instantaneous disappearance of the iodine. However, analysis of the ether layer revealed the presence of 0.44 mmol of iodide in 1 min, 1.02 mmol in 5 min, and 1.21 mmol in 15 min.

This result appears to rule out a mechanism involving a direct reaction of iodine with the vinyl–boron bond.[7] It suggests that the fast reaction of the neutralized vinylboronic acid and iodine results in an intermediate which is converted into the vinyl iodide relatively slowly. Further study is necessary to elaborate the nature of this intermediate.

It was previously reported that the stereospecific *trans*-1-alkenylmercuric acetates can be prepared from 1-alkynes *via* hydroboration with catecholborane.[8] In the present study the stereospecific *trans*-1-alkenyl iodides can likewise be prepared from these intermediates. Consequently, these alkenylboronic acids may provide valuable new intermediates leading to a variety of derivatives.

Irrespective of future developments, the present procedure provides a very simple, essentially quantitative synthesis of *trans*-1-alkenyl iodides. The alternative method for the synthesis of these compounds is the hydroalumination procedure of Zweifel and Whitney.[9] The *trans*-1-alkenyl iodides are finding important applications in the synthesis of prostaglandins.[10,11]

(7) We also observed that phenylboronic acid is not converted into phenyl iodide under the same conditions.

(8) R. C. Larock, S. K. Gupta, and H. C. Brown, *J. Amer. Chem. Soc.*, **94**, 4371 (1972).

(9) G. Zweifel and C. C. Whitney, *ibid.*, **89**, 2753 (1967).

(10) A. F. Kluge, K. G. Untch, and J. H. Fried, *ibid.*, **94**, 7827 (1972).

(11) C. J. Sih, P. Price, R. Sood, R. G. Salomon, G. Peruzzotti, and M. Casey, *ibid.*, **94**, 3643 (1972); C. J. Sih, J. B. Heather, G. P. Peruzzotti, P. Price, R. Sood, and L. F. H. Lee, *ibid.*, **95**, 1676 (1973).

(12) Visiting scholar on funds provided by the Fuji Photo Film Co., Ltd., Tokyo, Japan.

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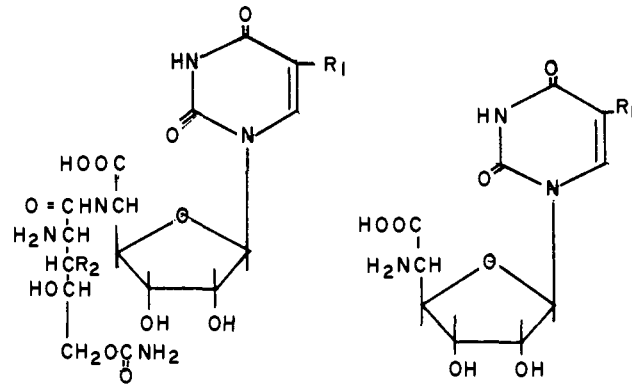
Biosynthesis of the 5-Fluoropolyoxins, Aberrant Nucleoside Antibiotics

Sir:

The polyoxins represent a new group of pyrimidine nucleoside peptide antibiotics which are elaborated by *Streptomyces cacaoi*.[1] They are extremely toxic toward phytopathogenic fungi, but do not inhibit bacteria, plants, or animals.[2,3] It is the structural similarity of the polyoxins with UDP–*N*-acetylglucosamine that makes these compounds inhibitors for chitin synthesis. Because the pyrimidine chromophore in ten of the polyoxins has either the 5-methyl, 5-hydroxymethyl, or 5-carboxy substituent, it was of interest to study the biosynthesis of these 5-substituted uracils. There is a new enzyme system in *S. cacaoi* that synthesizes the thymine (T) and/or hydroxymethyluracil (HMU) chromophore from uracil (U) and C-3 of serine without proceeding through thymidylate synthetase (to be published elsewhere). Because uracil was an efficient precursor of pyrimidine chromophore, we became interested in the possibility of biosynthesizing unnatural polyoxin by using uracil analogs in place of U. First, these experiments would define the specificity of the enzyme system that catalyzes the biosynthesis of the polyoxins. Second, the formation of an "aberrant nucleoside antibiotic" would be extremely useful in the preparation of a polyoxin with broader inhibitory properties. We have now been able to show that 5-fluorouracil (FU) is very efficiently incorporated and forms 5-fluoropolyoxin L (**1**) and 5-fluoropolyoxin M (**2**), which have broad activity to bacteria (see Chart I).

Chart I



1, R_1 = F; R_2 = OH
2, R_1 = F; R_2 = H
3, R_1 = H; R_2 = OH
4, R_1 = H; R_2 = H
5, R_1 = F
6, R_1 = H

S. cacaoi var *asoensis*[1] was fermented with an organic medium in shaking flasks.[3] At the stationary phase, FU was added (10^{-2} *M*). Three days later, polyoxin complex was isolated.[3] Each polyoxin was separated on a cellulose column. The main components were **1**, **2**, polyoxin L[1] (**3**), and polyoxin M (**4**).[4] FU was incorporated into polyoxins without any dilution of radioactivity. The base ratio of the polyoxin complex (FU:U:T:HMU $\simeq$ 0.6:1:0.1:0.1) is markedly different from the normal ratio (U:T:HMU $\simeq$ 1:2:3). Apparently, the fluoropolyoxins formed in the cell inhibit T and HMU chromophore formation.

5-Fluoropolyoxin L (**1**) was obtained as a white powder: $C_{16}H_{22}N_5O_{12}F$; $[\alpha]^{25}D$ +45.1° (*c* 1, H_2O); pK_a (3.1) 6.65, 7.85; uv_{max} (H_2O) 0.05 *N* HCl, 267 (ε 8100); 0.05 *N* NaOH, 268 (ε 6400); pmr (D_2O) δ 5.86 (br d, 1, H-1′), 7.91 (d, 1, H-6). Alkaline hydrolysis[2] gave FU, 5-fluorouracilpolyoxin C (**5**), 2-amino-2-deoxy-L-xylonic acid (**7**),[1] CO_2, and NH_3.

5-Fluoropolyoxin M (**2**) was obtained as a white powder: $C_{16}H_{22}N_5O_{11}F$; $[\alpha]^{25}D$ +42.5° (*c* 1, H_2O); pK_a (2.6), 7.05, 8.05; uv_{max} (H_2O) 0.05 *N* HCl, 267 (ε 7900); 0.05 *N* NaOH, 268 (ε 6400); pmr (D_2O) δ 5.84 (br d, 1, H-1), 7.84 (d, 1, H-6), 2.08 (m, 2″, 3″-CH_2). Alkaline hydrolysis gave FU, **5**, 2-amino-2,3-dideoxy-L-xylonic acid (**8**),[1] CO_2, and NH_3.

Compound **5** was crystallized with mp 225–226°

(1) K. Isono, K. Asahi, and S. Suzuki, *J. Amer. Chem. Soc.*, **91**, 7490 (1969).

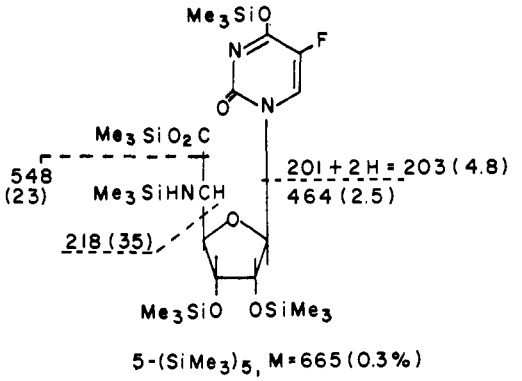
(2) K. Isono, J. Nagatsu, Y. Kawashima, and S. Suzuki, *Agr. Biol. Chem.*, **29**, 848 (1965).

(3) K. Isono, J. Nagatsu, K. Kobinata, K. Sasaki, and S. Suzuki, *Agr. Biol. Chem.*, **31**, 190 (1967).

(4) K. Isono, S. Suzuki, M. Tanaka, T. Nanbata, and K. Shibuya, *Tetrahedron Lett.*, 425 (1970).

dec; uv_{max} (H_2O) 0.05 *N* HCl, 267 (ε 8500); 0,05 *N* NaOH, 269 (ε 7000); mass spectrum of the trimethylsilyl derivative,[5] found for M − CH_3, *m/e* 650.2400; calcd for $C_{24}H_{49}N_3O_7Si_5F$, 650.2401. Principal fragment ions[6] agree with structure **5** (see Chart II) and

Chart II



correlate with the spectrum of **6**, with all base-containing ions shifted 17.991 ± 0.003 mass units higher due to fluorine. The pmr spectrum (100 MHz) of **5** (compared with **6**) is shown in Table I. Close resemblance of chemical shifts and coupling constants of 1′, 2′, 3′, 4′, and 5′ protons strongly suggests the same configuration and conformation in **5** and **6**. Moreover, typical coupling of H-1′ and H-6 with 5-fluorine was observed.[7]

Table I. Nuclear Magnetic Resonance Spectral Data of 5-Fluorouracil Polyoxin C and Uracil Polyoxin C in 20% DCl in D_2O

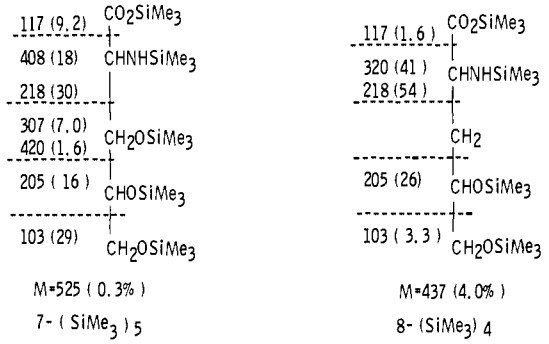
5-Fluorouracil polyoxin C (**5**)			Uracil polyoxin C (**6**)		
Assignment	Chem shift[a]	Coupling constant[b]	Assignment	Chem shift[a]	Coupling constant[b]
1′-H	5.81 (br d)	$J_{1',2'} = 4.0$[c]	1′-H	5.82 (d)	$J_{1',2'} = 3.8$[c]
2′-H	4.51 (q)	$J_{2',3'} = 6.2$	2′-H	4.54 (q)	$J_{2',3'} = 6.0$
3′-H	4.76 (q)	$J_{3',4'} = 6.6$	3′-H	4.77 (q)	$J_{3',4'} = 6.8$
4′-H	4.51 (q)	$J_{4',5'} = 3.0$	4′-H	4.52 (q)	$J_{4',5'} = 2.7$
5′-H	4.76 (d)		5′-H	4.75 (d)	
6-H	7.75 (d)	$J_{6\text{-}F} = 6.0$[d]	5-H	5.98 (d)	$J_{56} = 8.1$
		$J_{1'\text{-}F} \simeq 1$[d]	6-H	7.61 (d)	

[a] Shifts are given in ppm from DSS as an internal standard. [b] *J* values are in Hz; read from first-order splittings; d, doublet; q, quartet; br, broad. [c] Coupling was confirmed by the spin-decoupling experiment. [d] See ref for H_6–F and $H_{1'}$–F coupling of 5-fluorouracil nucleosides.

Compounds **7** and **8** were not crystallized. However, the R_f values of **7** and **8** were identical with authentic **7** and **8** (tlc; three solvents). Mass spectra (relative abundance) of the major ions shown below (Chart III) from gas chromatography–mass spectrometry[6] of the trimethylsilyl derivatives of **7** and **8** were the same as those derived from authentic **7** and **8** and clearly establish the overall structure as **1** and **2**.

Whereas the natural polyoxins only inhibit the fungi, **1** and **5** are extremely inhibitory to *Streptococcus faecalis* and *Escherichia coli* (10^{-5}–10^{-6} *M*). 5-Fluorouracil-2′-deoxyuridine 5′-monophosphate inhibits thymidylate synthetase.[8] With partially purified thymidylate synthetase from *E. coli*, the fluoropolyoxins (**1** and **5**) were not inhibitory. Therefore, the mode of action of the fluoropolyoxins is unclear. This mode of action is under study. Finally, **1** and **3** had the same inhibitory properties against purified chitin synthetase from *Saccaromyces cerevisiae* 5233C; **5** was not inhibitory.

Chart III



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(5) J. A. McCloskey, A. M. Lawson, K. Tsuboyama, P. M. Krueger, and R. N. Stillwell, *J. Amer. Chem. Soc.*, 90, 4182 (1968).

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(7) R. J. Cushley, I. Wempen, and J. J. Fox, *J. Amer. Chem. Soc.*, 90, 709 (1968).

(8) (a) T. I. Kalman, *Ann. N. Y. Acad. Sci.*, **186**, 166 (1971); (b) R. J. Landenbach, P. V. Danenberg, and C. Heidelberger, *Biochem. Biophys. Res. Commun.*, **48**, 1565 (1972); (c) D. V. Santi and C. McHenry, *Proc. Nat. Acad. Sci. U. S.*, **69**, 1855 (1972).

(9) This paper is part XVI of a series; the previous paper is T. Uematsu and R. J. Suhadolnik, *J. Med. Chem.*, in press.

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5-Chlorocytosine. Occurrence in Salmon Sperm Deoxyribonucleic Acid

Sir:

Fractionation of a deoxyribonucleic acid (DNA) hydrolysate from 900 kg of salmon sperm resulted in the isolation of 5-chlorocytosine (I). While numerous halogen-containing compounds have been isolated from marine organisms,[1] this is, to our knowledge, the first halogenated nucleic acid constituent to be isolated.[2,3]

(1) See, for example, J. J. Sims, W. Fenical, R. M. Wing, and P. Radlick, *J. Amer. Chem. Soc.*, **95**, 972 (1973); W. Fenical, J. J. Sims, and P. Radlick, *Tetrahedron Lett.*, 313 (1973); G. E. VanLear, G. O. Morton, and W. Fulmor, *ibid.*, 299 (1973); W. B. T. Cruse, M. N. G. James, A. A. Al-Shamma, J. K. Beal, and R. W. Doskotch, *Chem. Commun.*, 1278 (1971); J. J. Sims, W. Fenical, R. M. Wing, and P. Radlick, *J. Amer. Chem. Soc.*, **93**, 3774 (1971); S. Hunt and S. Breuer, *Biochem. Soc. Trans.*, 1, 215 (1973).

(2) Halogenated nucleosides, *e.g.*, 5-bromouridine, when administered to certain organisms are incorporated into nucleic acid chains. See P. Hackett and P. Hanawalt, *Biochim. Biophys. Acta*, 123, 356 (1966).

(3) Nucleocidin, an antibiotic nucleoside produced by *Streptomyces calvus*, has a fluoro substituent at C-4 of the ribosyl moiety. See G. O. Morton, J. E. Lancaster, G. E. Van Lear, W. Fulmor, and W. E. Meyer, *J. Amer. Chem. Soc.*, **91**, 1535 (1969).