 1-(2,5-dideoxy-β-D-*glycero*-pent-4-enofuranosyl)cytosine (**21b**) which, like its counterpart (**18**), could only be crystallized from pyridine as a crystalline solvate. In this case, however, the pyridine could be removed by drying *in vacuo* at 95° giving the free crystalline product.

The methods described in this paper make 4′,5′-unsaturated pyrimidine nucleosides readily available. Extension of this work to the purine series will shortly be described, as will a number of studies on addition reactions to both types of exocyclic vinyl ethers.[41]

Experimental Section

General Methods. The general methods used are similar to those described previously.[2] Melting points are obtained using a hot stage microscope and are corrected. We are particularly grateful to Mrs. J. Nelson and Dr. M. L. Maddox for their generous help and advice with nmr spectroscopy.

Reaction of 1a with Silver Fluoride. A suspension of silver fluoride (300 mg, 2.4 mmol)[35] in a solution of **1a** (591 mg, 1.5 mmol)[2a] in pyridine (10 ml) was stirred at 20° for 48 hr. The gray solid was removed by centrifugation and the supernatant evaporated leaving a residue that was partitioned between ethyl acetate and water, both phases being filtered through Celite. Evaporation of the aqueous phase gave a syrup (400 mg) that was shown to be almost exclusively 2,5′-anhydro-2′,3′-*O*-isopropylideneuridine (**3**) by its ultraviolet spectrum (λ_{max} 236 nm) and by tlc comparison (acetone) with an authentic sample.[2a] Evaporation of the organic phase left a syrup (90–150 mg in different experiments) that showed a single spot by tlc (CCl_4–acetone, 7:3) but which was shown by nmr to be a 3:1 mixture of 5′-deoxy-5′-fluoro-2′,3′-*O*-isopropylideneuridine (**1b**) and **2** (see Tables I and II).

1-(5-Deoxy-2,3-*O*-isopropylidene-β-D-*erythro*-pent-4-enofuranosyl)uracil (2). A solution of **1a** (1.18 g, 3 mmol) and potassium *tert*-butoxide (7.7 mmol) in anhydrous dimethyl sulfoxide (7 ml) was kept at 20° for 30 min. After addition of water (35 ml), the solution was neutralized with glacial acetic acid and extracted four times with chloroform. Evaporation of the dried extracts gave a residue that was purified by preparative tlc (CCl_4–acetone, 7:3) giving 670 mg (84%) of **2** as a homogeneous white solid that could not be induced to crystallize but which had an nmr spectrum identical with material prepared from 2′,3′-*O*-isopropylidene-5′-*O*-*p*-toluenesulfonyluridine as described by Robins *et al.*[16]

2′,3′-Di-*O*-acetyl-5′-deoxy-5′-iodouridine (5). A. Iodination of 2′,3′-di*O*-acetyluridine[20] as previously described[2a] gave **5** with mp 162–164° in 84% yield. The overall yield from uridine by this route was roughly 40%.

B. A solution of 5′-deoxy-5′-iodouridine (950 mg, 2.7 mmol)[2a] in dimethylformamide (10 ml), pyridine (1 ml), and acetic anhydride (10 ml) was kept at 20° for 3 hr and then evaporated to dryness. After co-evaporation of the crystalline residue with dimethylformamide, it was crystallized from chloroform–hexane giving 1.16 g (quantitative) of **5** with mp 163–164°. The overall yield of **5** from 2′,3′-*O*-isopropylideneuridine was 88% by this route.

1-(2,3-Di-*O*-acetyl-5-deoxy-β-D-*erythro*-pent-4-enofuranosyl)uracil (6a). A suspension of silver fluoride (600 mg, 4.8 mmol) in a solution of **5** (876 mg, 2 mmol) in pyridine (20 ml) was stirred in the dark for 4 days at room temperature. The mixture was then filtered through Celite and the filtrate and pyridine washings were evaporated almost to dryness. The residue was partitioned between ethyl acetate (50 ml) and water (50 ml), an insoluble substance being removed by filtration. Evaporation of the organic phase and preparative tlc of the residue using ethyl acetate gave a major ultraviolet absorbing band, elution of which gave 525 mg (85%) of **6a** as a homogeneous foam, λ_{max} (MeOH) 258 nm (ε 9500).

Anal. Calcd for $C_{13}H_{14}N_2O_7$ (310.26): C, 50.32; H, 4.55; N, 9.03. Found: C, 50.43; H, 4.86; N, 8.75.

1-(5-Deoxy-β-D-*erythro*-pent-4-enofuranosyl)uracil (6b). A solution of **6a** (835 mg, 2.7 mmol) in a mixture of methanol (8 ml) and concentrated ammonium hydroxide (8 ml) was kept at room temperature for 1 hr and then evaporated to dryness *in vacuo*. The residue was purified by preparative tlc (acetone–ethyl acetate, 1:1) giving 500 mg (87%) of pure, crystalline **6b**. An analytical sample

recrystallized from acetone had mp 169–170°, λ_{max} (MeOH) 261 nm (ϵ 9600).

Anal. Calcd for $C_9H_{10}N_2O_5$ (226.19): C, 47.79; H, 4.46; N, 12.39. Found: C, 47.89; H, 4.62; N, 12.21.

Reactions of Methyl 5-Deoxy-5-iodo-2,3-*O*-isopropylidene-β-D-ribofuranoside (4) with Silver Salts. Solutions of 4 (32 mg, 0.1 mmol) in pyridine (0.5 ml) were stirred in the dark at room temperature for 48 hr in the presence of 0.1 mmol of silver fluoride, silver oxide, silver perchlorate, silver nitrate, silver acetate, and mercuric fluoride. The mixtures were then filtered and the filtrates were examined directly by glc using a 6-ft column of 1% NPGS on Gas-Chrom Q[36] programmed from 100° to 200° at 8° per min. Under these conditions, the reaction with silver fluoride efficiently gave the desired olefin as reported by Hough and Otter.[12] The other added salts led to no significant reactions with the exception of silver acetate, which led to the formation of a modest yield of methyl 5-*O*-acetyl-2,3-*O*-isopropylidene-β-D-ribofuranose, which was identified by comparison with an authentic sample.[18]

1-(3-*O*-Acetyl-2,5-dideoxy-β-D-*glycero*-pent-4-enofuranosyl)thymine (8a). A suspension of silver fluoride (1.5 g, 12 mmol) in a solution of **7** (1.92 g, 4.9 mmol)[2a] in pyridine (100 ml) was stirred in the dark for 3 days and then filtered through Celite. The filtrate and pyridine washings were evaporated leaving a syrup that was partitioned between water and ethyl acetate with removal of a precipitate by filtration. Evaporation of the organic phase left a residue that was purified by preparative tlc using CCl_4–acetone (2:1). Elution of the major band with acetone gave 850 mg (66%) of **8a** as a homogeneous white foam, λ_{max} (MeOH) 265 nm (ϵ 9300).

Anal. Calcd for $C_{12}H_{14}N_2O_5$ (266.25): C, 54.12; H, 5.30; N, 10.52. Found: C, 54.26; H, 5.40; N, 10.18.

1-(2,5-Dideoxy-β-D-*glycero*-pent-4-enofuranosyl)thymine (8b). A solution of **8a** (850 mg, 3.2 mmol) in methanol (8 ml) and concentrated ammonium hydroxide (8 ml) was kept at room temperature for 1 hr and then evaporated *in vacuo* to dryness. Crystallization of the residue from methanol gave 580 mg (85%) of **8b** which melted at 208–210°, resolidified and remelted at 270° (reported[22] mp 196–197.5°), λ_{max} (MeOH) 267 nm (ϵ 9500).

Anal. Calcd for $C_{10}H_{12}N_2O_4$ (224.21): C, 53.57; H, 5.40; N, 12.50. Found: C, 53.98; H, 5.58; N, 12.65.

1-(2,3,5-Trideoxy-5-iodo-β-D-*glycero*-pent-2-enofuranosyl)thymine (11b).[23] A solution of **11a** (224 mg, 1 mmol)[24] and methyltriphenoxyphosphonium iodide (600 mg, 1.3 mmol) in dimethylformamide (3 ml) was kept at room temperature for 3 min. Methanol (2 ml) was added and the solvents were evaporated *in vacuo*. Addition of ethyl acetate (3 ml) to the residue gave a white precipitate which was removed by filtration and washed with ethyl acetate giving 307 mg of **11b**. The filtrates were washed with aqueous sodium thiosulfate and water, dried ($MgSO_4$), and evaporated leaving a residue that was crystallized from ethanol giving 15 mg of crystalline **11b**. Recrystallization of both solid fractions from ethanol gave 273 mg (82%) of pure **11b** with mp 113–115° dec, λ_{max} (MeOH) 265 nm (ϵ 10,000), $[\alpha]^{23}D$ −32.3° (*c* 0.13, MeOH).

Anal. Calcd for $C_{10}H_{11}N_2O_3I$ (334.12): C, 35.94; H, 3.32; N, 8.39. Found: C, 36.06; H, 3.40; N, 8.39.

2-Methylene-5-(*R*)-(thymin-1-yl)-2,5-dihydrofuran (10). A.[23] A solution of **11b** (167 mg, 0.5 mmol) and 1,5-diazabicyclo-[4.3.0]non-5-ene (124 mg, 1 mmol) in acetonitrile (10 ml) was kept at 100° for 30 min and then evaporated to dryness. The residue was directly purified by preparative tlc ($CHCl_3$MeOH, 9:1), the major band being eluted with acetone and crystallized from ethanol giving 77 mg (75%) of **10** with mp 163–165°, λ_{max} (dioxane) 264 nm (ϵ 16,900), $[\alpha]^{23}D$ 229.7° (*c* 0.1, dioxane).

Anal. Calcd for $C_{10}H_{10}N_2O_3$ (206.20): C, 58.24; H, 4.89; N, 13.59. Found: C, 58.13; H, 5.02; N, 13.56.

B. A solution of 3′,5′-dideoxy-3′,5′-diiodothymidine (**9**, 462 mg, 1 mmol)[2b] in pyridine (10 ml) was shaken in the dark at room temperature with silver fluoride (300 mg, 2.4 mmol) for 65 hr. The mixture was worked up just as described for **8a**, using preparative tlc with acetone–ethyl acetate (1:1). Elution of the major band gave 85 mg (41%) of **10** identical with the product isolated above.

N^4-Acetyl-2′,3′-*O*-isopropylidenecytidine (16a). Perchloric acid (2 ml of 60%) was added dropwise with vigorous stirring to a suspension of N^4-acetylcytidine (5.4 g, 19 mmol)[29] in a mixture of acetone (300 ml) and 2,2-dimethoxypropane (50 ml). After 1 hr at 20°, concentrated ammonium hydroxide (2.4 ml) was added to the clear solution and the solvents were removed *in vacuo*. The residue was dissolved in hot ethyl acetate (100 ml) and, upon cooling, crude **16a** separated. Recrystallization from water gave 4.32 g (70%) of pure **16a** with mp 125–129° (reported[37] mp 117–120° without details); λ_{max} (MeOH) 213 nm (ϵ 18,100), 247 (15,700), 297 (7100).

Anal. Calcd for $C_{14}H_{19}N_3O_6$ (325.32): C, 51.68; H, 5.89; N, 12.92. Found: C, 51.52; H, 6.01; N, 13.10.

N^4-Acetyl-5′-deoxy-2′,3′-*O*-isopropylidene-5′-iodocytidine (16b). A solution of **16a** (3.67 g, 11.3 mmol) and methyltriphenoxyphosphonium iodide (8.56 g, 20 mmol) in dimethylformamide (100 ml) was kept at room temperature for 3 hr. After addition of methanol (3 ml), the solvents were evaporated, the residue was dissolved in chloroform and washed with aqueous sodium thiosulfate, sodium bicarbonate, and water. The dried organic phase was evaporated and the residue crystallized from chloroform–hexane giving 4.47 g (91%) of **16b** with mp 194–195°; λ_{max} (MeOH) 298 nm (ϵ 6000), 249 (16,200), 210 (24,500).

Anal. Calcd for $C_{14}H_{18}N_3O_5I$ (435.21): C, 38.63; H, 4.17; N, 9.66; I, 29.16. Found: C, 38.53; H, 4.23; N, 9.44; I, 29.30.

N^4-Acetyl-5′-deoxy-5′-iodocytidine (17a). A solution of **16b** (2.175 g, 5 mmol) in 80% formic acid (50 ml) was kept at 20° for 20 hr and then evaporated to dryness *in vacuo*. Crystallization of the residue from methanol gave 1.55 g (78%) of pure **17a**. An analytical sample recrystallized from dimethylformamide–acetone had mp 203–203.5°; λ_{max} (MeOH) 210 nm (ϵ 20,400), 246 (16,500), 298 (7900).

Anal. Calcd for $C_{11}H_{14}N_3O_5I$ (395.15): C, 33.43; H, 3.57; N, 10.63; I, 32.12. Found: C, 33.70; H, 3.45; N, 10.51; I, 32.43.

N^4,$O^{2'}$,$O^{3'}$-Triacetyl-5′-deoxy-5′-iodocytidine (17b). A solution of **17a** (500 mg, 1.26 mmol) in a mixture of dimethylformamide (5 ml), acetic anhydride (5 ml), and pyridine (0.5 ml) was kept at room temperature for 3.5 hr and then evaporated to dryness. The residue was co-evaporated with methanol and then crystallized from methanol to give 582 mg (96%) of **17b** with mp 193–193.5°; λ_{max} (MeOH) 208 nm (ϵ 16,000), 247 (15,000), 296 (6600).

Anal. Calcd for $C_{15}H_{18}N_3O_7I$ (479.22): C, 37.59; H, 3.79; N, 8.77; I, 26.48. Found: C, 37.50; H, 3.67; N, 8.79; I, 26.67.

1-(5-Deoxy-β-D-*erythro*-pent-4-enofuranosyl)cytosine (18). A solution of **17b** (479 mg, 1 mmol) and 1,5-diazabicyclo[4.3.0]-non-5-ene (248 mg, 2 mmol) in dimethylformamide (10 ml) was kept at room temperature for 1 hr and then evaporated to dryness.[38] The residue was directly treated at room temperature for 30 min with methanol (6 ml) and concentrated ammonium hydroxide (3 ml) and then evaporated to dryness. An aqueous solution of the residue was applied to a 1.6 × 17.5 cm column of Bio Rad AG1-X 2 (OH^-) resin. Elution of the column first with water and then with methanol–water (1:4) gave 36 mg (15%) of cytidine while continued elution with methanol–water (3:7) gave 147 mg (63%) of **18** that was homogeneous by tlc and nmr. Crystallization from pyridine[39] gave highly crystalline **18** as the pyridine solvate with mp 108–109.5° (the pyridine could not be removed by drying *in vacuo* at 80° for 24 hr); λ_{max} (0.01 *N* NaOH, MeOH) 251 nm (ϵ 10,700), 257 (11,000), 263 (10,500), 270 (9300).

Anal. Calcd for $C_9H_{11}N_3O_4 \cdot C_5H_5N$ (304.30): C, 55.25; H, 5.30; N, 18.41. Found: C, 55.31; H, 5.40; N, 18.63.

N^4-Acetyl-5′-deoxy-2′,3′-*O*-isopropylidenecytidine (16c). A solution of **16b** (1.3 g, 3 mmol) and sodium acetate (700 mg) in a mixture of methanol (80 ml) and water (8 ml) was vigorously stirred for 1 hr in an atmosphere of hydrogen in the presence of 10% palladium/carbon catalyst (210 mg). The mixture was then filtered through Celite and the evaporated filtrate was dissolved in ethyl acetate and washed with a minimum amount of aqueous sodium thiosulfate and water. Evaporation of the dried organic phase and crystallization of the residue from chloroform–hexane gave 764 mg (83%) of **16c** with mp 214–215°; λ_{max} (MeOH) 214 nm (ϵ 19,800), 248 (17,000), 298 (7200).

Anal. Calcd for $C_{14}H_{19}N_3O_5$ (309.31): C, 54.36; H, 6.19; N, 13.58. Found: C, 54.15; H, 6.25; N, 13.29.

5′-Deoxycytidine Hydrochloride (19 HCl). Concentrated ammonium hydroxide (5 ml) was added to a solution of **16c** (700 mg, 2.26 mmol) in hot methanol (4 ml) and the mixture was heated under reflux for 10 min. It was then evaporated to dryness and the residue was co-evaporated with ethanol–benzene to give a white foam. This material was dissolved in methanol (3 ml) and concentrated hydrochloric acid (0.3 ml) was added. White crystals formed quite rapidly and recrystallization from methanol gave 295 mg (50%) of the hydrochloride of **19** with mp 193–194° dec; λ_{max} (pH 2) 212 nm (ϵ 9700), 279 (12,800).

Anal. Calcd for $C_9H_{13}N_3O_4 \cdot HCl$ (263.67): C, 40.99; H, 5.35; N, 15.94. Found: C, 40.70; H, 5.55; N, 15.75.

N^4-Benzoyl-2′,5′-dideoxy-5′-iodocytidine (20b). A solution of N^4-benzoyl-2′-deoxycytidine (**20a**, 331 mg, 1 mmol)[34] and methyltriphenoxyphosphonium iodide (600 mg, 1.3 mmol) in dimethyl-

formamide (5 ml) was kept at room temperature for 10 min and then evaporated to dryness after addition of methanol (0.5 ml). The residue was vigorously stirred with ether (25 ml) and the resulting brown precipitate was washed several times with fresh ether giving a yellow powder (620 mg). This was dissolved in hot acetone and purified by preparative tlc using ethyl acetate–acetone (1:1). Elution of the major band and crystallization from dimethylformamide–ethyl acetate gave 62 mg (14%)[40] of **20b** with mp 175° dec followed by gradual recrystallization and sublimation at ~300°; λ_{max} (MeOH) 259 nm (ϵ 21,700), 304 (9300).

Anal. Calcd for $C_{16}H_{16}N_3O_4I$ (441.2): C, 43.55; H, 3.66; N, 9.52. Found: C, 43.58; H, 3.59; N, 9.39.

N^4-Benzoyl-5′-bromo-2′,5′-dideoxycytidine (20c). A solution of **20a** (1.99 g, 6 mmol), triphenylphosphine (1.57 g, 6 mmol), and carbon tetrabromide (1.99 g, 6 mmol) in dimethylacetamide (20 ml) was kept at room temperature for 2 hr. Since some unreacted **20a** remained, further 1.2-mmol portions of the two reagents were added and, after 2 hr, the reaction was quenched with methanol and evaporated to dryness. Direct crystallization of the residue from chloroform (20 ml) gave 1.35 g (57%) of **20c** which was sufficiently pure for direct use. An analytical sample could be obtained by preparative tlc (chloroform–ethanol, 9:1) followed by crystallization from dimethylformamide–ethyl acetate with mp 180° dec followed by partial recrystallization and sublimation at ~300°; λ_{max} (MeOH) 259 nm (ϵ 20,700), 303 (8500).

Anal. Calcd for $C_{16}H_{16}N_3O_4Br$ (394.23): C, 48.74; H, 4.09; N, 10.66. Found: C, 48.42; H, 3.94; N, 10.58.

N^4-Benzoyl-1-(2,5-dideoxy-β-D-*glycero*-pent-4-enofuranosyl)cytosine (21a). Potassium *tert*-butoxide (560 mg, 5 mmol) was added to a suspension of crude **20c** (975 mg, 3.5 mmol) in dimethylformamide (20 ml) and the mixture was stirred at room temperature for 20 hr. It was then neutralized with glacial acetic acid (0.2 ml) and evaporated to dryness. The brown residue was extracted with acetone (100 ml) and filtered, and the filtrate was evaporated. The residue was once again suspended in acetone (10 ml) and the resulting precipitate (340 mg) was collected by centrifugation. Addition of ether (30 ml) to the concentrated supernatant (3 ml) gave a precipitate that was triturated with ether and combined with the earlier precipitate giving a total of 560 mg (72%) of essentially pure **21a** suitable for the next step. An analytical sample prepared by preparative tlc using ethyl acetate–acetone (2:1) followed by crystallization from acetone had mp 217° dec; λ_{max} (MeOH) 260 nm (ϵ 23,600), 304 (10,000).

Anal. Calcd for $C_{16}H_{15}N_3O_4$ (313.30): C, 61.33; H, 4.83; N, 13.41. Found: C, 61.60; H, 4.87; N, 13.20.

1-(2,5-Dideoxy-β-D-*glycero*-pent-4-enofuranosyl)cytosine (21b). A suspension of crude **21a** (220 mg, 0.7 mmol) in a mixture of methanol (3 ml) and concentrated ammonium hydroxide (3 ml) was gently warmed until it was homogeneous and then stored at room temperature for 2 hr. After evaporation of the solvents, the residue was purified by preparative tlc using ethyl acetate–methanol (7:3). Elution of the major band gave 60 mg (41%) of **21b** which crystallized from pyridine as a pyridine solvate with mp 165–166°. After drying *in vacuo* at 95° for 10 hr, free **21b** was obtained with mp 159–160°; λ_{max} (0.1 *N* NaOH) 229 nm (ϵ 8300), 270 (9000).

Anal. Calcd for $C_9H_{11}N_3O_3$ (209.21): C, 51.67; H, 5.30; N, 20.09. Found: C, 51.77; H, 5.44; N, 20.30.

Registry No.—**1a,** 14671-65-9; **2,** 17331-67-8; **4,** 38838-06-1; **5,** 14842-09-2; **6a,** 14365-62-9; **6b,** 14365-63-0; **7,** 14046-57-2; **8a,** 52523-37-2; **8b,** 28034-72-2; **9,** 14260-87-8; **10,** 52523-38-3; **11a,** 3056-17-5; **11b,** 29108-95-0; **16a,** 16667-80-4; **16b,** 30685-49-5; **16c,** 52523-39-4; **17a,** 52523-40-7; **17b,** 52523-41-8; **18,** 52523-42-9; **19** HCl, 52523-43-0; **20a,** 4836-13-9; **20b,** 52523-44-1; **20c,** 52523-45-2; **21a,** 52523-46-3; **21b,** 52523-47-4; N^4-acetylcytidine, 3768-18-1.

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(38) No separation of **17b** and **18** could be achieved by tlc in several systems. Completion of the reaction was determined by periodic removal of aliquots from a reaction followed by treatment first with methanol–concentrated ammonium hydroxide (1:1) for 30 min at 20° and then with 80% acetic acid at 100° for 5 min. Under these conditions **17b** is converted to 5′-deoxy-5′-iodocytidine while **18** is hydrolyzed to cytosine.
(39) We have not succeeded in obtaining **18** in crystalline form from any solvent but pyridine.
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