Synthesis of novel psoralen analogues and their anti-proliferative effect on human cancer cell lines

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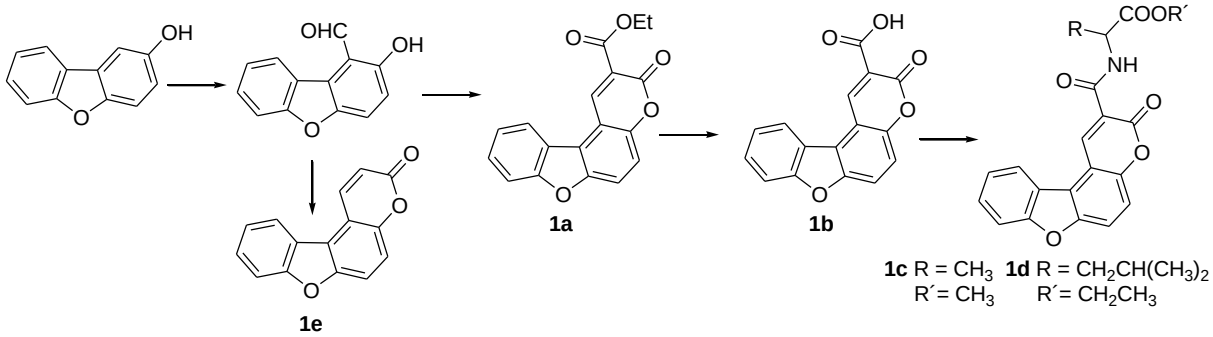
Psoralen derivatives have been used as photosensitizing drugs in the treatment of various skin diseases, blood decontamination and some AIDS-related infections.[1] These compounds were found to be effective in inhibiting the in vitro growth of different human tumor cell lines.[2]

In the present work we describe the synthesis of 3*H*-benzofuro[3,2-*f*]chromen-3-ones **1**. Compound **1a** was prepared from 2-hydroxydibenzofuran by Reimer-Tiemann formylation followed by condensation with diethyl malonate to build the pyranone ring. To synthesize **1e** (R = H) the method of Harayama and Ishii was used where the cinnamate was obtained by the Wittig reaction followed by ring closure. Compound **1b** was obtained by basic hydrolysis of **1a** and was coupled to amino acids to give products **1c** and **1d**. 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-MB231 and HeLa) was evaluated using a commercial MTS assay. Results suggest that the synthesized psoralen analogues possess a potent cytotoxic effect against the cell lines studied.



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References

(1) Oliveira, A. M. A. G. et al. *Chem. & Biodiversity* **2007**, *4*, 980.

(2) Leite, V. C.; Santos, R. F.; Chen, L. C.; Guillo, R. A. *J. Photochem. Photobiol. B: Biol*. **2004**, *76*, 49.