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[54] 14-HALO-CAMPTOTHECINS

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Related U.S. Application Data


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[58] Field of Search 546/48

References Cited

U.S. PATENT DOCUMENTS
4,578,381 3/1986 Uchida et al. 514/233
4,894,456 1/1990 Wall et al. 546/41
5,162,532 11/1992 Comins et al. 546/48
5,191,082 5/1993 Comins et al. 546/116
5,212,317 5/1993 Comins et al. 546/301
5,243,050 9/1993 Comins et al. 546/116
5,342,947 8/1994 Lackey et al. 546/41

FOREIGN PATENT DOCUMENTS

OTHER PUBLICATIONS
J. A. Bristol et al; Synthetic Approaches to Camptothecin; Abstracts, 23d International Congress of Pure and Applied Chemistry (Boston, Mass. 1971) pp. 67.

A method of making racemic DE ring intermediates for the synthesis of camptothecin and camptothecin analogs employing novel intermediates of Formula (XX) and (XXI):

wherein R₂₀ is loweralkyl, R is loweralkyl, Y is H or halogen, and R₃₁ is loweralkoxy; as precursors to the DE ring intermediate.

The present invention also provides a camptothecin analog of Formula (I-A):

wherein:
Hal is a halogen;
and the remainder of the variables are as defined in the specification.

Additionally, other novel compounds useful in the preparation of the compounds of Formula (I-A) and methods of producing compounds of (I-A) are also provided.

8 Claims, No Drawings