

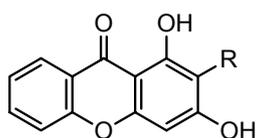
PRENYLATED XANTHONIC DERIVATIVES: SYNTHESIS, STRUCTURE ELUCIDATION AND INHIBITION OF GROWTH OF HUMAN TUMOUR CELL LINES

Raquel Castanheiro ^a, Madalena Pinto ^{a,b*}, Artur Silva ^c, Sara Cravo ^{a,b}, Madalena Pedro ^a,
Rujida Wilairat ^{a,d}, Naïr Nazareth ^a, Maria S. J. Nascimento ^{a,e}

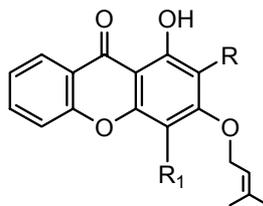
^aCentro de Estudos de Química Orgânica, Fitoquímica e Farmacologia da Universidade do Porto; ^bLaboratório de Química Orgânica; ^c Departamento de Química, Universidade de Aveiro, 3810 Aveiro, Portugal; ^dFaculty of Pharmacy, Chiang Mai University, Thailand; ^eLaboratório de Microbiologia; ^{a,b,e} Faculdade de Farmácia da Universidade do Porto, R. Aníbal Cunha 164, 4050-047 Porto, Portugal

Recently we have investigated the effect of several hydroxy and methoxyxanthenes on the *in vitro* growth of human tumour cell lines [1]. In order to improve the antitumor activity we have synthesized new prenylated derivatives, so in this work we describe the synthesis, structure elucidation and biological activity of nine xanthenes **1-9**. [2-4]. Xanthenes **1** and **2** were used as building blocks for prenylation, being compounds **3** and **4** obtained from **1** and **5**, **6**, **7** and **8** from compound **2**. The cyclic derivative **9** was obtained from the prenylated xanthone **4** [4].

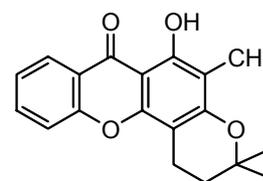
Structures were established by IR, UV, MS and NMR (¹H, ¹³C, HSQC and HMBC). The effects of the compounds on the *in vitro* growth of four human tumour cell lines: MCF-7 (breast), NCI- H460 (non-small cell lung), SF-268 (central nervous system) and UACC-62 (melanoma) were evaluated. Compounds **6**, **7** and **9** were found to be selective and highly potent against the MCF-7 cell line.



1 R=CH₃
2 R=H



3 R=CH₃, R₁=3,3-dimethylallyl
4 R=CH₃, R₁=H
5 R=H, R₁=H
6 R=H, R₁=1,1-dimethylallyl
7 R=H, R₁=3,3-dimethylallyl
8 R=3,3-dimethylallyl, R₁=H



9

[1] M. Pedro, F. Cerqueira, M. E. Sousa, Pinto, *Bioorg. Med. Chem.*, **2002**, *10*, 3725.

[2] P. K. Grover, G. D. Shah and R. C. Shah, *J. Chem. Soc.*, **1995**, 3982.

[3] M. M. Pinto, J. Polónia, *Helv. Chim. Acta*, **1974**, *57* (8), 2613.

[4] G. S. R. Subba Rao and S. Raghavan, *J. Indian Inst. Sci.*, **2001**, *81*, 393.

M. S. J. Nascimento and M.

ACKNOWLEDGEMENTS

FCT (I&D 226/94), FEDER, POCTI and for the PhD grant to Raquel Castanheiro (SFRH/BD/13167/2003) and Madalena Pedro (SFRH/BD/1456/2000).

* madalena@ff.up.pt