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## Nucleosides, Nucleotides and Nucleic Acids

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### 2'-Deoxycoformycin: Biosynthesis and Enzymatic Conversion of 8-Keto-Deoxycoformycin to 2'-Deoxycoformycin by Streptomyces Antibioticus

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2'-DEOXYCOFORMYCIN: BIOSYNTHESIS AND ENZYMATIC CONVERSION OF 8-KETO-DEOXYCOFORMYCIN TO 2'-DEOXYCOFORMYCIN BY STREPTOMYCES ANTIBIOTICUS

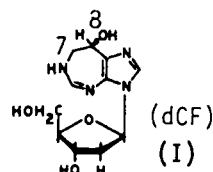
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Studies on the biosynthesis of the N-nucleoside antibiotics have established that the purine and pyrimidine nucleosides/nucleotides serve as the carbon and nitrogen skeleton, whereas with the C-nucleoside antibiotics, the C-N precursor for the aglycon is either acetate or glutamate<sup>1</sup>. With the pyrrolopyrimidine nucleoside antibiotics (toyocamycin, tubercidin, and sangivamycin), either two or three carbons of the N-ribose/ribotide of GTP contribute to carbons 5 and 6 of the pyrrole ring and the cyano or carboxamide group<sup>2</sup>. With the naturally occurring nucleoside antibiotic containing the 1,3-diazepine seven-membered ring, 2'-deoxycoformycin (dCF)(I), the precursor is not immediately obvious.

Initial studies from this laboratory reported that adenosine contributed ten of the eleven carbons in the biosynthesis of dCF<sup>3</sup>.

This communication presents data which show the biosynthetic origin of the -CH<sub>2</sub>- (i.e., carbon-7) of dCF. Two pathways were con-



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sidered for the insertion of the one-carbon unit between N-1 and C-6 of the purine ring of adenosine. One pathway proposed that serine contributed carbon-3 to the one-carbon pool via tetrahydrofolate. The second pathway proposed that carbon-1 of D-ribose was the one-carbon donor. <sup>13</sup>C-NMR analyses of dCF isolated from cultures of Streptomyces antibioticus to which either [3-<sup>13</sup>C]serine or [1-<sup>13</sup>C]D-ribose was added revealed that carbon-7 of dCF was enriched with <sup>13</sup>C from D-ribose, but not from serine. A biosynthetic mechanism for the

utilization of carbon-1 of D-ribose would involve conversion to PRPP which is then covalently linked at N-1 of the adenine ring (presumably ATP). This mechanism is similar to the biosynthesis of histidine with the exception that only carbon-1 of D-ribose is utilized by S. antibioticus. One of the postulated intermediates in the biosynthesis of dCF, 8-ketodeoxycoformycin, is converted to dCF by the enzyme, 8-ketodCF dehydrogenase. This enzyme has been isolated and partially purified from cell extracts of S. antibioticus. The enzyme requires NADPH and removes only the proS hydrogen. The enzymatic reduction of 8-ketodCF proceeds such that the 8-hydroxyl of dCF has the R configuration. Supported by NIH research grant AI22296.

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