Abstract

Four series of bifunctional ligands have been synthesized as DNA-binding combilexins. These novel agents contain a triazeno-benzene sulfonamide linker moiety that is attached to an intercalating acridine or acridone chromophore by a functionalized amide or ester residue. In order to obtain these combilexins three series of the anticipated antitumor triazeno-benzene sulfonamide were synthesized. The synthesis and bioscreening of the new antineoplastic compounds are depending on the structural correlation with several reported antineoplastic acridines. 2-Chlorobenzoic acid was reacted with anthranilic acid to give N-(2-carboxyphenyl) anthranilic acid which upon cyclodehydration with sulfuric acid afforded 9-oxo-9. 10-dihydrocicridine-4-carboxylic acid, (acridone-4-carboxylic acid) 8. This latter intermediate has been converted to 9-chloroacridine carbonyl chloride 9 using thionyl chloride. Selective substitution of 9 with derivatives of 4-(piperazine-1-yldiazenyl) benzenesulfonamides 4a-e or derivatives of 4-(2-hydroxyethyl)piperazine-1-yl)diazenyl) benzenesulfomaides 5a-e to yield their 9-chloroacridine-4-carboxamides 10a-e and 9-chloroacridine-4-carboxlic acid esters 13a-e respectively. Those intermediates have been reacted either with different sulfonamides to give derivatives of 4-{4-[4-(4 sulfamoylphenyldiazenyl)piperazine-1-carbonyl]-9-ylamino}benzenesulfonamides 11a-h and derivatives of 2-[(4-(4-sulfamoyl-phenyl)diazenyl)perazine-1-yl]ethyl 9-(4-sulfamoylphenylamino)-9,10-dihydroacridine-4-carboxylates 14a-i respectively or subjected to mild acid hydrolysis to yield derivatives of 4-{4-[(9-oxo-9,10-dihydroacridine-4-carbonyl)piperazine-1-yl]diazenyl}-benzenesulfonamide 12a-e and derivatives of 2-{4-[(4-sulfamoyl-phenyl)diazenyl]piperazine-1-yl}ethyl-9-oxo-9,10-dihydroacridine-4-carboxylate 15a-e respectively. Besides, the synthesis of derivatives of 4-(piperazine-1-yldiazenyl) benzenesulfonamides 4a-e and derivatives of 4-(2-hydroxyethyl)piperazine-1-yl)diazenyl) benzenesulfonamides 5a-e has been achieved via diazotization Of various substituted benzene sulfonamides with sodium nitrite and hydrochloric acid followed by various amines coupling to yield the target triazeno-benzene sulfonamides. Fourteen new compounds were selected for screening their antitumor activity against breast cell line in National Cancer Institute. Six of them were found to be active as antitumor agents, while two were found to be mild active.