[PD1-8] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Design and Synthesis of N-Aryl 8,9-Dihydro-7H-isoindolo[5,6-g]quinoxaline-7,9-dione Derivatives as Potential Antitumor Agent

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We have previously reported the synthesis and cytotoxic activities of a series of azaanthraquinone derivatives using doxorubicin as a lead compound. Doxorubicin is known to intercalate into DNA and to inhibit topoisomerase II activity. But in the case of quinone compounds like Dox, its use is limited because of systemic toxicities, primarily cardiotoxicity and myelosuppression. In this study, we discuss the synthesis of isoindolobenzoquinoxaline derivatives. The quinone group of the azaanthraquinone derivatives were removed in the target compounds. The removal of the quinone group was intended to lessen the cardiotoxicity of the doxorubicin. The target compounds were designed based on the structural features of acridine-4-carboxamide DACA and amonafide. DACA has a neutral chromophore and acridine moiety and poisons both topoisomerases I and II with DNA intercalating activity. In order to delineate the SAR of isoindolobenzoquinoxaline derivatives, various aryl substituents were introduced to the nitrogen of the target compounds. The synthesis of the target compounds used Diels-Alder rout as a key step.

[PD1-9] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

AHL inhibition of Beckerelide and Fimbrolide

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Quorum sensing, a gene expression in response to population density, is regulated by chemical signals, most of which are acylated homoserine lactones (AHLs). The AHL derivatives have been reported to regulate bioluminescence, virulence factors and / or swarming motility in bacteria. It is hypothesized that higher organisms may have evolved specific means to interfere with bacterial communication as exemplified in the AHL-antagonistic activity of halogenated furanones isolated from the Australian macroalga Delisea pulchra. In order to explore the structure-activity relationship of these furanones, analogues were synthesized as described by Manny et. al. while the AHL inhibition activity was tested in a convenient colorimetric liquid culture assay system using the AHL-responsive recombinant Agrobacterium tumefaciens strain. Among the furanone analogues tested, (5Z)-4-bromo-5-(bromoethylene)-3-butyl-2(5H)-furanone, a fimbrolide analogue showed moderate AHL-antagonistic activity while 3-butyl-4-bromo-5-dibromomethyl-5-hydroxy-2(5H)-furanone, a beckerelide showed a more potent AHL-antagonistic activity.

[PD1-10] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Detection, Identification and Characterization of In vitro GSH Metabolites Formed by 1- and 2-Bromopropane

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1- and 2-Bromopropane were reported as the causative agents for reproductive toxicity and immunotoxicity. The glutathione (GSH) metabolites resulting from in vitro treatment of 1- and 2-bromopropane were detected, identified and characterized. For the facile identification, expected GSH metabolites formed by 1- and 2-bromopropane were chemically synthesized as reference materials (positive controls) and characterized by ^{1}H-