Synthesis of novel psoralen analogues and in vitro antitumor activity

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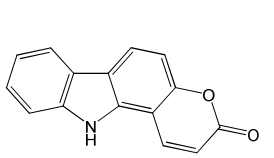
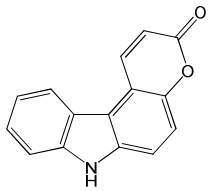
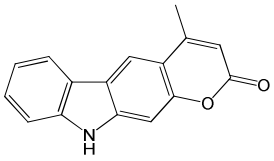
Psoralens are natural products present in several plant families that are extremely toxic to a wide variety of prokaryotic and eukaryotic organisms. They are potentially active in diseases such as vitiligo, psoriasis, and several types of cancer. Following our interest on this type of compounds [1] four new psoralen analogues were prepared, **1a**-**1c** and **1e**. To synthesize **1a** (R = H) the method of Harayama and Ishii was used where the cinnamate was obtained by the Wittig reaction followed by ring closure. Condensation of 1-formyl-2-hydroxycarbazole with diethyl malonate gave **1b** which by basic hydrolysis yielded compound **1c**. Compound **1d** was prepared before.[2] Condensation of the 2-hydroxycarbazole with ethyl acetoacetate gave **1e**. The products were characterized by elemental analysis, ^{1}H and ^{13}C NMR. Moreover, the anti-proliferative effect of compounds **1a**-**1e** on human cancer cell lines (MDA-MB 231, HeLa and TCC-SUP) was evaluated. Results suggest that these psoralen analogues possess a potent cytotoxic effect against the cell lines studied. Computational and molecular docking studies are being carried out.



1a R = H
1b R = COOEt
1c R = COOH



1d



1e

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References

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(2) Francisco, C. S.; Oliveira-Campos, A. M. F.; Rodrigues, L. M. 5th Brazilian Symposium on Medicinal Chemistry, 2010, Ouro Preto, Brazil, Poster PO39.