Synthesis and Cytotoxicity of 9-Alkoxy-1,5-Dichloroanthracene Derivatives in Murine and Human Cultured Tumor Cells

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摘要

Abstract

9-Alkoxy-1,5-dichloroanthracenes were successfully prepared. Their cytotoxicity was evaluated in vitro on rat glioma C6 cell lines and human hepatoma G2 cell lines, respectively. Alkylation of 1,5-dichloro-9(10H)-anthracenone with either the appropriate alcohols or alkyl chlorides in the presence of sulfuric acid or sodium hydride, respectively, furnished this structural class of anthracenes. Contrary to mitoxantrone, cytotoxic properties were observed as documented by the reactivity of the novel compounds and potent in vitro activity against C6 cells and hep G2 cells over a wide range of structural variants. Among these compounds, 5c, 5h, 5l and 5n are potent cytotoxins. They inhibit C6 cell growth in culture, indicated by using 2,3-bis(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide sodium salt (XTT) colorimetric assay. By using this assay it was also shown that 5c, 5d and 5l possess potent cytotoxicity on hep G2 cells. The most active compound displaying in vitro cytotoxicity was the9-butoxy derivative 5h with IC50 values 0.02 microM against C6 cells, as compared with mitoxantrone with IC50 values 0.07 microM. The most active compound displaying in vitro cytotoxicity against hep G2 cells was 5c with IC50 values1.7 microM (mitoxantrone: 0.8 microM). Structure-activity relationships (SAR) of these compounds with respect to the nature of the alkoxy substitution in the 9 position are discussed for both cell lines.