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United States Patent [19]

Comins et al.

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[54] METHODS AND INTERMEDIATES FOR THE ASSYMMETRIC SYNTHESIS OF CAMPTOTHECIN AND CAMPTOTHECIN ANALOGS

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[21] Appl. No.: 900,650

[22] Filed: Jun. 18, 1992

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 632,970, Dec. 20, 1990, Pat. No. 5,162,532.

[51] Int. Cl.[5] C07D 213/64

[52] U.S. Cl. 546/301; 546/302; 546/116

[58] Field of Search 546/301, 302

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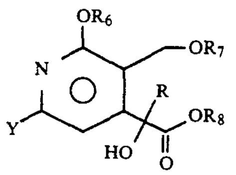
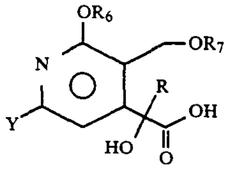
[57] **ABSTRACT**

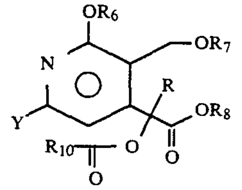
Processes for making compounds of Formulae XIV, XV, and XVII



XIV

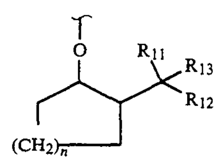


XV



XVII

wherein R_6 is lower alkyl, R_7 is lower alkyl, R is lower alkyl, Y is H, F or Cl, R_8 is a moiety of Formula XVIII



(XVIII)

wherein n is 1, 2, or 3, R_{11} is C_1–C_4 alkyl and R_{12} is the same as R_{11}, or R_{11} and R_{12} together form cyclopentane or cyclohexane, and R_{13} is:

(a) phenyl substituted 1 to 5 times with C_3–C_7 secondary alkyl or C_4–C_7 tertiary alkyl, or

(b) selected from the group consisting of naphthyl, anthryl, and phenanthryl optionally substituted 1 to 5 times with C_3–C_7 secondary alkyl or C_4–C_7 tertiary alkyl groups,

R_{10} is C_6–C_{10} alkyl, aryl or alkyl aryl,

and Y is H, F or Cl,

are disclosed. These processes can be used to make optically enhanced and optically pure forms of the compounds, which are useful in the making of camptothecin and analogs thereof.

51 Claims, No Drawings