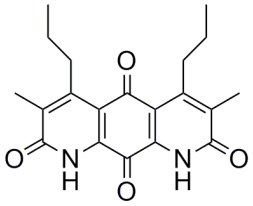
Diazaanthracenetetraones: Synthesis and Cytotoxic Properties

Joseph S. Bair and Paul J. Hergenrother

Diazaanthracenetetraones, such as diazaquinomycin (**1**), CV-65 (**2**), and SCH 538415 (**3**), have been shown to be potent antibacterial, antifungal, and antineoplastic compounds. Postulated mechanisms of cytotoxicity include thymidylate synthase inhibition, disruption of cell signaling pathways, and generation of reactive oxygen species. Definitive biological studies and generation of derivatives with desirable drug-like properties have been hampered by inefficient synthetic strategies.

We present a cross coupling-based approach which allows for rapid and modular construction of this class of molecules. Key to this strategy is a sequence of palladium-mediated borylation, Suzuki coupling and intramolecular aryl amidation which generates the tricyclic core. Initial structure-activity relationships and mode-of-action studies are also reported.



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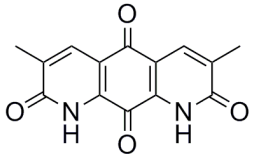

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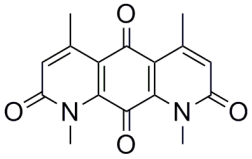

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