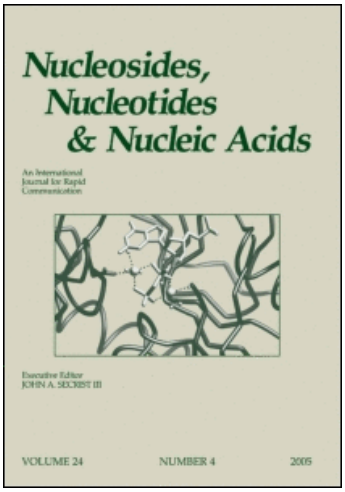


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

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

Jeffery C. Hanvey[a]; Elma Smal[a]; Robert J. Suhadolnik[a]; David C. Baker[a]
[a] Department of Biochemistry, Temple University School of Medicine, Philadelphia, PA

To cite this Article Hanvey, Jeffery C. , Smal, Elma , Suhadolnik, Robert J. and Baker, David C.(1987) '2'-Deoxycoformycin: Biosynthesis and Enzymatic Conversion of 8-Keto-Deoxycoformycin to 2'-Deoxycoformycin by Streptomyces Antibioticus', Nucleosides, Nucleotides and Nucleic Acids, 6: 1, 495 — 496
To link to this Article: DOI: 10.1080/07328318708056267
URL: http://dx.doi.org/10.1080/07328318708056267

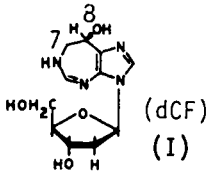
NUCLEOSIDES & NUCLEOTIDES, 6(1&2), 495-496 (1987)

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

Jeffery C. Hanvey, Elma Smal, Robert J. Suhadolnik*and David C. Baker

Department of Biochemistry, Temple University School of Medicine, Philadelphia, PA 19140; Department of Chemistry, University of Alabama, University, AL 35486

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 antibioticus, the C-N precursor for the aglycon is either acetate or glutamate[1]. With the pyrrolopyrimidine nucleoside antibiotics (toyocamycin, tubercidin, and sangivamycin), either two or three carbons of the N-riboside/ribotide of GTP contribute to carbons 5 and 6 of the pyrrole ring and the cyano or carboxamide group[2]. With the naturally occurring nucleoside antibiotic containing the 1,3-diazepine seven-membered ring, 2'-deoxycoformycin (dCF)(I), the precursor is not immediately obvious.



(dCF)
(I)
2'-DEOXYCOFORMYCIN

Initial studies from this laboratory reported that adenosine contributed ten of the eleven carbons in the biosynthesis of dCF[3]. This communication presents data which show the biosynthetic origin of the $-CH_2-$ (i.e., carbon-7) of dCF. Two pathways were considered 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. ^{13}C-NMR analyses of dCF isolated from cultures of Streptomyces antibioticus to which either [3-^{13}C]serine or [1-^{13}C]D-ribose was added revealed that carbon-7 of dCF was enriched with ^{13}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.

REFERENCES

1. Suhadolnik, R.J. (1979) Nucleosides as Biological Probes, John Wiley & Sons, Inc., New York.
2. Suhadolnik, R.J., & Uematsu, T. (1970) J. Biol. Chem. 245, 4365-4371.
3. Hanvey, J.C., Hardman, J.K., Suhadolnik, R.J., & Baker, D.C. (1984) Biochemistry 23, 904-907.