US006071906A

United States Patent [19]

Hansen, Jr. et al.

[11] **Patent Number: 6,071,906**

[45] **Date of Patent: Jun. 6, 2000**

[54] **IMIDINO PIPERIDINE DERIVATIVES USEFUL AS NITRIC OXIDE SYNTHASE INHIBITORS**

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[21] Appl. No.: **09/123,822**

[22] Filed: **Jul. 28, 1998**

Related U.S. Application Data

[60] Division of application No. 08/448,473, Jun. 6, 1995, Pat. No. 5,854,234, which is a continuation-in-part of application No. 08/141,168, Oct. 21, 1993.

[51] **Int. Cl.**[7] **C07D 239/02**; C07D 279/04; C07D 413/02

[52] **U.S. Cl.** **514/227.2**; 546/242; 546/244

[58] **Field of Search** 514/211, 212, 514/218, 227.2, 228.8, 256, 349, 352; 540/488, 492, 527, 544, 553, 596, 605, 606; 544/53, 54, 55, 88, 96, 97, 330, 331, 332; 546/242, 244

[56] **References Cited**

U.S. PATENT DOCUMENTS

2,049,582	8/1936	Ziegler	260/127
3,109,848	11/1963	Bortnick et al.	260/313
3,121,093	2/1964	Bortnick et al.	260/313
3,132,151	5/1964	Bortnick et al.	260/313
3,501,487	3/1970	Poos	260/296
3,563,994	2/1971	Wollweber et al.	260/293
3,694,432	9/1972	Hershenson	260/239
3,725,435	4/1973	Poos	260/326.5
3,816,457	6/1974	Grisar et al.	260/329
4,046,909	9/1977	Rasmussen et al.	424/274
4,061,746	12/1977	Blohm et al.	424/244
4,126,613	11/1978	Grisar et al.	260/239
4,126,621	11/1978	Grisar et al.	260/329
4,153,235	5/1979	Grisar et al.	260/239
4,443,468	4/1984	Maillard et al.	424/274
4,523,020	6/1985	Moormann et al.	548/353
4,525,476	6/1985	Butler et al.	514/326
4,533,739	8/1985	Pitzele et al.	548/554
4,556,674	12/1985	Maillard et al.	514/426
4,579,951	4/1986	Pitzele et al.	546/223
4,699,918	10/1987	Maillard et al.	514/426

(List continued on next page.)

FOREIGN PATENT DOCUMENTS

191584	12/1981	Czechoslovakia .
0 042 279	12/1981	European Pat. Off. .
0 309 422	3/1989	European Pat. Off. .
0370320	5/1990	European Pat. Off. .
0446699	9/1991	European Pat. Off. .
0462948	12/1991	European Pat. Off. .
0676196	10/1995	European Pat. Off. .
0713704	5/1996	European Pat. Off. .
0713876	5/1996	European Pat. Off. .
0717040	6/1996	European Pat. Off. .
1367598	9/1974	United Kingdom .
2240041	7/1991	United Kingdom .
91/04023	4/1991	WIPO .
91/04024	4/1991	WIPO .
93/13055	7/1993	WIPO .
93/16721	9/1993	WIPO .
93/24126	12/1993	WIPO .
94/12163	6/1994	WIPO .
94/12165	6/1994	WIPO .
94/14780	7/1994	WIPO .
94/16729	8/1994	WIPO .
95/05363	2/1995	WIPO .
95/11231	4/1995	WIPO .
95/31987	11/1995	WIPO .
95/32203	11/1995	WIPO .
96/14842	5/1996	WIPO .
96/14844	5/1996	WIPO .
96/18616	6/1996	WIPO .
97/16430	5/1997	WIPO .

OTHER PUBLICATIONS

Kato et al., Studies on Ketene and Its Derivatives. CIII. Synthesis of Fused 4–Pyrimidones and Their Photoreactions, Heterocycles, vol. 15, No. 1, pp. 399–402, Jan. 1981.

Tatsuta et al., The Structure of Chymostatin, A Chymotrypsin Inhibitor, The Journal of Antibiotics, vol. 26, No. 11, pp. 625–646, Nov. 1973.

Kato et al., Reaction of Triethyloxonium Fluoroborate with Acid Amide. I. Formation of Cyclic Amidine and Tetrahydropyrimidine, Chemical & Pharmaceutical Bulletin, vol. 20, No. 5, pp. 901–904, May 1972.

Kunzi et al., Ammonolysis of Nitroarginine and Nitroarginine–Conatining Peptides; Some Side Reaction, Helvetica Chimica Acta, vol. 57, No. 3, pp. 566–572, 1974.

Culvenor, C.C.J. et al, *Aust. J. Chem.,* 24 (1971)371–375 (Beilstein Registry ID Only).

Caujolle, R. et al, *Eur. J. Med. Chem. Chim. Ther.,* 28(1) (1993) 29–35 (Beilstein Registry ID Only).

Kato et al, *Chem. Pharm. Bull.,* 20 (1972) 901 (Beilstein Registry ID Only).

Anderson, Wayne K. et al, *Synth. Commun.,* 19(13–14) (1989) 2237–2242 (Beilstein Registry ID Only).

(List continued on next page.)

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[57] **ABSTRACT**

The current invention discloses useful pharmaceutical compositions containing amidino derivative useful as nitric oxide synthase inhibitors.

20 Claims, 1 Drawing Sheet