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# United States Patent [19]

Bailey et al.

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[54] **INTERMEDIATES AND A PROCESS FOR SYNTHESIS OF TETRAHYDROPTERIDINE C6-STEREOISOMERS, INCLUDING (6S)-TETRAHYDROFOLATE AND N5-FORMYL-(6S)-TETRAHYDROFOLATE**

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[21] Appl. No.: **981,778**

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**Related U.S. Application Data**

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[51] **Int. Cl.**[5] ..... **C07D 475/04**

[52] **U.S. Cl.** ..... **544/258;** 544/258; 544/298; 544/323

[58] **Field of Search** ..... 544/323, 320, 257, 258, 544/259, 260, 261, 298; A61K 31/505

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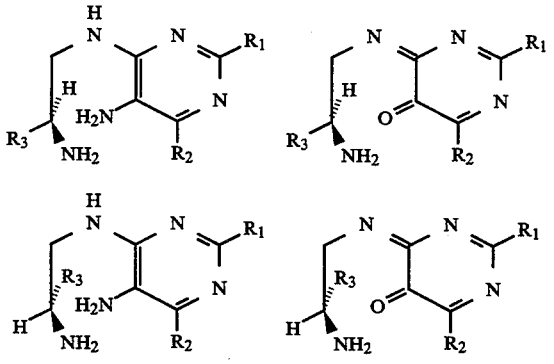
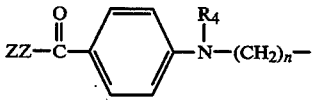
[57] **ABSTRACT**

Intermediates and a process for the synthesis of 6-monosubstituted tetrahydropteridine C6-stereoisomers, including (6S)-tetrahydrofolic acid. The intermediates are shown in their two enantiomeric forms as follows:



wherein $R_1$ and $R_2$ are the same or different and represent hydrogen, methyl, hydroxy, amino, alkyl or dialkylamino, alkoxy, benzyloxy, or benzylthio; $R_3$ represents an alkene, alkyne, cycloalkyl, benzyl, alkyl (substituted with hydroxy, acetoxy, benzyloxy, alkoxy, alkylthio, amino, carboxy, oxo, or phosphate), a protected aldehyde, or



wherein n=1 or 2, $R_4$ is hydrogen, formyl, methyl, or propargyl, and ZZ represents an amino acid or amino acid polymer.

**8 Claims, No Drawings**