United States Patent [19]

Wong et al.

[11] **Patent Number: 5,075,225**

[45] **Date of Patent: Dec. 24, 1991**

[54] **PROCESS FOR THE ENZYMATIC SYNTHESIS OF NUCLEOSIDES**

[75] Inventors: **Chi-Huey Wong; William J. Hennen,** both of College Station, Tex.

[73] Assignee: **The Texas A&M University System,** College Station, Tex.

[21] Appl. No.: **334,699**

[22] Filed: **Apr. 6, 1989**

[51] **Int. Cl.**[5] **C12P 19/38;** C12P 19/40; C12P 19/30; C12N 9/12

[52] **U.S. Cl.** **435/87;** 435/88; 435/89; 435/194

[58] **Field of Search** 435/87, 88, 194, 89

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,347,315	8/1982	Krenitsky et al.	435/87
4,381,344	4/1983	Rideout et al.	435/87
4,594,320	6/1986	Fujishima	435/89
4,594,321	6/1986	Fujishima	435/88

OTHER PUBLICATIONS

Krenitsky, et al., J. Med. Chem., 1986, vol. 29, pp. 138–143.
Krenitsky, et al., Carbohydrate Research, 1981, vol. 97, pp. 139–146.
Krenitsky et al., Biochemistry, 1981, vol. 20, pp. 3615–3621.
Krenitsky, et al., J. Med. Chem., 1982, vol. 25, pp. 32–35.
Rideout, et al., J. Med. Chem., 1982, vol. 25, pp. 1040–1044.
Utagawa, et al., Agric. Biol. Chem., 1986, vol. 50(1), pp. 121–126.
Jones, et al., J. Am. Chem., 1963, vol. 85, pp. 193–201.
Kulikowska, et al., Biochem. Biophys. Acta., 1986, vol. 874, pp. 355–363.
Stoeckler, et al., Fed. Proc. Fed. Am. Soc. Exp. Biol., 1986, vol. 45, pp. 2773–2778.
Witkowski et al., J. Med. Chem., 1972, vol. 15 (11), pp. 1150–1154.
Rousseau, et al., Biochemistry, 1966, vol. 5, pp. 756–760.
Stoltzfus, et al., J. Virol., 1981, vol. 38, pp. 173–183.
Oivanen, et al., J. Tet., 1987, vol. 43, pp. 1133–1140.
Ryba, et al., J. Chromatography, 1981, vol. 211, pp. 337–346.
Tener, et al., J. Chem. Soc., 1957, vol. 79, pp. 441–443.
Enzyme Nomenclature, Academic Press, 1984.
Hupe, et al., Ann. Reports in Medicinal Chemistry, Bailey, Ed., Academic Press, New York, 1986, vol. 21, Ch. 23.
Mansuri, et al., Ann. Reports in Medicinal Chemistry, Bailey, Ed., Academic Press, New York, 1987, vol. 22, Ch. 15.
Mansuri, et al., Ann. Reports in Medicinal Chemistry, Allen, Ed., Academic Press, New York, 1988, vol. 23, Ch. 17.
Ezzell, Nature, 1987, vol. 326, p. 430.
DeClerg, Trends in Pharmacol. Sci., 1987, vol. 8, pp. 339–345.
Lerch, Antiviral Res., 1987, vol. 7, pp. 257–270.
Vanek, et al., J. Coll. Czech. Chem. Commun., 1984, vol. 49, pp. 2492–2495.
Sidewall, et al., Science, 1972, vol. 177, pp. 705–706.
Utagawa, et al., Agric. Biol. Chem., 1985, vol. 49, p. 3229.
Nucleoside Analogues; Chemistry, Biology and Medicinal Applications, Walker, et al., Eds., NATO Advanced Study Institutes Seires, Plenum, New York, 1979, vol. 26.
Suhadolnik, Nucleoside Antibiotics, J. Wiley, New York, 1970.
Suhadolnik, Nucleosides as Biological Probes, J. Wiley, New York, 1979.
Robbins, et al., Can. J. Chem., 1973, vol. 51, p. 3161.
Mizuno, et al., Chem. Pharm. Bull., 1964, vol. 12, p. 866.

Primary Examiner—Herbert J. Lilling
Attorney, Agent, or Firm—Arnold, White & Durkee

[57] **ABSTRACT**

A process for synthesizing nucleosides is disclosed. The process includes the reaction of an alkylated nucleoside (such as 7-methylguanosine or 7-methylinosine) with a heterocyclic base (such as adenine, 3-deazaadenine or 1,2,4-triazole-3-carboxamide) in the presence of a nucleoside-forming enzyme to form a nucleoside that includes a glycosyl component, donate by the alkylated nucleoside, bonded to the heterocyclic base.

19 Claims, 3 Drawing Sheets