Synthesis of new cytotoxic aminoanthraquinone derivatives via nucleophilic substitution reactions

ABSTRACT

Aminoanthraquinones were successfully synthesized via two reaction steps. 1,4-Dihydroxyanthraquinone (1) was first subjected to methylation, reduction and acylation to give an excellent yield of anthracene-1,4-dione (3), 1,4-dimethoxyanthracene-9,10-dione (5) and 9,10-dioxo-9,10-dihydroanthracene-1,4-diyl diacetate (7). Treatment of 1, 3, 5 and 7 with BuNH2 in the presence of PhI(OAc)2 as catalyst produced seven aminoanthraquinone derivatives 1a, b, 3a, and 5a–d. Amination of 3 and 5 afforded three new aminoanthraquinones, namely 2-(butylamino)anthracene-1,4-dione (3a), 2-(butylamino)anthracene-9,10-dione (5a) and 2,3-(dibutylamino)anthracene-9,10-dione (5b). All newly synthesised aminoanthraquinones were examined for their cytotoxic activity against MCF-7 (estrogen receptor positive human breast) and Hep-G2 (human hepatocellular liver carcinoma) cancer cells using MTT assay. Aminoanthraquinones 3a, 5a and 5b exhibited strong cytotoxicity towards both cancer cell lines (IC50 1.1–13.0 µg/mL).

Keyword: Acylation; Amination; Aminoanthraquinone; Cytotoxic; Hep-G2; MCF-7; Mechanism; Methylation; Reduction; Substitution.