Synthesis of Novel 4-Pyridone Annelated-Isatin Derivatives as Potential Antitumor Agents

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Abstract

A new 6-ethyl-1,1-dihydroxy-2,9-dioxo-2,3,6,9-tetrahydro-1H-pyrrolo[3,2-*f*]quinoline-8-carboxylic acid (**7**) has been synthesized *via* the interaction of 6-amino-1-ethyl-4-oxoquinoline-3-carboxylic ester with chloral hydrate and hydroxylamine hydrochloride that gave the corresponding isonitroso-acetamido derivative which, upon treatment with concentrated sulfuric acid, was converted regioselectively into 1,2,9-trioxopyrrolo[3,2-*f*]quinoline-8-carboxylic acid. This novel tricyclic system was reacted with selected substituted oxindoles in acidic medium to deliver the corresponding isoindigo compounds (**9a-f**). Newpyrrolidine-2-spiro-3-(2-oxindole) fused to 4-oxopyridine-3-carboxylate derivatives (**10a-o**) were also synthesized *via* 1,3-dipolar cycloaddition reaction of compound (**7**) utilizing several (α)-amino acids in a methanol/water medium, through formation of the azomethineylides, followed by 1,3-dipolar cyclo addition of the dipolarophile N-methylmaleimide. The newly synthesized compounds were characterized by spectroscopic techniques (^{1}H-NMR,^{13}C-NMR, DEPT, 2D-NMR (COSY, HMQC and HMBC)) experiments, IR and High Resolution Mass Spectrometry (HRMS).