Scheme I

CH₂OR′ H

CH_3OH, $h\nu$

t-BuOK

2, R = H
3, R = Ac

4, R = Ac; R′ = H
5, R = Ac; R′ = Ms
6, R = R′ = H

OH⁻

7

1

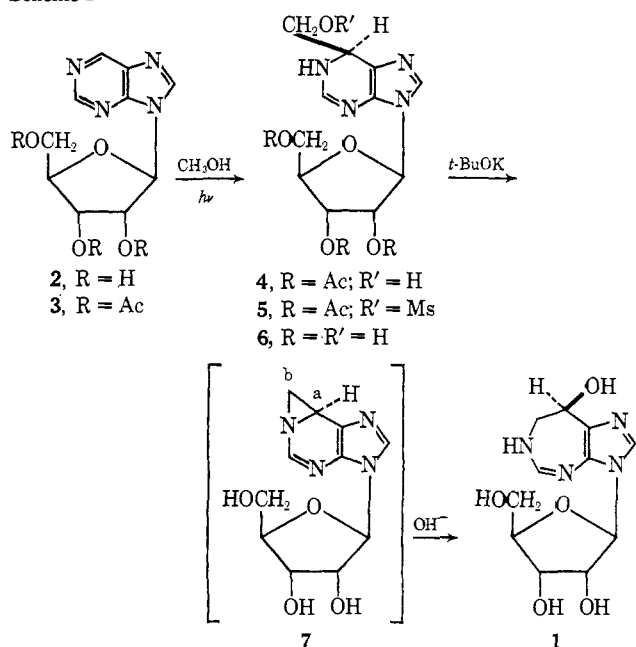296 nm (ϵ 9000), 244 (5500)]. This photoadduct was considered to be free of isomeric impurities[6] as determined by thin-layer chromatography[7] and the careful analysis of the hydrolysis product 6.[8] The photoadduct 4 was treated with mesyl chloride in the presence of sodium hydride[9] in anhydrous dimethoxyethane at 0° for 17 hr to afford a pale yellow oil [M⁺ 488, uv_{max} (CH₃OH) 293 nm (ϵ 7600), 246 (sh) (5400)] in 91% yield. The mesylate 5[10] was immediately treated with potassium $tert$-butoxide in dimethoxyethane at 0° for 18 hr to afford a brown precipitate. The precipitate was dissolved in water at room temperature (30 min) and treated with active charcoal to adsorb the reaction product.[11] The extract of the charcoal with 50% aqueous acetone gave a pale yellow glassy material which was treated with Dowex 1-X2 (OH⁻) and adjusted to pH 8–8.5 at room temperature for 17 hr. The product was subjected to preparative thin-layer chromatography, affording coformycin (1) in 38% yield.[12]

(6) This result was markedly different from that of the photoaddition of methanol to 2: B. Evans and R. Wolfenden, *J. Amer. Chem. Soc.*, **92**, 4751 (1970).

(7) This was carried out using three solvent systems with benzene–methanol (5:1, R_f = 0.22), chloroform–methanol (7:3, R_f = 0.25), and ethyl acetate–methanol (3:1, R_f = 0.15).

(8) 4 was treated with Dowex 1-X2 (OH⁻) in water at room temperature overnight, and the product was analyzed according to the procedure of Evans and Wolfenden.[6]

(9) The hydroxyl group in alcohol 4 is very strongly hydrogen bonded by the N-7, judging from the ir spectrum, which is the reason why attempted sulfonylation with tosyl chloride–pyridine or mesyl chloride–pyridine was completely unsuccessful in our case and for a similar preparation of benzyl tosylates using sodium hydride; see K. I. H. Williams, S. E. Cremer, F. W. Kent, E. J. Sehm, and D. S. Tarbell, *J. Amer. Chem. Soc.*, **82**, 3982 (1960).

(10) The mesylate 5 was very unstable, giving three spots by tlc after dissolving it in chloroform at room temperature for 2–3 hr.

(11) During the synthetic experiment, it was found that a complex salt was formed from coformycin and potassium methanesulfonate and easily adsorbed by active charcoal and coformycin was easily recovered by the treatment of the salt with a strong anion-exchange resin.

(12) The synthetic coformycin was confirmed to be free of the diastereomer by tlc using different solvent systems such as benzene–methanol (1:1, R_f = 0.31) and butanol–ethanol–chloroform–17% NH₃ in H₂O (4:5:2:4, R_f = 0.39). Besides 1, there was obtained another product of higher mobility in 20% yield which was considered to be a compound with aromatic purine nucleus[6] based on the uv spectrum (263 nm, ϵ 6550). The characterization of the compound will be published in a full paper.

The identity of the synthetic coformycin (1) with the natural one was confirmed by mixture melting point, tlc, spectroscopic data including ir, uv, and nmr, [α]D, and ORD.

The successful ring expansion of the mesylate 5 strongly suggests that the product 1 was formed exclusively through fission at a of aziridine intermediate 7, although an attempt to isolate 7 was unsuccessful.[13] Since the stereochemistry of the hydroxyl group of the base moiety of 1 is R configuration,[1] the stereochemistry of the hydroxymethyl group of 4 must also be R configuration based on SN2 character of the solvolysis of the intermediate 7.[14] Therefore, the photoaddition of methanol to 2 is stereospecific.

(13) The fission at b of the aziridine intermediate 7 will give original 4 unstable and easily oxidized. On the other hand, the vinylic bond (C₄– C₅ bond) of 4 is also properly disposed for a 1,2 shift, but such rearrangement will require an unfavorable intermediate highly strained. For ring expansion of dihydro heterocycles, see G. F. Field, W. J. Zally, and L. H. Sternbach, *J. Org. Chem.*, **36**, 2968 (1971).

(14) The cleavage reaction of such an aziridine intermediate is considered to be stereospecific with retention of configuration for 7 to 1. See, for instance, D. R. Crist and N. J. Leonard, *Angew. Chem., Int. Ed. Engl.*, **8**, 965 (1969).

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Structure of Coformycin, an Unusual Nucleoside of Microbial Origin

Sir:

Coformycin was discovered in culture filtrates of *Nocardia interforma* and *Streptomyces kaniharaensis* SF-557[1] which produced formycin. Coformycin showed a strong synergistic activity with formycin[2] in inhibiting the growth of bacteria,[1] although coformycin alone did not exhibit antibacterial activity. It was also confirmed to be the strongest inhibitor of adenosine deaminase which deaminates adenosine and formycin.[3] We would like to report the structure of coformycin (1), an unusual nucleoside of microbial origin with dihydrohomopurine nucleus.

Coformycin (1) has the formula C₁₁H₁₆N₄O₅ (M⁺ 284.110): mp 182–184°; [α]²⁴D +34 (c 1.0, H₂O); pK_a 5.3; uv_{max} (H₂O) 282 nm (ϵ 8250); ORD Cotton effect (H₂O), negative at 270 nm and positive at 307 nm. As D-ribose was obtained by acid hydrolysis, 1 was considered to be a ribonucleoside linked by the usual C–N glycosyl bond.[4] A close structural relationship[5] with a purine riboside was strongly considered based on the spectroscopic and chemical evidences mentioned above and the competitive nature of inhibition to enzymatic deamination of substrate such as adenosine.[3]

(1) A preliminary report of the isolation and characterization of coformycin was given: T. Niida, *et al.*, 153rd Scientific Meeting of Japan Antibiotics Research Association, Tokyo, Jan 27, 1967. See also R. J. Suhadolnik, "Nucleoside Antibiotics," Wiley-Interscience, New York, N. Y., 1970, p 366.

(2) G. Koyama, K. Maeda, H. Umezawa, and Y. Iitaka, *Tetrahedron Lett.*, 597 (1966).

(3) T. Sawa, Y. Fukagawa, H. Homma, T. Takeuchi, and H. Umezawa, *J. Antibiot., Ser. A*, **20**, 227 (1967), and reference contained therein.

(4) T. Tsuruoka, T. Ito, and T. Niida, unpublished result.

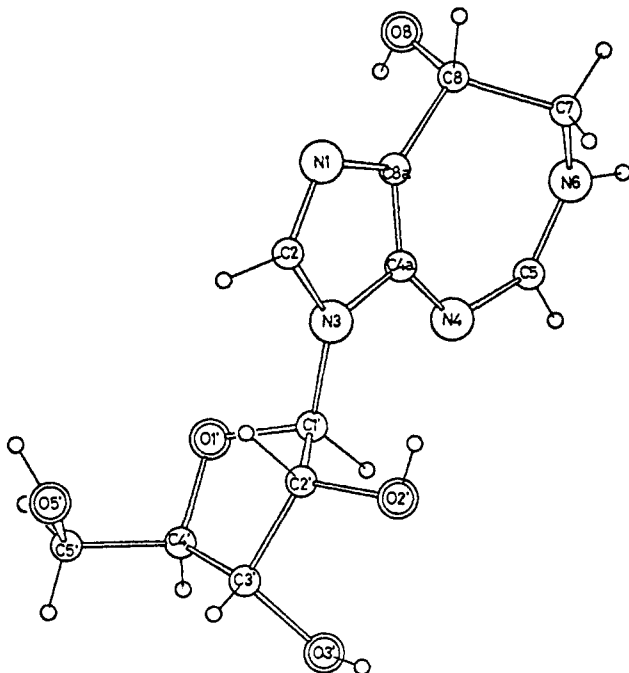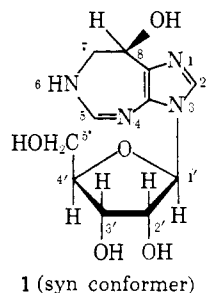(5) The detailed spectral interpretation will be reported in a full paper.

Figure 1.

The unequivocal formulation of the structure as **1**

1 (syn conformer)

has been accomplished by the X-ray crystallographic study of coformycin itself.[5] The crystals of coformycin were grown from an aqueous solution as colorless thin plates. Lattice constants and intensities were measured by a four-circle X-ray diffractometer using Ni-filtered Cu Kα radiation. Crystal data for coformycin sesquihydrate, $C_{11}H_{16}N_4O_5 \cdot 1.5H_2O$: formula weight = 311.3; orthorhombic; a = 11.96$_0$, b = 23.50$_0$, c = 4.935 Å; D_χ = 1.49 g cm^{-3}, Z = 4; absent reflections, $h00$ when $h \neq 2n$, $0k0$ when $k \neq 2n$; space group $P2_1 2_1 2$. Integrated intensities were measured by the $\omega-2\theta$ scanning method with a scan speed of 4° 2θ min^{-1}. The crystal was about 0.13 × 0.025 × 0.9 mm in size and no correction was applied for absorption. A total of 1021 independent reflections with $F > 3\sigma(F)$ were measured. These structure factors were then converted to the normalized structure factors; E and the phases of 81 reflections with $E > 1.8$ were determined by the symbolic addition procedure. These phases were then refined and extended to 182 reflections with $E > 1.49$. The resulting E map showed the locations of 17 non-hydrogen atoms. Refinement of the atomic parameters for these 17 atoms was carried out by the least-squares method. Subsequent Fourier and difference Fourier syntheses revealed the whole structure including hydrogen atoms. The R value at the present stage of the refinement is 0.057 for 1021 reflections. Thus, the

present analysis establishes the structure of coformycin to be 3-(β-D-ribofuranosyl)-6,7,8-trihydroimidazo[4,5-d] [1,3]diazepin-8(R)-ol. The structure resembles that of formycin B in some respects, but the base moiety is modified and links to the sugar moiety through a usual carbon–nitrogen glycosyl bond. Figure 1 illustrates the conformation of the molecule. The conjugated system of the base is interrupted at C(7) and the seven-membered ring takes a puckered form. Thus the ten atoms comprising the base are nearly coplanar except for C(7). The C(7) atom deviates from the plane formed by the remaining nine atoms (they are planar within ±0.06 Å) by 0.72 Å in the opposite direction to O(8). The glycosyl torsion angle χ [C(2)–N(3)–C(1')–O(1')], 73°, lies in the range of usual anti conformation which is different from that found in either formycin hydrobromide monohydrate[2] or formycin monohydrate.[6] The torsion angles of the furanose ring are $\tau_0 = -40°$, $\tau_1 = 45°$, $\tau_2 = -33°$, $\tau_3 = 12°$, and $\tau_4 = 17°$, and the conformation of the ring is C(2')-endo–C(1')-exo. Similar conformation has been found in formycin monohydrate.[6] The conformation about the C(4')–C(5') bond is gauche–gauche with $\phi_{OO} = 74°$ and $\phi_{OC} = 45°$, which also differs from that of formycins.[2,6] As a whole, the conformation about the glycosyl bond, furanose ring, and the C(4')–C(5') bond are those which have been most commonly observed in nucleoside and nucleotides.

(6) P. Prusiner, T. Brennan, and M. Sundaralingam, *Biochemistry*, **12**, 1196 (1973).
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Organic Transition States. II. The Methylenecyclopropane Rearrangement. A Two-Step Diradical Pathway with a Secondary Minimum[1]

Sir:

Methylenecyclopane, first as Feist's acid, then as a variety of other derivatives, has been found to undergo facile degenerate rearrangement.[2] This reaction is interesting since in principle appropriate labeling can distinguish between Woodward–Hoffmann allowed,[3] Woodward–Hoffmann forbidden but subjacent al-

(1) Part I: Y. Jean, L. Salem, J. S. Wright, J. A. Horsley, C. Moser, and R. M. Stevens, *Pure Appl. Chem., Suppl.*, **1**, 197 (1971); J. A. Horsley, Y. Jean, C. Moser, L. Salem, R. M. Stevens, and J. S. Wright, *J. Amer. Chem. Soc.*, **94**, 279 (1972); Y. Jean, These d'Etat, Université de Paris-Sud, Centre d'Orsay, 1973.
(2) (a) E. F. Ullmann, *J. Amer. Chem. Soc.*, **82**, 505 (1960); (b) W. v. E. Doering and L. Birladeanu, *Tetrahedron*, **29**, 449 (1973); (c) J. J. Gajewski, *J. Amer. Chem. Soc.*, **93**, 4450 (1971); (d) J. C. Gilbert and D. P. Higley, *Tetrahedron Lett.*, 2075 (1973).
(3) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).