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[54] **METHOD OF MAKING INTERMEDIATES FOR CAMPTOTHECIN AND ITS ANALOGS**

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Related U.S. Application Data

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[51] **Int. Cl.**[6] **C07D 491/052**

[52] **U.S. Cl.** **546/116**

[58] **Field of Search** 546/116

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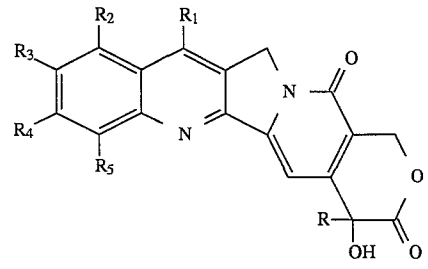
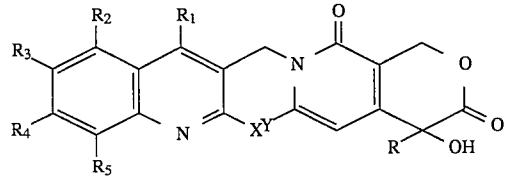
[57] **ABSTRACT**

Disclosed are new methods of making camptothecin and camptothecin analogs defined by Formula I:



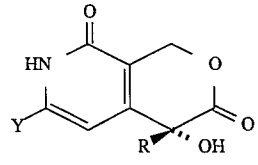
I

wherein R is loweralkyl; R_1 is H, loweralkyl, loweralkoxy, or halo; and R_2, R_3, R_4 and R_5 are each independently H, amino, hydroxy, loweralkyl, loweralkoxy, loweralkylthiol, di(loweralkyl)amino, cyano, methylenedioxy, formyl, nitro, halo, trifluoromethyl, aminomethyl, azido, amido, hydrazino, or any of the twenty standard amino acids bonded to the A ring via the amino-nitrogen atom. The methods comprise cyclizing a compound of Formula IV:



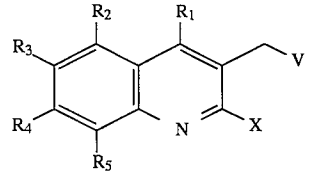
IV

wherein X is Br or I, and Y is H, by an Aryl-to-Aryl free radical coupling reaction to yield a compound of Formula I. Compounds of Formula IV are made by alkylating a compound of Formula III:



III

wherein R is loweralkyl and Y is H with a compound of Formula II-x:



II-x

wherein X is a Br or I and V is hydroxy, by a Mitsunobu reaction to yield the compound of Formula IV.

7 Claims, No Drawings