ing temperature is *n*-hexyl alcohol, *n*-hexyl ether, *n*-Bu_3P, internal standard, and *n*-Bu_3PO.

1,2-Dioxane was prepared by the method of Criegee[9] in 18% yield. The product had bp 49° (67 mm) [lit.[9] bp 61–62° (110 mm)]; $n^{20}D$ 1.4261 (lit.[7] $n^{20}D$ 1.4262). Ir, mass, and nmr spectra confirm the structure. 1,4-Butanediol was trapped from the glc effluent of a reduced sample of 1,2-dioxane for comparison with an authentic sample.

The best column for quantitative glc analysis of the components of a reduced sample of 1,2-dioxane was a 10 ft × 0.25 in. Carbowax 20M (16.7%) on AW Chromosorb P (60–80 mesh); 2-dodecanone was used as internal standard.

Di-*tert*-butyl peroxide was obtained from Lucidol and was 99.9% pure by glc.

Ascaridole was obtained from K & K. The reduction product, *p*-menthene-1,4-diol, was prepared by hydride reduction. Ascaridole (1.7 g, 1.01×10^{-2} mol) in 30 ml of benzene was refluxed with $NaAlH_2(OCH_2CH_2OCH_3)_2$ (2.86×10^{-2} mol) for 2 hr. On cooling, 50 ml of water was added, benzene was removed on a Rotavapor, and the aqueous phase was extracted with four 300-ml portions of 1:1 ether–*n*-pentane. Removal of the solvent provided 1.8 g of residue which on two crystallizations from cyclohexane gave 1.6 g of crystals: mp 80–81° (lit.[18] mp 82°); nmr ($CDCl_3$) δ 0.8–1.0 (2 d, 6 H, methyl), 1.25 (s, 3 H, methyl), 1.5–2.0 (m, 5 H, methylene + methine), 2.3 (1 H, OH), 2.7 (1 H, OH), 5.4–5.9 (2 d, 2 H, olefinic); the OH resonance is shifted by addition of D_2O and CF_3CO_2H. The glycol as a mixture with *n*-Bu_3PO was also obtained by chromatograpic separation of a Bu_3P-reduced sample of ascaridole on basic alumina (Alcoa, pH 9).

The product mixture from *n*-Bu_3P reduction was analyzed by glc on a 5 ft × 0.25-in. Carbowax 20M (5%) on Percopak T column using methyl heptanoate as internal standard. The order of elution was internal standard, *n*-Bu_3P, ascaridole decomposition peaks, 1,4-diol, and *n*-Bu_3PO.

(18) M. Matic and D. A. Sutton, *J. Chem. Soc.*, 2679 (1952).

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Registry No.—**1**, 40735-15-7; **2**, 40735-16-8; **3**, 40735-17-9; styrene polyperoxide, 27379-77-7; triphenylphosphine, 603-35-0; 1,3-octadiene polyperoxide, 40742-13-0; *n*-hexyl peroxide, 3903-89-7; tributylphosphine, 998-40-3; 1,2-dioxane, 5703-46-8; *tert*-butyl peroxide, 110-05-4; ascaridole, 512-85-6; styrene oxide, 96-09-3; *p*-menthene-1,4-diol, 40735-19-1.

Reactions of 2-Acyloxyisobutyryl Halides with Nucleosides. III.[1] Reactions of Tubercidin and Formycin

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The reaction of tubercidin with 2-acetoxyisobutyryl halides gives exclusively the 2′-*O*-acetyl-3′-halo-3′-deoxy-β-D-xylofuranosyl nucleoside (**3**) substituted at the 5′ position with a trimethyldioxolanone moiety. Treatment of **3** with methanolic ammonia rapidly removed both the acetyl and dioxolanone groups to give crystalline 4-amino-7-(3-deoxy-3-halo-β-D-xylofuranosyl)-pyrrolo[2,3-*d*]pyrimidines (**4**) which could be converted to 2′,3′-anhydrotubercidin with sodium methoxide. Catalytic hydrogenolysis of the 3′-bromo nucleoside (**4b**) gave 3′-deoxytubercidin while similar treatment of the bromo acetate (**3b**) gave both 3′-deoxytubercidin and 2′,3′-dideoxytubercidin. Similar reactions of formycin with 2-acetoxyisobutyryl bromide gave both 2′-*O*-acetyl-3′-bromo-3′-deoxy-β-D-xylofuranosyl and 3′-*O*-acetyl-2′-bromo-2′-deoxy-β-D-arabinofuranosyl nucleosides (**9** and **10**) substituted at the 5′ position as 2-acetoxyisobutyryl esters. The acetyl and acetoxyisobutyryl esters could be sequentially removed by treatment with ammonia and catalytic hydrogenolysis of the appropriate compounds gave 2′-deoxy-, 3′-deoxy-, and 2′,3′-dideoxyformycin. Treatment of **9** and **10** with sodium methoxide gave 2′,3′-anhydroformycin.

Several recent papers from this laboratory have described the reactions of 2-acetoxyisobutyryl halides (**1**) with uridine[4] and adenosine.[1] These studies, based upon earlier work by Mattocks, showed that simple cis vicinal diols react with **1** to form trans halo acetates *via* intermediate acetoxonium ions. In the case of the reaction of **1** with uridine the major products proved to be derivatives of 3′-*O*-acetyl-2′-deoxy-2′-halouridine, the unusual cis configuration of the acetyl and halo functions being explained by interaction of the C_2 carbonyl group of the uracil ring with the intermediate 2′,3′-acetoxonium intermediate.[4] On the other hand, the reaction of adenosine with **1** led predominantly to the formation of 2′-*O*-acetyl-3′-deoxy-3′-halo and 3′-*O*-acetyl-2′-deoxy-2′-halo nucleosides with the D-xylo and D-arabino configurations in a ratio of roughly 10:1.[1] These products were entirely to be expected on the assumption that the intermediate 2′,3′-acetoxonium ion was opened by halide attack without participation of the purine ring. The halo nucleosides obtained from adenosine and **1** were shown to be useful intermediates for the preparation of 3′-deoxy- and 2′,3′-dideoxyadenosine as well as of 2′,3′-anhydroadenosine.

In recent years numerous nucleoside antibiotics have been isolated from nature.[5] Analogs of adenosine have been particularly prevalent in this class and antibiotics such as 4-amino-7-(β-D-ribofuranosyl)pyrrolo-[2,3-*d*]pyrimidine (**2**, tubercidin) and 7-amino-3-(β-D-ribofuranosyl)-pyrazolo[4,3-*d*]pyrimidine (**8**, formycin) have been widely studied.[5,6] The interesting spectrum of biological activities shown by tubercidin and formycin has made the chemical modification of these molecules an attractive exercise and has led to both work on total synthesis[7] and to preparation of a variety of

(1) For part II, see A. F. Russell, S. Greenberg, and J. G. Moffatt, *J. Amer. Chem. Soc.*, **95**, 4025 (1973).
(2) Syntex Postdoctoral Fellow, 1971–1973.
(3) Syntex Postdoctoral Fellow, 1968–1970.
(4) S. Greenberg and J. G. Moffatt, *J. Amer. Chem. Soc.* **95**, 4016 (1973).
(5) R. J. Suhadolnik, "Nucleoside Antibiotics," Wiley-Interscience, New York, N. Y., 1970.
(6) C. G. Smith, G. D. Gray, R. G. Carlson, and A. R. Hanze, *Advan. Enzyme Regul.*, **5**, 121 (1967).
(7) R. L. Tolman, R. K. Robins, and L. B. Townsend, *J. Amer. Chem. Soc.*, **91**, 2102 (1969).

TABLE I

NMR CHEMICAL SHIFTS (PARTS PER MILLION) AT 100 MHz IN DMSO-d_6

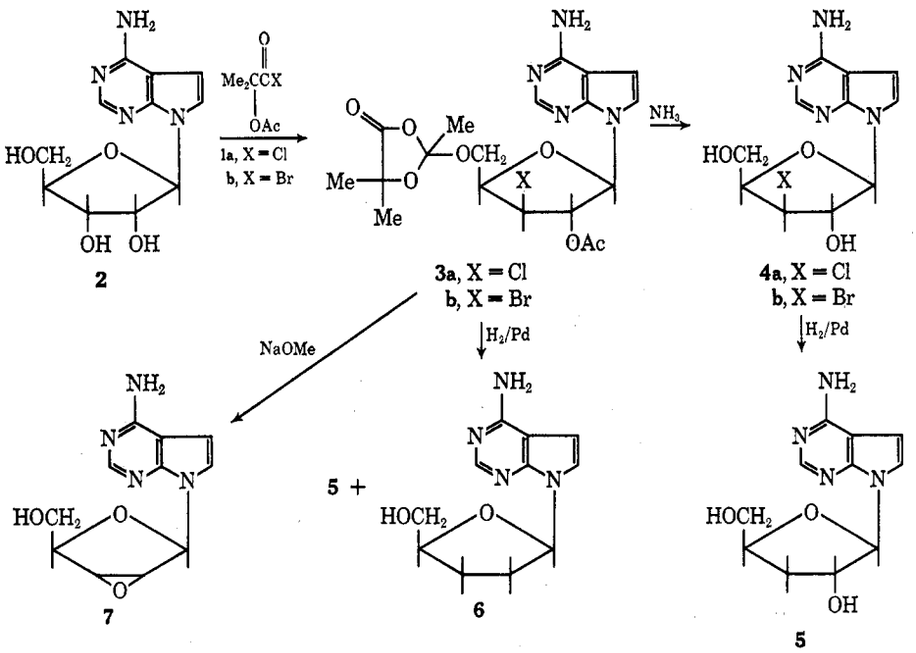
Compd	$C_{1'}$ H	$C_{2'}$ H	$C_{3'}$ H	$C_{4'}$ H	$C_{5'}$ H_a	$C_{5'}$ H_b	C_2 H[a]	C_5 H	C_6 H	Other
2	5.97 (d)	4.42 (dd)[b]	4.08 (dd)[b]	3.91 (dt)	3.59 (d)[b]		8.04 (s)	6.59 (d)	7.32 (d)	
3a free base	6.30 (d)	5.47 (dd)[c]	4.86 (m)[c]	4.50 (br dt)	3.72 (dd)	3.92 (dd)	8.06 (s)	6.66 (d)	7.25 (d)	1.44, 1.47 (s, 3, CMe_2), 1.71 (s, 3, $MeCO_3$), 2.05 (s, 3, OAc), 7.08 (s, 2, NH_2)
3b free base	6.29 (d)	5.60 (m)[c]	4.86 (m)[c]	4.38 (m)	3.76 (dd)	3.88 (dd)	8.06 (s)	6.66 (d)	7.30 (d)	1.45, 1.48 (s, 3, CMe_2), 1.72 (s, 3, $MeCO_3$), 2.06 (s, 3, OAc), 7.09 (s, 2, NH_2)
4a	6.02 (d)	4.56 (dd)[b]	4.44 (d)	4.29 (dt)	3.68 (dd)		8.04 (s)	6.60 (d)	7.26 (d)	6.23 (d, 1, $C_{2'}$ OH), 5.13 (t, 1, $C_{5'}$ OH), 7.01 (s, 2, NH_2)
4b	5.98 (d)	4.68 (ddd)	4.48 (dd)	4.18 (dt)	3.67 (dd)		8.04 (s)	6.60 (d)	7.31 (d)	6.21 (d, 1, $C_{2'}$ OH), 5.16 (t, 1, $C_{5'}$ OH), 6.99 (s, 2, NH_2)
5	6.00 (d)	4.4 (m)	1.90 (ddd) 2.16 (ddd)	4.4 (m)	3.56 (m)		8.04 (s)	6.56 (d)	7.31 (d)	5.49 (d, 1, $C_{2'}$ OH), 5.04 (t, 1, $C_{5'}$ OH), 6.95 (s, 2, NH_2)
6	6.33 (dd)	2.0–2.3 (m)	2.0–2.3 (m)	4.02 (m)	3.43 (dd)[b]	3.57 (dd)[b]	8.02 (s)	6.54 (d)	7.31 (d)	5.16 (m, 1, $C_{5'}$ OH), 6.97 (s, 2, NH_2)
7	6.28 (s)	4.28 (d)	4.17 (d)	4.11 (t)	3.55 (m)[b]		8.08 (s)	6.61 (d)	7.34 (d)	5.07 (m, 1, $C_{5'}$ OH), 7.05 (s, 2, NH_2)
8	4.94 (d)	4.47 (dd)[b]	4.09 (dd)[b]	3.96 (m)	4.6 (m)		8.13 (s)			
9[d]	5.19 (d)	6.19 (dd)	4.75 (dd)	4.4 (m)	4.21 (dd)	4.35 (dd)	8.17 (s)			1.47 (s, 6, CMe_2), 1.99 (s, 3, *t*-OAc), 2.04 (s, 3, OAc), 7.37 (s, 2, NH_2)
11a	4.89 (d)	5.21 (dd)[b]	4.49 (dd)	4.28 (m)	4.22 (dd)	4.35 (dd)	8.14 (s)			1.46 (s, 6, CMe_2), 1.96 (s, 3, *t*-OAc), 6.0 (br, 2′ OH), 7.27 (s, 2, NH_2)
11b	4.79 (d)	4.95 (dd)[b]	4.47 (dd)	4.19 (m)	3.57 (dd)	3.74 (dd)	8.14 (s)			5.85 (m, 2, OH), 7.38 (s, 2, NH_2)
12a	5.57 (d)	4.73 (dd)	4.7 (m)	3.90 (m)	4.29 (dd)	4.48 (dd)	8.15 (s)			1.46 (s, 6, CMe_2), 1.97 (s, 3, *t*-OAc), 7.29 (s, 2, NH_2)
12b	5.56 (d)	4.70 (dd)	4.58 (dd)[b]	3.73 (m)	3.73 (m)		8.07 (s)			7.78 (br s, 2, NH_2)
13a	5.01 (d)	4.70 (m)	1.95 (m) 2.30 (m)	4.37 (m)	4.13 (dd)	4.24 (dd)	8.13 (s)			1.40, 1.42 (s, 3, CMe_2), 1.95 (s, 3, *t*-OAc)
13b free base	4.91 (d)	4.58 (dt)[b]	1.88 (ddd) 2.25 (m)	4.25 (m)	3.38 (dd)[b]	3.63 (dd)[b]	8.10 (s)			7.4 (br s, 2, NH_2)
14 HCl	5.46 (dd)	2.15–2.35 (m)	4.32 (m)	3.88 (m)	3.56 (d)		8.52 (s)			9.8 (br s, 3, NH_3^+)

TABLE I
(*Continued*)

Compd	$C_{1'}$ H	$C_{2'}$ H	$C_{3'}$ H	$C_{4'}$ H	$C_{5'}$ H_a	$C_{5'}$ H_b	C_2 H[a]	C_5 H	C_6 H	Other
15	5.34 (s)	4.17 (d)	4.10 (d)	4.08 (t)	3.39 (dd)[b]	3.62 (dd)[b]	8.18 (s)			7.34 (s, 2, NH_2), 5.2 br, 1, $C_{5'}$ OH)
16 free base	5.16 (dd)	2.0-2.4 (m)	2.0-2.4 (m)	4.1 (m)	3.37 (dd)	3.61 (dd)	8.12 (s)			7.39 (s, 2, NH_2)

[a] C_2 H refers only to tubercidin derivatives and is replaced by C_5 H in the case of formycin derivatives. [b] After addition of D_2O. [c] The signals for $C_{2'}$ H and $C_{3'}$ H clearly showed slight doubling due to the chiral dioxolanone grouping. The spectrum of the hydrochloride was very similar except for the chemical shifts of C_2 H, C_5 H, and C_6 H which appeared at 8.41, 7.12 and 7.54 ppm, respectively. [d] The 2′-bromo isomer (**10**) can be recognized by its $C_{1'}$ H (5.58 ppm, d, $J_{1',2'}$ = 5 Hz), $C_{2'}$ H (4.97 ppm, dd, $J_{2',3'}$ = 4 Hz), $C_{3'}$ H (5.70 ppm, dd, $J_{3',4'}$ = 4 Hz), and 3′ OAc (2.12 ppm, s) signals.

SCHEME I



base analogs.[8] On the other hand, while 2′-deoxytubercidin has been isolated following incubation of radioactive **2** with L cells in tissue culture, little work has been done on modification of the sugar moiety of these interesting compounds.[9] In this paper we describe the reactions of tubercidin and formycin with **1** leading to syntheses of the corresponding 3′-deoxy, 2′,3′-dideoxy, and 2′,3′-anhydro analogs. The work with tubercidin has been presented previously.[10]

As an initial model, a suspension of tubercidin (**2**) in acetonitrile was treated with 2-acetoxyisobutyryl chloride (**1a**)[4] and gave a homogeneous reaction mixture after 18 hr at 37°. Following a simple work-up using either precipitation or extraction techniques a crude product was isolated in essentially quantitative yield and was shown by tlc to be predominantly a single spot with only traces of more polar by-products. The nmr spectrum of this crude product was very sharp and clearly indicated the presence of essentially a single compound identified as 4-amino-7-[2-*O*-acetyl-3-chloro-3-deoxy-5-*O*-(2,5,5-trimethyl-1,3-dioxolan-4-on-2-yl)-β-D-xylofuranosyl]pyrrolo[2,3-*d*]pyrimidine (**3a**). The nature of the 5′ substituent was clear from the nmr spectrum (Table I, nonequivalent CMe_2 singlets at 1.44 and 1.47 ppm, and $MeCO_3$ at 1.71 ppm),[1,4] as was the location of the acetyl group, the $C_{2'}$ H being strongly deshielded relative to that in tubercidin. The β-D-xylo configuration of the 3′-chloro group was expected on mechanistic grounds[1,4] and was confirmed by the facile conversion of **3a** into crystalline 2′,3′-anhydrotubercidin (**7**) upon treatment with sodium methoxide (Scheme I). The nmr spectrum of **7** is very similar to those of other 2′,3′-anhydro nucleosides that we have prepared[1,11] and shows values of $J_{1',2'}$ and of $J_{3',4'}$ = 0 (Table II).

Quite unlike the situations observed during reactions of adenosine,[1] guanosine,[11] and inosine[11] with **1**, it is clear from the nmr spectrum of crude **3a** that no significant formation of 3′-*O*-acetyl-2′-chloro-2′-deoxy-β-D-arabinofuranosyl nucleoside occurred. For the moment we see no explanation for the apparently complete regiospecificity shown in the tubercidin reaction. It should also be noted that **3a** should be present as a

(8) See, *e.g.*, (a) S. Watanabe, G. Matsuhashi, S. Fukatsu, G. Koyama, K. Maeda, and H. Umezawa, *J. Antibiot. Ser. A*, **19**, 93 (1966); (b) R. L. Tolman, G. L. Tolman, R. K. Robins, and L. B. Townsend, *J. Heterocycl. Chem.*, **7**, 799 (1970); (c) R. A. Long, A. F. Lewis, R. K. Robins, and L. B. Townsend, *J. Chem. Soc. C*, 2443 (1971).

(9) (a) J. A. Montgomery and K. Hewson, *J. Med. Chem.*, **10**, 665 (1967); (b) M. Bobek, R. L. Whistler, and A. Block, *ibid.*, **15**, 168 (1972).

(10) A. F. Russell, S. Greenberg, and J. G. Moffatt, Abstracts of the 158th National Meeting of the American Chemical Society, New York, N. Y., Sept 1969, CARB 14.

(11) Unpublished work by T. C. Jain, A. F. Russell, and J. G. Moffatt; see T. C. Jain and J. G. Moffatt, Abstracts of the 165th National Meeting of the American Chemical Society, Dallas, Texas, April 1973, CARB 15.

TABLE II
FIRST-ORDER COUPLING CONSTANTS (HERTZ)

Compd	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'a}$	$J_{4',5'b}$	$J_{5'a,5'b}$	$J_{5,6}$	Other
2	6	5.5	3	3	3	0	3.5	
3a	3.5	5.5	4.5	5	3.5	10	3.5	
3b	3.5	*a*	*a*	*a*	3	11	3.5	
4a	4	3	4.5	4.5	4.5	0	3.5	$J_{2',OH} = J_{5',OH} = 5$
4b	4.5	3.5	4.5	4.5	4.5	0	3.5	$J_{2',OH} = J_{5',OH} = 5$
5	2.5	3.5, 5[b]	6, 8[b]	*a*	*a*	*a*	3.5	$J_{3'a,3'b} = 13$
6	5, 5.5	*a*	*a*	4.5	4	11	3.5	
7	0	2.5	0	6	6	*a*	3.5	
8	7	5	2.5	*a*	*a*	*a*		
9	5	2	3.5	3.5	3.5	12		
11a	6	3.5	3.5	3	3	12		
11b	7	5.5	5.5	3.5	3.5	11		
12a	5.5	5.5	*a*	7	4	11		
12b	5.5	5	5	*a*	*a*	*a*		
13a	3	*a*	*a*	4	3.5	10		
13b	4.5	5, 5	7[c]	4	3	12		$J_{3'a,3'b} = 14$
14	7, 8.5	*a*	*a*	4	4	0		
15	0	2.5	0	6	6	11		
16	6, 8	*a*	*a*	3.5	3.5	11		

[a] Unresolved. [b] The relative assignments of J values are based upon analogy with the spectrum of 3′-deoxyadenosine[1] and in the present case cannot be confirmed by decoupling studies since $C_{2'}$ H and $C_{4'}$ H are very close together. [c] The $C_{3'b}$ H signal is not readily subject to first-order analysis.

pair of diastereoisomers owing to the chiral nature of the dioxolanone grouping. In the adenosine and uridine series[1,4] this was always reflected in the nmr spectra by a doubling of the signals for various heterocyclic ring or sugar protons. In the case of **3a**, at least in DMSO-d_6, there is no indication whatsoever for multiple signals due to C_2 H, C_5 H, or C_6 H of the heterocyclic ring or for $C_{1'}$ H of the sugar, all of which appeared as very sharp signals. The presence of diastereomers could only be detected in the $C_{2'}$ H and $C_{3'}$ H signals, both of which appeared as closely overlapping doublets of doublets.

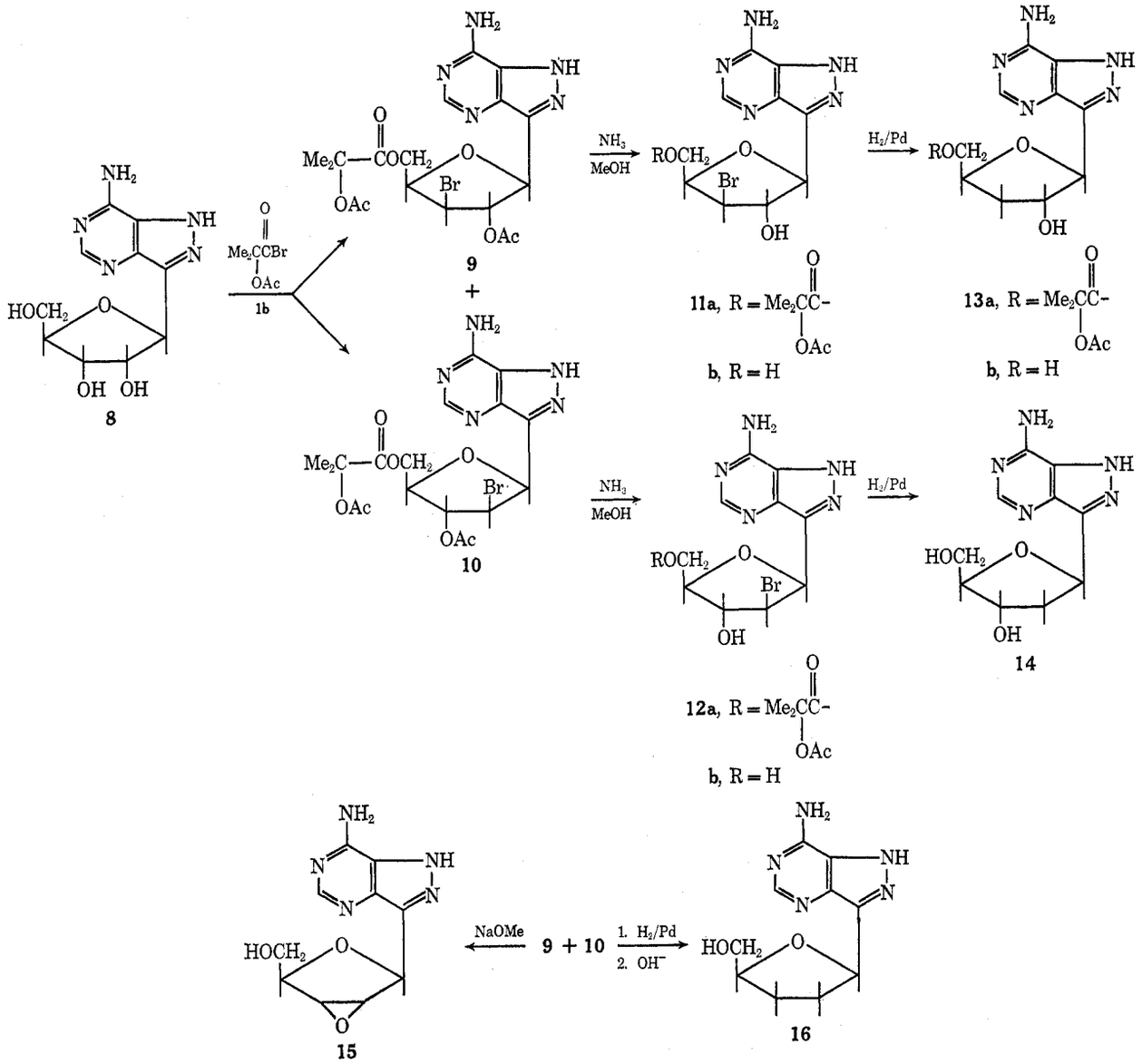
One of our principal interests was the preparation of various deoxy analogs of tubercidin and formycin *via* catalytic hydrogenolysis of the corresponding halo compounds. We have previously found that chloro compounds are generally unsuited for this purpose and accordingly studied the reaction of tubercidin with 2-acetoxyisobutyryl bromide (**1b**).[1] As in the case of the corresponding reaction with adenosine,[1] the reaction of **1b** and **2** took place within an hour at room temperature. The crude product, isolated in almost quantitative yield, was shown by tlc to consist predominantly of the 3′-bromo nucleoside (**3b**) together with only a trace amount of the comparable product from which the labile 5′-*O*-dioxolanone grouping had been lost. Once again the nmr spectrum of the crude product gave no indication of the presence of any 2′-bromo isomer and showed the 5′ position to be blocked by a dioxolanone group. As in the case of **3a**, treatment of crude **3b** with sodium methoxide at room temperature gave the epoxide in 73% yield.

In our previous studies we have made use of mild acidic hydrolysis for the stepwise removal of both dioxolanone and *O*-acetyl protecting groups. While the former were removed very rapidly by treatment with roughly 0.1 *N* methanolic hydrogen chloride, complete deacetylation under these acidic conditions took 4–8 days at room temperature. We have now observed that brief treatment of **3a** or **3b** with saturated methanolic ammonia leads to rapid cleavage of both the dioxolanone and acetyl groups giving the corresponding 4-amino-7-(3-halo-3-deoxy-β-D-xylofuranosyl)pyrrolo[2,3-*d*]pyrimidines (**4a** and **4b**) without significant epoxide formation. In this way the bromohydrin (**4b**) and the chlorohydrin (**4a**) were obtained in crystalline form in overall yields of 65 and 47% from tubercidin without any serious effort to maximize the yields through reworking the mother liquors. Catalytic hydrogenolysis of **4b** in the presence of a palladium catalyst went very smoothly and gave crystalline 3′-deoxytubercidin (**5**) in 62% yield. The structure of **5** was obvious from its nmr spectrum, the sugar portion of which was very similar to that of 3′-deoxyadenosine and showed the presence of free hydroxyl groups at both the $C_{2'}$ and $C_{5'}$ positions. In addition, the two $C_{3'}$ protons appeared as clearly separated, geminately coupled eight-line patterns at 1.90 and 2.16 ppm. Similar catalytic hydrogenolysis of the protected 3-bromo nucleoside (**3a**), followed by hydrolysis of the 3′ and 5′ substituents gave, however, two principal products that were isolated by preparative tlc and shown to be 3′-deoxytubercidin (**5**) and 2′,3′-dideoxytubercidin (**6**) in roughly equal amounts. Once again the nmr spectrum of **6** closely resembled that of 2′,3′-dideoxyadenosine and showed the 2′- and 3′-methylene groups as overlapping multiplets at 2.0–2.3 ppm.

The formation of 2′,3′-dideoxy nucleosides was previously reported in the adenosine series during hydrogenolysis of a trans bromo acetate and has been explained *via* a palladium-catalyzed trans elimination of the acetate group giving a 2′,3′ olefin which is concomitantly reduced.[1] In the absence of the 2′-*O*-acetyl group such an elimination is blocked and simple hydrogenolysis to the 3′-deoxy nucleoside is observed as above.

The reaction of formycin (**8**) with **1b** follows a puzzlingly different course. Complete reaction occurred once again at room temperature and the crude product could be isolated in quantitative yield as either the free base or the hydrobromide by use of partition or precipitation work-ups, respectively. The crude ma-

SCHEME II



terial proved to be an analytically pure but inseparable mixture of the 2′-*O*-acetyl-3′-bromo-3′-deoxy-β-D-xylofuranosyl and 3′-*O*-acetyl-2′-bromo-2′-deoxy-β-D-arabinofuranosyl nucleosides (**9** and **10**, Scheme II) in a ratio of 3:1 by nmr analysis. Unlike the results in the tubercidin series, these products showed none of the characteristics of dioxolanone groupings in either their nmr or ir spectra.[4] They were, however, clearly 5′-*O*-(2-acetoxyisobutyrate) esters, their nmr spectrum showing a *gem*-dimethyl group as a six-proton singlet at 1.47 ppm and a tertiary acetate at 1.99 ppm while the ir spectrum showed no bands near 1805 cm^{-1}. The location of the acetyl groups was readily apparent from the nmr spectrum of the mixture, and the trans stereochemistry of the bromo and acetyl functions was once again confirmed by conversion in 46% yield of the mixture to crystalline 2′,3′-anhydroformycin (**15**) upon treatment with sodium methoxide.

Brief treatment of the mixture of **9** and **10** quite selectively removed the acetyl groups while having little effect upon the acetoxyisobutyrates. The resulting isomeric trans bromohydrins (**11a** and **12a**) could be cleanly separated by preparative tlc giving the pure 3′-bromo-D-xylo (**11a**) and 2′-bromo-D-arabino (**12a**) isomers in yields of 61 and 26%, respectively, together with only 9% bromo diols (**11b** and **12b**) resulting from hydrolysis of the 5′ substituent. While we have not actually done the experiment, the very low solubility of the 2′-bromo compound (**12a**) in ethyl acetate suggests that this compound could be directly isolated from the mixture by crystallization. Complete removal of the acetoxyisobutyrate ester from **11a** and **12a** requires treatment with saturated methanolic ammonia for 48 hr at room temperature and even under these conditions is accompanied by relatively little (8%) formation of the epoxide **15**. The isomeric bromo diols (**11b** and **12b**) were readily separated by preparative tlc giving the pure isomers in yields of 57 and 18%, respectively, together with 8% of crystalline **15**, identical with that described above.

As in the tubercidin series, palladium-catalyzed hydrogenolysis of the trans bromohydrin **11b** gave 5′-*O*-(2-acetoxyisobutyryl)-3′-deoxyformycin (**13a**) in 65% yield and subsequent hydrolysis with methanolic ammonia converted this to 3′-deoxyformycin (**13b**). Similar hydrogenolysis of the bromo diol (**11b**) directly

gave analytically and spectroscopically pure **13b** both as the amorphous free base and the crystalline hydrochloride. In a similar way direct hydrogenolysis of the 2′-bromo diol (**12b**) gave 2′-deoxyformycin (**14**) which was isolated as its crystalline hydrochloride. The isomeric deoxyformycins (**13b**, **14**) could be distinguished from one another by tlc using several developments with chloroform–methanol (85:15). As expected, hydrogenolysis of the pure 5′-protected 2′-bromo nucleoside (**12a**), followed by hydrolysis with methanolic ammonia, also gave **14** uncontaminated by its 3′-deoxy isomer. Also, in agreement with what has been previously shown in the adenosine and tubercidin series, direct hydrogenolysis of the mixture of fully blocked bromo acetates (**9** and **10**), followed by removal of the 5′-substituent and preparative tlc, gave as the major product (44%) 2′,3′-dideoxyformycin (**16**). Smaller amounts of 3′-deoxyformycin (**13b**, 28%) and 2′-deoxyformycin (**14**, 3%) were also isolated and all three compounds could be obtained as their crystalline hydrochlorides. The various deoxy and dideoxy analogs of tubercidin and formycin are currently being examined for biological activities, and these results will be described elsewhere.

For the moment it is very difficult to explain the different courses followed by tubercidin and formycin in their reactions with 2-acetoxyisobutyryl halides. Thus the reaction of tubercidin leads exclusively to introduction of halogen at the 3′ position and to substitution of the 5′-hydroxyl group by a dioxolanone group. On the other hand, formycin, which is grossly very similar in structure, gives both 3′- and 2′-bromo derivatives in a ratio of roughly 3:1 and is exclusively substituted at $C_{5'}$ by an acetoxyisobutyryl ester. A possible contributing factor could be the known syn conformation of formycin at least in the crystal state[12] and in certain polynucleotides.[13] At first glance, however, one might feel that attack by halide ion from the β face at $C_{2'}$ of a 2′,3′-acetoxonium ion intermediate would be sterically inhibited if the nucleoside were preferentially in a syn conformation. Such an argument would suggest that the reaction of formycin with **1** would lead to less 2′-halogenation (**10**) than was observed with tubercidin or adenosine, a situation that is clearly not so. The reason for the clear-cut difference in the nature of the 5′ substituent is equally obscure and we are unable to provide any meaningful suggestions. A similar preference for either dioxolanone or acetoxyisobutyrate substitution at $C_{5'}$ was previously observed in the uridine series depending upon the solvent used for the reaction.[4] One possible factor that we have considered is that formycin exists as a very tenacious monohydrate that is not removed upon drying *in vacuo* at 50°. Because of this a slightly larger excess of **1b** was used and the formation of an equivalent of hydrogen bromide would be expected. The addition of 1 equiv of water to a reaction of adenosine with **1b** exactly as above does not, however, lead to any observable changes in the products. We are, accordingly, unable to provide any adequate explanation for the subtle differences observed in the reactions of tubercidin and formycin at this time.

The reactions of **1** with ribonucleosides such as tubercidin and formycin clearly provide a novel and facile route to a variety of deoxy and epoxide derivatives. These compounds are currently being examined for possible biological activities and the results of these studies will be reported elsewhere.

(12) G. Koyama, K. Maeda, and H. Umezawa, *Tetrahedron Lett.*, 579 (1966).

(13) (a) D. C. Ward and E. Reich, *Proc. Nat. Acad. Sci.*, **61**, 1494 (1968). (b) D. C. Ward, W. Fuller, and E. Reich, *ibid.*, **62**, 581 (1969). For a review of the data concerning the conformation of formycin, see ref 5, Chapter 9.

Experimental Section

General Methods.—The general methods used are similar to those described earlier.[4] Melting points were obtained on a hot-stage microscope and are corrected.

4-Amino-7-[2-*O*-acetyl-3-chloro-3-deoxy-5-*O*-(2,5,5-trimethyl-1,3-dioxolan-4-on-2-yl)-β-D-xylofuranosyl]pyrrolo[2,3-*d*]pyrimidine (3a).—A suspension of tubercidin (1.3 g, 4.88 mmol)[14] and **1a** (2.24 g, 13.6 mmol) in anhydrous acetonitrile was stirred at 37° for 18 hr. The resulting clear solution was evaporated *in vacuo* to a syrup that was triturated with ether giving a white precipitate that was dried *in vacuo*. This material (2.33 g, 97%) was homogeneous by tlc (chloroform–methanol, 9:1) and gave a very sharp nmr spectrum indicating the presence of a single compound shown by its elemental analysis to be the hydrochloride of **3a**: λ_{max}^{MeOH,H^+} 227 nm (ε 22,600), 271 (11,000); $\lambda_{max}^{MeOH,OH^-}$ 271 nm (ε 11,700); $[\alpha]^{23}D$ −16.9° (*c* 1.0, $CHCl_3$); ORD (MeOH) $[\Phi]_{280}^{tr}$ − 3000°, $[\Phi]_{255}$ 0°, $[\Phi]_{248}$ 1300°; ν_{max} (KBr) 1805 (dioxolanone), 1755, 1675 cm^{-1}.

For analytical purposes this material was converted with quantitative recovery into the free base by partitioning between ethyl acetate and aqueous sodium bicarbonate. The organic phase was dried and evaporated leaving a dry foam. In some experiments the free base was isolated directly (85% yield) by omitting the ether precipitation step and directly using the partitioning process.

Anal. Calcd for $C_{19}H_{23}N_4O_7Cl$ (454.86): C, 50.17; H, 5.10; N, 12.32. Found: C, 50.29; H, 5.32; N, 12.24.

4-Amino-7-[2-*O*-acetyl-3-bromo-3-deoxy-5-*O*-(2,5,5,-trimethyl-1,3-dioxolan-4-on-2-yl)-β-D-xylofuranosyl]pyrrolo[2,3-*d*]pyrimidine (3b).—A suspension of tubercidin (1.3 g, 4.88 mmol) and **1b** (3.13 g, 15 mmol) in acetonitrile (50 ml) was stirred at room temperature for 1 hr. The solvent was largely removed *in vacuo* and the residue was partitioned between ethyl acetate and aqueous sodium bicarbonate. The organic phase was washed once more with bicarbonate and then with water, dried ($MgSO_4$), and evaporated leaving crude **3b** as a white froth in quantitative yield. As obtained, this material showed essentially one spot by tlc (chloroform–methanol, 9:1) and only traces of a more polar material lacking the dioxolanone group. The nmr spectrum of the crude product confirmed that it was essentially homogeneous and for analytical purposes an aliquot was purified by preparative tlc using the above system giving **3b** with excellent recovery as a froth that could not be crystallized: λ_{max}^{MeOH,H^+} 227 nm (ε 24,500), 271 (11,500); $\lambda_{max}^{MeOH,OH^-}$ 271 nm (ε 11,800); $[\alpha]^{23}D$ −4.7° (*c* 0.7, $CHCl_3$); ORD (MeOH) $[\Phi]_{280}^{tr}$ − 1950°, $[\Phi]_{264}$ 0°, $[\Phi]_{242}^{pk}$ 4100°; ν_{max} (KBr) 1808, 1755, 1635 cm^{-1}.

Anal. Calcd for $C_{19}H_{23}N_4O_7Br$ (499.32): C, 45.70; H, 4.64; N, 11.22; Br, 16.00. Found: C, 45.93; H, 4.79; N, 11.03; Br, 15.86.

In one experiment the hydrobromide of **3b** was isolated in essentially quantitative yield by the direct precipitation process described for **3a**. This material was entirely satisfactory for direct use in subsequent steps.

4-Amino-7-(3-chloro-3-deoxy-β-D-xylofuranosyl)pyrrolo[2,3-*d*]-pyrimidine (4a).—A solution of the crude hydrochloride of **3a** (1.8 g, 3.66 mmol) in saturated methanolic ammonia (100 ml) was kept at room temperature for 5 hr and then evaporated to dryness *in vacuo*. The residue was partitioned between chloroform and water, the bulk of the nucleoside material being found in the aqueous phase. The aqueous phase was freed of salts by preparative tlc using chloroform–methanol (4:1) giving 808 mg (78%) of a foam that contained a minor slower moving impurity by tlc. Crystallization from methanol gave 490 mg (47%) of pure **4a**: mp 188–189°; λ_{max}^{MeOH,H^+} 228 nm (ε 24,700), 272 (11,200); $\lambda_{max}^{MeOH,OH^-}$ 270 nm (ε 12,400); $[\alpha]^{23}D$ −37.2° (*c* 0.5, MeOH);

(14) Obtained through the kindness of Dr. A. R. Hanze of The Upjohn Co., Kalamazoo, Mich.

ORD (MeOH) $[\Phi]^{tr}_{288}$ −1600°, $[\Phi]_{260}$ 0°, $[\Phi]^{pk}_{250}$ 450°, $[\Phi]_{230}$ 0°; mass spectrum *m/e* 284, 286 (M^+), 249 (M − Cl), 163 [base (B) + CH_2O], 135 (base + 2 H), 134 (base + H).

Anal. Calcd for $C_{11}H_{13}N_4O_3Cl$ (284.70): C, 46.40; H, 4.60; N, 19.68; Cl, 12.45. Found: C, 46.48; H, 4.70; N, 19.58; Cl, 12.34.

4-Amino-7-(3-bromo-3-deoxy-β-D-xylofuranosyl)pyrrolo[2,3-*d*]pyrimidine (4b).—A solution of the crude hydrobromide salt of **3b** (1.5 g, 2.58 mmol) in saturated methanolic ammonia (150 ml) was kept at room temperature for 2 hr and then evaporated to dryness. The residue was purified by preparative tlc on three plates using four developments with chloroform–methanol (9:1). The major band was eluted and crystallized from methanol–ethyl acetate giving 554 mg (65%) of **4b**: mp 179.5–180°; λ_{max}^{MeOH,H^+} 228 nm (ε 25,300), 272 (11,400); $\lambda_{max}^{MeOH,OH^-}$ 270 nm (ε 12,300); $[\alpha]^{23}D$ −21.5° (*c* 0.65, MeOH); ORD (MeOH) $[\Phi]^{tr}_{292}$ −2200°, $[\Phi]_{270}$ 0°, $[\Phi]^{pk}_{246}$ 1700°.

Anal. Calcd for $C_{11}H_{13}N_4O_3Br$ (329.16): C, 40.14; H, 3.98; N, 17.02; Br, 24.28. Found: C, 40.28; H, 4.10; N, 16.88; Br, 24.11.

3′-Deoxytubercidin (5).—A solution of **4b** (474 mg, 1.44 mmol) in methanol (100 ml) and ethyl acetate (50 ml) containing triethylamine (0.5 ml) was vigorously stirred in an atmosphere of hydrogen in the presence of a 10% palladium-on-carbon catalyst (1.0 g) for 3 days. The mixture was filtered and the filtrate was desalted by preparative tlc using chloroform–methanol (9:1). Crystallization of the uv-absorbing material from ethyl acetate gave 224 mg (62%) of **5**: mp 178–179°; λ_{max}^{MeOH,H^+} 230 nm (ε 24,200), 273 (11,100); $\lambda_{max}^{MeOH,OH^-}$ 271 nm (ε 11,200); $[\alpha]^{23}D$ −74.6° (*c* 1.0, EtOH); ORD (MeOH) $[\Phi]^{tr}_{292}$ −2400°, $[\Phi]_{267}$ 0°, $[\Phi]^{pk}_{256}$ 600°, $[\Phi]_{240}$ 0°, $[\Phi]^{tr}_{238}$ −550°, $[\Phi]_{234}$ 0°; mass spectrum (20 eV) *m/e* 251 (M + H), 250 (M^+), 177 (BH—CH=CHOH), 163 (BHCHO), 136 (B + 2 H), 135 (B + H).

Anal. Calcd for $C_{11}H_{14}N_4O_3$ (250.25): C, 52.79; H, 5.64; N, 22.39; O, 19.18. Found: C, 52.64; H, 5.73; N, 22.27; O, 19.28.

2′,3′-Dideoxytubercidin (6).—A solution of crude **3b** (from 2.25 mmol of tubercidin) in ethyl acetate (100 ml) was stirred in an atmosphere of hydrogen in the presence of triethylamine (0.35 ml) and 10% palladium on carbon (500 mg) for 22 hr. The filtered and evaporated mixture was treated with methanolic ammonia for 6 hr and then purified first on a column of silicic acid and then by preparative tlc using two developments with chloroform–methanol (9:1). Elution of the major band gave 230 mg (40%) of 3′-deoxytubercidin (**5**) identical with that above, while elution of a somewhat less polar band gave 294 mg (56%) of **6** as a homogeneous foam that could not be obtained crystalline and tenaciously held water: λ_{max}^{MeOH,H^+} 219 nm (ε 19,100), 275 nm (ε 8400); $\lambda_{max}^{MeOH,OH^-}$ 272 nm (ε 9000); $[\alpha]^{23}D$ −20.8° (*c* 1.0, MeOH); ORD (MeOH) $[\Phi]^{tr}_{288}$ −1000°, $[\Phi]_{260}$ 0°, $[\Phi]^{pk}_{250}$ 300°, $[\Phi]^{tr}_{240}$ 100°; mass spectrum (70 eV) *m/e* 234 (M^+), 134 (B + H, base peak); mass spectrum (20 eV) *m/e* 234 (M^+), 134 (B + H, base peak).

Anal. Calcd for $C_{11}H_{14}N_4O_2 \cdot 2H_2O$ (266.25): C, 48.88; H, 6.71. Found: C, 48.91; H, 6.92.

2′,3′-Anhydrotubercidin (7). A. From the Bromohydrin (4b).—A solution of **4b** (250 mg, 0.75 mmol) in methanol (10 ml) containing 0.76 mmol of sodium methoxide was kept under nitrogen at room temperature for 3 hr. The solution was then neutralized with Dowex 50 (H^+) resin and evaporated leaving a syrup that was purified by preparative tlc using several developments with chloroform–methanol (9:1) giving a major band moving just faster than **4b**. Elution of this band and crystallization from methanol–ethyl acetate gave 106 mg (57%) of **7** which decomposed gradually at 145–176° (*cf.* 2′,3′-anhydroadenosine, which decomposes above 180° without melting[14]): $\lambda_{max}^{H^+}$ 228 nm (ε 22,700), 272 (11,200); $\lambda_{max}^{OH^-}$ 270 nm (ε 12,200); $[\alpha]^{23}D$ −42.6° (*c* 0.2, MeOH); mass spectrum (70 eV) *m/e* 248 (M^+), 221 (M − HCN), 134 (B + H, base peak), 163 (B + 30).

Anal. Calcd for $C_{11}H_{12}N_4O_3$ (248.24): C, 53.22; H, 4.86; N, 22.57. Found: C, 53.19; H, 4.99; N, 22.57.

B. From Tubercidin.—The total crude extracted product from tubercidin (266 mg, 1 mmol) and **1b** as above (600 mg) was dissolved in methanol (20 ml) containing 5 mmol of sodium methoxide and stored overnight at room temperature. The solution was then heated under reflux for 30 min, neutralized with Dowex 50 (H^+) resin, and evaporated *in vacuo*. The residue was purified by preparative tlc using chloroform–methanol (85:15) giving 180 mg (73%) of chromatographically homogeneous **7** which crystallized on standing and had an nmr spectrum identical with that of the analytical sample above.

Analogous treatment of the crude chloro nucleoside (**3a**) gave **7** in the same way.

Reaction of Formycin with 1b.—Formycin monohydrate (1.14 g, 4 mmol)[15] and **1b** (2.48 ml, 16 mmol) were stirred together in acetonitrile for 3 hr. The resulting clear solution was largely evaporated *in vacuo* and a solution of the residue in ethyl acetate was washed twice with saturated aqueous sodium bicarbonate and then with water. Evaporation of the dried ($MgSO_4$) solution left 2.10 g (100%) of a mixture of **9** and **10** (3:1 by nmr) which behaved as a single spot on tlc with chloroform–methanol (9:1) but could not be crystallized: λ_{max}^{MeOH,H^+} 235 nm (ε 8300), 297 (10,800); $\lambda_{max}^{MeOH,OH^-}$ 235 nm (ε 18,900), 305 (7600); ν_{max} 1665, 1740 cm^{-1}, no peaks near 1805 cm^{-1}.

Anal. Calcd for $C_{18}H_{22}N_5O_7Br$ (500.32): C, 43.21; H, 4.43; N, 14.00. Found: C, 43.58; H, 4.67; N, 14.28.

A similar reaction on 1.3 g of formycin but using ether precipitation rather than the partitioning work-up gave 2.9 g of the almost homogeneous hydrobromide of **9** and **10** containing a small amount of deacetylated material.

7-Amino-3-[5-*O*-(2-acetoxyisobutyryl)-3-bromo-3-deoxy-β-D-xylofuranosyl]pyrazolo[4,3-*d*]pyrimidine (11a).—A solution of the mixture of **9** and **10** above (1.0 g, 2 mmol) in saturated methanolic ammonia (10 ml) was kept at room temperature for 2.5 hr and then evaporated to dryness. The residue was applied to four preparative tlc plates and developed four times with chloroform–methanol (9:1) giving a clean separation of two major bands. Elution of the faster band gave 560 mg (61%) of **11a** as a chromatographically and spectroscopically homogeneous foam that could not be crystallized: λ_{max}^{MeOH,H^+} 236 nm (ε 8600), 298 (10,100); $\lambda_{max}^{MeOH,OH^-}$ 235 nm (ε 16,800), 304 (10,000); $[\alpha]^{23}D$ 7.1° (*c* 1.0, MeOH); ORD (MeOH) $[\Phi]^{tr}_{318}$ −1400°, $[\Phi]_{302}$ 0°, $[\Phi]^{pk}_{276}$ 1850°, $[\Phi]^{tr}_{260}$ 1450°, $[\Phi]^{pk}_{236}$ 4100°; ν_{max} (KBr) 1735, 1645 cm^{-1}.

Anal. Calcd for $C_{16}H_{20}N_5O_6Br$ (458.27): C, 41.93; H, 4.40; N, 15.28; Br, 17.44. Found: C, 41.69; H, 4.82; N, 15.13; Br, 17.78.

A sample of this material was converted into its hydrochloride, which was precipitated from methanol with ether giving a dry white powder.

Anal. Calcd for $C_{16}H_{20}N_5O_6Br \cdot HCl$ (480.73): C, 39.97; H, 4.40; N, 11.65; Br, 16.62. Found: C, 39.82; H, 4.55; N, 11.88; Br, 16.37.

7-Amino-3-[5-*O*-(2-acetoxyisobutyryl)-2-bromo-2-deoxy-β-D-arabinofuranosyl]pyrazolo[4,3-*d*]pyrimidine (12a).—Elution of the slower band from the above ammonia-treated product gave 240 mg (26%) of homogeneous **12a** which was crystallized from ethyl acetate giving 200 mg with mp 200–205° dec from ethyl acetate: λ_{max}^{MeOH,H^+} 237 nm (ε 8500), 298 (11,400); $\lambda_{max}^{MeOH,OH^-}$ 236 nm (ε 17,800), 306 (7100); $[\alpha]^{23}D$ 37.4° (*c* 1.0, MeOH); ORD (MeOH) $[\Phi]^{tr}_{320}$ −1000°, $[\Phi]_{308}$ 0°, $[\Phi]^{pk}_{240}$ 15,600°; ν_{max} (KBr) 1735, 1640 cm^{-1}.

Anal. Calcd for $C_{16}H_{20}N_5O_6Br$ (458.27): C, 41.93; H, 4.40; N, 15.28; Br, 17.44. Found: C, 41.78; H, 4.53; N, 15.14, Br, 17.57.

A small amount (60 mg, 9%) of a mixture of **11b** and **12b** was also eluted from a much more polar band on the above plates. See below.

7-Amino-3-(3-bromo-3-deoxy-β-D-xylofuranosyl)pyrazolo[4,3-*d*]pyrimidine (11b).—A solution of the crude mixture of **9** and **10** (500 mg, 1 mmol) in saturated methanolic ammonia (5 ml) was kept at room temperature for 50 hr and then evaporated to dryness. The residue was chromatographed on two preparative plates using four developments with chloroform–methanol (85:15) which clearly separated two major slow bands from lesser amounts of epoxide (**15**, 20 mg, 8%, after crystallization from ethanol), **11a** (39 mg, 8%), and **12a** (17 mg, 3%, mp 199–202° from ethyl acetate). Elution of the faster band gave 190 mg (57%) of **11b** as a chromatographically homogeneous syrup that was crystallized from ethanol: mp 202–204° dec; λ_{max}^{MeOH,H^+} 238 nm (ε 8500), 298 (12,000); $\lambda_{max}^{MeOH,OH^-}$ 213 nm (ε 26,400), 236 (19,900), 305 (8100); $[\alpha]^{23}D$ 8.3° (*c* 1.0, MeOH); ORD (MeOH) $[\Phi]^{pk}_{296}$ 1700°, $[\Phi]_{258}$ 0°, $[\Phi]^{tr}_{234}$ −12,400°.

Anal. Calcd for $C_{10}H_{12}N_5O_3Br$ (330.15): C, 36.38; H, 3.66; N, 21.21; Br, 24.21. Found: C, 36.54; H, 3.61; N, 21.21; Br, 24.23.

7-Amino-3-(2-bromo-2-deoxy-β-D-arabinofuranosyl)pyrazolo-

(15) Obtained from Meiji Seika Kaisha, Ltd., Kawasaki, Japan, through the kindness of Dr. Kenji Maeda of the Institute of Microbial Chemistry, Tokyo, Japan. This material proved to be a tenacious monohydrate and was used as such.

[4,3-*d*]**pyrimidine** (**12b**).—Elution of the slower band from the isolation of **11b** gave 60 mg (18%) of **12b**, which was crystallized from ethanol giving 45 mg of crystals that underwent a loss of crystal structure at 165° and then slowly decomposed above 200°: λ_{max}^{MeOH,H^+} 236 nm (ε 7800), 298 (ε 10,500); $\lambda_{max}^{MeOH,OH^-}$ 236 nm (ε 18,800), 306 (7400).

Anal. Calcd for $C_{10}H_{12}N_5O_3Br$ (330.15): C, 36.38; H, 3.66. Found: C, 36.44; H, 3.99.

5′-*O*-(2-Acetoxyisobutyryl)-3′-deoxyformycin (**13a**).—A solution of **11a** (576 mg, 1.25 mmol) in methanol (100 ml) and ethyl acetate (50 ml) containing triethylamine (0.5 ml) was vigorously stirred in an atmosphere of hydrogen for 24 hr in the presence of a 10% palladium on carbon catalyst (1 g). The mixture was filtered and the filtrate desalted by preparative tlc using chloroform–methanol (9:1) to give 308 mg (65%) of **13a** as a homogeneous foam that could not be crystallized: λ_{max}^{MeOH,H^+} 236 nm (ε 9100), 297 (10,800); $\lambda_{max}^{MeOH,OH^-}$ 212 nm (ε 25,900), 236 (16,600), 305 (6700); $[\alpha]^{23}D$ −21.0° (*c* 0.7, MeOH); ORD (MeOH) $[\Phi]_{314}^{tr}$ −1400°, $[\Phi]_{290}$ 0°, $[\Phi]_{238}^{pk}$ 5200 °.

Anal. Calcd for $C_{16}H_{21}N_5O_6$ (379.37): C, 50.65; H, 5.58; N, 18.46. Found: C, 50.41; H, 5.57; N, 18.29.

3′-Deoxyformycin (**13b**). **A. From 11b.**—A solution of **11b** (350 mg, 1.06 mmol) in methanol (180 ml) and ethyl acetate (90 ml) containing triethylamine (0.5 ml) was vigorously stirred in an atmosphere of hydrogen for 48 hr in the presence of a 10% palladium on carbon catalyst. The filtered and evaporated mixture was desalted by preparative tlc using chloroform–methanol (85:15) giving 154 mg (60%) of **13b** as a chromatographically homogeneous but hygroscopic white foam.

Anal. Calcd for $C_{10}H_{13}N_5O_3$ (251.24): C, 47.80; H, 5.22; N, 27.88. Found: C, 47.59; H, 5.27; N, 27.72.

Treatment of a portion of this substance with a small excess of methanolic hydrogen chloride gave the crystalline hydrochloride in quantitative yield with mp 207–209° from ethanol: λ_{max}^{MeOH,H^+} 234 nm (ε 8500), 295 (10,500); $\lambda_{max}^{MeOH,OH^-}$ 234 nm (ε 16,800), 303 (7800); $[\alpha]D$ −32.4° (*c* 0.4, H_2O); ORD (H_2O) $[\Phi]_{308}^{tr}$ −850°, $[\Phi]_{293}$ 0°, $[\Phi]_{260}^{pk}$ 2100°, $[\Phi]_{232}$ 0°, $[\Phi]_{220}^{tr}$ −4300°.

Anal. Calcd for $C_{10}H_{14}N_5O_3Cl$ (287.70): C, 41.74; H, 4.90; N, 24.34. Found: C, 41.58; H, 4.75; N, 24.49.

B. From 13a.—A solution of **13a** (236 mg, 0.62 mmol) in saturated methanolic ammonia (100 ml) was kept at room temperature for 2 days. Preparative tlc using chloroform–methanol (85:15) showed that a trace of **13a** still remained, and elution of the major band gave 140 mg (90%) of **13b** identical with that above.

2′-Deoxyformycin (**14**).—A solution of **12a** (410 mg, 0.89 mmol) in methanol (100 ml) was hydrogenated as above in the presence of a palladium-on-carbon catalyst (400 mg). The mixture was then filtered and evaporated leaving a crude 2′-deoxy nucleoside that gave a single spot on tlc using chloroform–methanol (85:15). This material was dried, treated with methanolic sodium methoxide at room temperature for 3 hr, and then passed through a column of Dowex 50 (NH_4^+) resin. The eluate was concentrated and purified by preparative tlc using multiple developments with chloroform–methanol (4:1). The eluted material (140 mg, 63%) was treated with an excess of methanolic hydrogen chloride and crystallized from ethanol giving the hydrochloride of **14**: mp 194–196°; λ_{max}^{MeOH,H^-} 233 nm (ε 8900), 295 (10,700); $\lambda_{max}^{MeOH,OH^-}$ 234 nm (ε 16,500), 304 (7300); $[\alpha]^{23}D$ 20.8° (*c* 1.0, H_2O); ORD (H_2O) $[\Phi]_{320}^{tr}$ −500°, $[\Phi]_{303}$ 0°, $[\Phi]_{260}^{pk}$ 1300°, $[\Phi]_{241}$ 0°, $[\Phi]_{224}^{tr}$ −5900°.

Anal. Calcd for $C_{10}H_{14}N_5O_3Cl$ (287.70): C, 41.74; H, 4.90; N, 24.34; Cl, 12.32. Found: C, 42.00; H, 4.87; N, 24.14; Cl, 12.36.

2′,3′-Dideoxyformycin (**16**).—A solution of the crude product from formycin (3.45 mmol) and **1b** (as above) in methanol (100 ml) was vigorously stirred in the presence of triethylamine (0.5 ml) and a 10% palladium-on-carbon catalyst (500 mg) for 5 days. After filtration and evaporation, the residue was treated with methanolic sodium methoxide for 3 hr and then passed through a column of Dowex 50 (NH_4^+) resin. The residue was chromatographed on four preparative plates using eight developments with chloroform–methanol (85:15) which clearly separated three bands. Elution of the slowest band gave 35 mg (3%) of pure **14** which was isolated as the crystalline hydrochloride. Elution of the middle band gave 320 mg (28%) of **13b** which was isolated as its crystalline hydrochloride with mp 205–209° as above. Elution of the fastest band gave 360 mg (44%) of chromatographically and spectroscopically homogeneous **16** as a foam. This material was converted to its hydrochloride and crystallized from ethanol giving 275 mg of needles with mp 182–185°. The remaining material was precipitated with ether for other studies: λ_{max}^{MeOH,H^+} 234 nm (ε 8900), 296 (10,200); $\lambda_{max}^{MeOH,OH^-}$ 234 nm (ε 17,200), 304 (8000); $[\alpha]^{23}D$ 30.2° (*c* 1.0, H_2O); ORD (MeOH) $[\Phi]_{254}^{pk}$ 1800°, $[\Phi]_{239}$ 0°, $[\Phi]_{226}^{tr}$ −3600°; mass spectrum (hydrochloride, 20 and 70 eV) *m/e* 235 (M^+), 162 (B + 28, base peak).[16]

Anal. Calcd for $C_{10}H_{14}N_5O_2Cl$ (271.71): C, 44.20; H, 5.19; N, 25.77; Cl, 13.05. Found: C, 44.03; H, 5.18; N, 25.53; Cl, 13.24.

2′,3′-Anhydroformycin (**15**).—A solution of crude **9** and **10** (500 mg, 1 mmole) in methanol (35 ml) containing 2.7 mmol of sodium methoxide was kept at room temperature for 72 hr, at which point tlc showed the presence of a single product. The mixture was neutralized by portionwise addition of Dowex 50 (H^+) resin, filtered, and evaporated. The residue was purified by preparative tlc using chloroform–methanol (4:1) and the major uv-absorbing product was crystallized from methanol–ethyl acetate giving 115 mg (46%) of **15** which decomposed gradually above 190° without melting: λ_{max}^{MeOH,H^+} 235 nm (ε 8300), 297 (11,100); $\lambda_{max}^{MeOH,OH^-}$ 235 nm (ε 18,300), 305 (7700); $[\alpha]^{23}D$ 17.4° (*c* 0.5, MeOH); ORD (MeOH) $[\Phi]_{240}^{pk}$ 4600°, $[\Phi]_{230}$ 0°, $[\Phi]_{222}$ −8300°.

Anal. Calcd for $C_{10}H_{11}N_5O_3$ (249.23): C, 48.19; H, 4.45; N, 28.01. Found: C, 48.38; H, 4.62; N, 27.84.

Registry No.—**1a**, 40635-66-3; **1b**, 40635-67-4; **2**, 69-33-0; **3a**, 40627-07-4; **3a** HCl, 40627-08-5; **3b**, 40627-09-6; **3b** HBr, 40627-10-9; **4a**, 40627-11-0; **4b**, 40627-12-1; **5**, 40725-89-1; **6**, 40627-30-3; **7**, 40627-31-4; **8**, 6742-12-7; **9**, 40627-32-5; **10**, 40627-33-6; **11a**, 40627-34-7; **11a** HCl, 40627-35-8; **11b**, 40627-36-9; **12a**, 40627-37-0; **12b**, 40627-38-1; **13a**, 40627-39-2; **13b**, 40725-90-4; **13b** HCl, 40627-13-2; **14**, 40627-14-3; **14** HCl, 40627-15-4; **15**, 40627-16-5; **16**, 40627-17-6; **16** HCl, 40627-18-7.

(16) The mass spectra of a number of compounds in this paper will be discussed in detail elsewhere.