

## [54] BIOPTERIN ANALOGS

[75] Inventors: Charles A. Nichol; John F. Reinhard, Jr., both of Durham; Gary K. Smith, Raleigh; Eric C. Bigham, Chapel Hill, all of N.C.

[73] Assignee: Burroughs Wellcome Co., Research Triangle Park, N.C.

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[58] Field of Search ..... 514/249; 544/258

## [56] References Cited

## U.S. PATENT DOCUMENTS

3,959,278 5/1976 Wood et al. .... 544/258  
4,073,786 2/1978 Wood et al. .... 544/258  
4,540,783 9/1985 Viscontini ..... 544/258  
4,560,685 12/1985 Roch et al. .... 514/249

## FOREIGN PATENT DOCUMENTS

79574 5/1983 European Pat. Off. .  
WO84/04040 10/1984 PCT Int'l Appl. .  
1293541 10/1972 United Kingdom .

## OTHER PUBLICATIONS

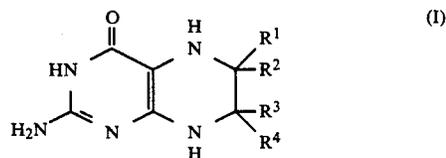
Kapatos et al., *Science*, 212, May 1981, pp. 955-956.  
Armarego et al., *Aust. J. Chem.*, 34 (1981), pp. 1921-1933.  
Armarego et al., *J. Chem. Res.*, pp. 3911-3914, (1980).  
Nagatsu, *TIPS*, Oct., pp. 276-279, (1981).  
Ayling et al., *Biochem. and Clin. Asp. of Pteridines*, vol. 2, (1983), pp. 147-163.  
Bailey et al., *Biochemistry*, vol. 22, pp. 1790-1798 (1983).

Primary Examiner—Robert Gerstl

Assistant Examiner—Stephen M. Kapner  
Attorney, Agent, or Firm—Donald Brown

## [57] ABSTRACT

The compounds of formula (I)



wherein R<sup>1</sup> is hydrogen, lower alkyl of 1-4 carbons, lower alkenyl of 2-4 carbons, —B—X—R<sup>5</sup>), or —B—Z—B—X—R<sup>5</sup>—<sub>n</sub>; n=0 when X is halogen or n=1 when X is —O—, —NR<sup>6</sup>— (where R<sup>6</sup> is hydrogen or lower alkyl of 1-4 carbons) or —S(O)<sub>q</sub>— where q=0 to 2); B is lower alkanyl (straight or branched) of 1-5 carbons; R<sup>5</sup> is hydrogen, aralkyl of 7 to 12 carbons or alkyl of 1-10 carbons; Z is —O—, NR<sup>6</sup>—, or —S(O)<sub>q</sub>—; R<sup>2</sup> is hydrogen or lower alkyl of 1-4 carbons or lower alkenyl of 2-4 carbons or either R<sup>1</sup> and R<sup>2</sup> together with the carbon atom in the pteridine ring structures to which they are attached, form a spirocycloalkyl ring system having 3 to 7 carbon atoms; R<sup>3</sup> and R<sup>4</sup> are hydrogen or methyl; R<sup>2</sup> and R<sup>3</sup>, together with the carbon atoms in the pteridine ring structure to which they are attached, form a cycloalkyl ring system having 5 to 7 carbon atoms; provided that at least one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> is hydrogen, and further provided that one of R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup>, R<sup>4</sup> represents gem disubstitution; have been found to selectively cofactor the biological conversion of tyrosine to dopamine, and are useful in the treatment of diseases resulting from a deficiency of dopamine in the brain such as Parkinson's disease. A further aspect of this invention comprises novel compounds of formula (I) defined above with the proviso that when both R<sup>3</sup> and R<sup>4</sup> are methyl neither R<sup>1</sup> and R<sup>2</sup> may be methyl, and R<sup>1</sup> and R<sup>2</sup> may not both be hydrogen, or a pharmaceutically acceptable salt thereof.

2 Claims, No Drawings