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Antimitotic Epothilone Analogues as Anticancer Agents

Microtubule-stabilizing agents accelerate the polymerization of tubulin to microtubules and stabilize them, thus inhibiting their depolymerization, an essential process during cell division. The clinically used anticancer drug paclitaxel (taxol) exerts its cytotoxic activity by a mechanism invoking the stabilization of microtubules. However, the susceptibility of taxol to multiple drug resistance has stimulated an extensive research for molecules with a paclitaxel-like mechanism of action. The most extensively investigated of the new molecular entities discovered are the epothilones, a class of macrolide natural products initially isolated from a soil bacterium. Some epothilones exhibit more potent anticancer activity than paclitaxel and have favorable attributes that may improve their pharmacological profile. Extensive studies on structure-activity relationship of epothilones have been reported and a few epothilone analogues are in various stages of clinical development. Given the interest in the therapeutic utility of epothilones, it is desirable to investigate additional analogues and to develop methodologies capable of providing significant quantities of epothilones for clinical trials and for large-scale preparation. Therefore, a method of synthesizing epothilone analogues has been developed.

The University of Toledo is seeking a company interested in utilizing this method of synthesizing epothilone analogues as anticancer agents.

Applications:

1. Synthesis of a new classes of epothilone analogues
2. Providing significant quantities of epothilone analogues

Advantages:

1. Ability to synthesize new classes of epothilone analogues with selective activity by altering the epothilone structure
2. Ability to easily synthesize conformationally restrained and open-chain epothilones that will be attractive as drug candidates
3. One synthesized analogue shows selective activity against CNS (SNB-75) and ovarian cancer (OVCAR-4) cell lines
4. Ability to easily provide significant quantities of epothilones for clinical trials and large-scale preparation

This invention is patent pending

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