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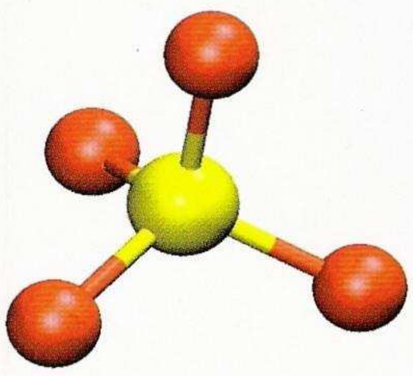
ABSTRACTS



15th European Symposium on Organic Chemistry

8 – 13 July 2007

University College Dublin – Ireland

EDITORS Professor Pat Guiry and Ann Mooney

Polyhydroxy-2,3-diarylxanthones: a total synthesis

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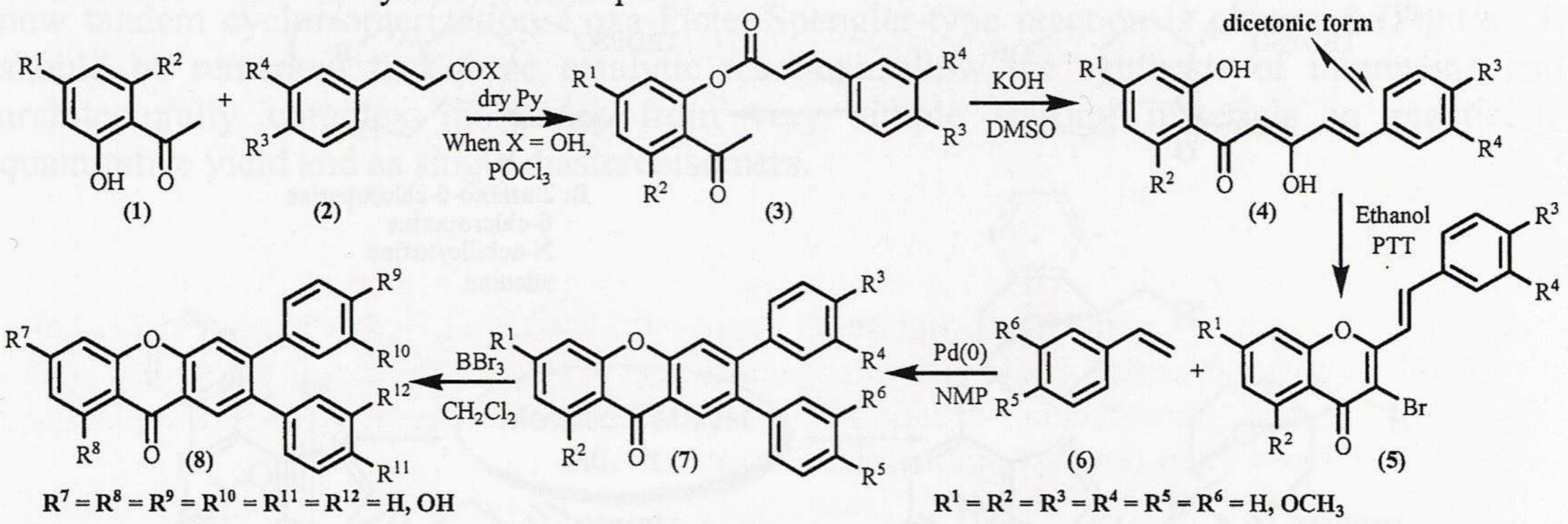
Xanthones are a class of oxygenated heterocyclic compounds and their biological properties are extensively reported in the literature, namely anti-fungal, anti-inflammatory, anti-tumour, as well as antioxidant activities [1,2]. Structure-activity studies on the antioxidant activity of polyphenolic compounds revealed the features for a high antioxidant activity are the presence of hydroxyl groups at certain positions of their skeleton [3]. Taking that in consideration, we started a project aiming the synthesis of polyhydroxy-2,3-diarylxanthones for further evaluation of their antioxidant activity [4].

Various methods are described for the synthesis of xanthones [5], however, the synthesis of derivatives bearing aryl groups are scarce and no natural or synthetic derivatives with a 2,3-diaryl substitution pattern were reported. So, we develop a new route for the synthesis of polyhydroxy-2,3-diarylxanthones, starting with 2'-hydroxyacetophenones **1** and cinnamic acid derivatives **2** (Scheme 1). The Baker-Venkataraman transformation followed by bromination/cyclization with PTT led to the formation of 3-bromo-2-styrylchromones **5**. The Heck reaction of **5** with styrenes **6** gives the polymethoxy-2,3-arylxanthones **7**. The final step consists in the cleavage of protective groups to obtain the desired polyhydroxy-2,3-diarylxanthones **8**. In this communication we will present the synthetic details of all described transformations as well as the structural characterisation by 1D and 2D NMR studies of the synthesised compounds.



Scheme 1

Acknowledgements: Thanks are due to the University of Aveiro, FCT and FEDER for funding the Organic Chemistry Research Unit and the project POCI/QUI/59284/2004. One of us (C.M.M. Santos) is also grateful to PRODEP 5.3 for financial support.

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POLYHYDROXY-2,3-DIARYLXANTHONES: A TOTAL SYNTHESIS

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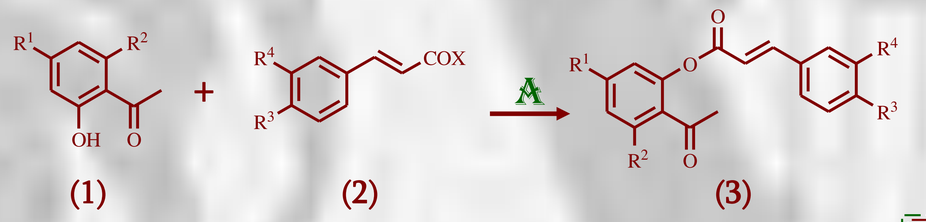
INTRODUCTION

Xanthones are a class of oxygenated heterocyclic compounds and their biological properties are extensively reported in the literature, namely anti-fungal, anti-inflammatory, anti-tumour, as well as antioxidant activities [1,2]. Structure-activity studies on the antioxidant activity of polyphenolic compounds revealed the features for a high antioxidant activity are the presence of hydroxyl groups at certain positions of their skeleton [3].

Taking that in consideration, we started a project aiming the synthesis of polyhydroxy-2,3-diarylxanthones for further assessment of their antioxidant activity [4].

Various methods are described for the synthesis of xanthones [5], however, the synthesis of derivatives bearing aryl groups are scarce and no natural or synthetic derivatives with a 2,3-diaryl substitution pattern were reported. So, we develop a new route for the synthesis of polyhydroxy-2,3-diarylxanthones, starting from 2'-hydroxyacetophenones 1 and cinnamic acid derivatives 2.

GENERAL PROCEDURE



SCHEME I

A: x = Cl, dry Py, r.t., 2h
x = OH, dry Py, $POCl_3$, 60 °C, 2h

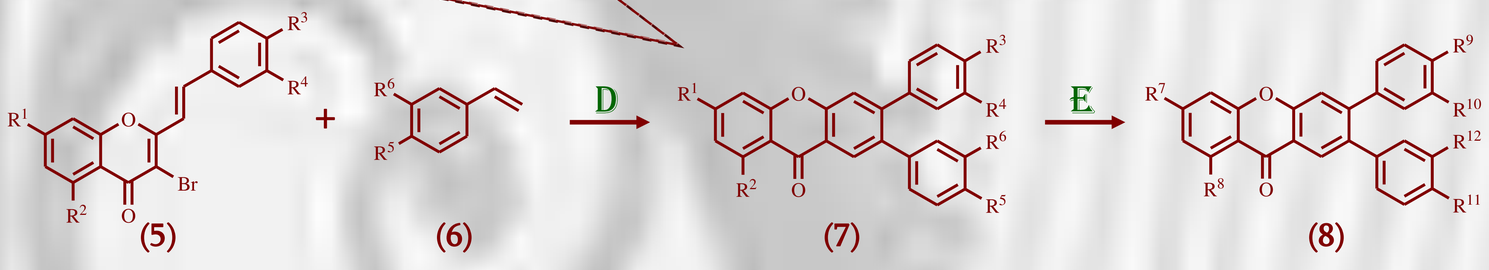
B: DMSO, KOH, r.t., 2h

C: Ethanol, PTT, r.t., 12h

Baker-Venkataraman transformation followed by bromination/cyclization with PTT led to the formation of 3-bromo-2-styrylchromones **5** (Scheme I).

	R^1	R^2	R^3	R^4	Yield 3 (%)	Yield 4 (%)	Yield 5 (%)
a	H	H	H	H	97	82	67
b	H	H	OCH_3	H	52	95	53
c	H	H	OCH_3	OCH_3	70	73	64
d	OCH_3	H	H	H	87	81	97
e	H	OCH_3	H	H	85	93	84
f	OCH_3	OCH_3	H	H	94	80	49

The Heck reaction of **5** with styrenes **6** gives the polymethoxy-2,3-diarylxanthones 7. The final step consists in the cleavage of the protecting groups to obtain the desired polyhydroxy-2,3-diarylxanthones **8** (Scheme II).



D: NMP, 1 equiv. Et_3N, 0.1 equiv. PPh_3, 0.05 equiv. $Pd(PPh_3)_4$

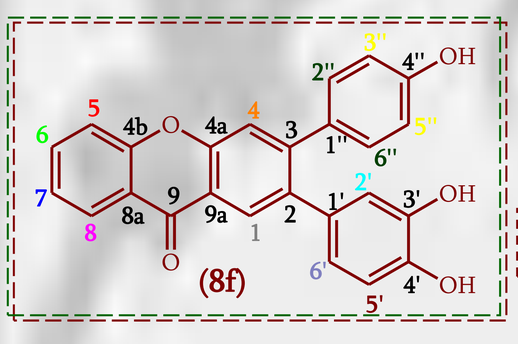
E: CH_2Cl_2, BBr_3, -78°C to r.t., N_2

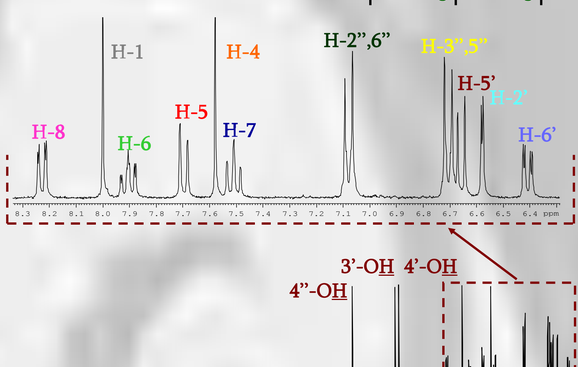
SCHEME II

	R^1	R^2	R^3	R^4	R^5	R^6	Conditions	Yield 7 (%)
a	H	H	H	H	H	H	160 °C, 9h	56
b	H	H	H	H	OCH_3	H	160 °C, 3h	66
c	H	H	H	H	OCH_3	OCH_3	160 °C, 12h	45
d	H	H	OCH_3	H	H	H	reflux, 9h	60
e	H	H	OCH_3	H	OCH_3	H	reflux, 9h	62
f	H	H	OCH_3	H	OCH_3	OCH_3	reflux, 9h	28
g	H	H	OCH_3	OCH_3	H	H	reflux, 9h	62
h	H	H	OCH_3	OCH_3	OCH_3	H	reflux, 9h	80
i	H	H	OCH_3	OCH_3	OCH_3	OCH_3	reflux, 3h	70
j	OCH_3	H	H	H	H	H	reflux, 6h	47
k	H	OCH_3	H	H	H	H	reflux, 9h	58
l	OCH_3	OCH_3	H	H	H	H	reflux, 6h	42

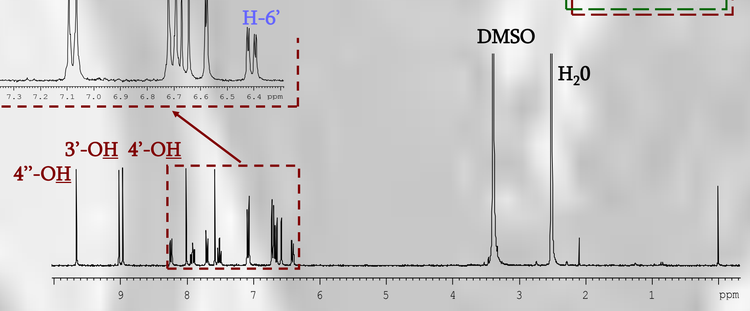
	R^7	R^8	R^9	R^{10}	R^{11}	R^{12}	Time	Yield 8 (%)
b	H	H	H	H	OH	H	1h	72
c	H	H	H	H	OH	OH	2h	80
d	H	H	OH	H	H	H	1h	82
e	H	H	OH	H	OH	H	2h	94
f	H	H	OH	H	OH	OH	3h	80
g	H	H	OH	OH	H	H	2h	80
h	H	H	OH	OH	OH	H	4h	94
i	H	H	OH	OH	OH	OH	4h	70
j	OH	H	H	H	H	H	72h	37
k	H	OH	H	H	H	H	1h	63
l	OH	OH	H	H	H	H	120h	60

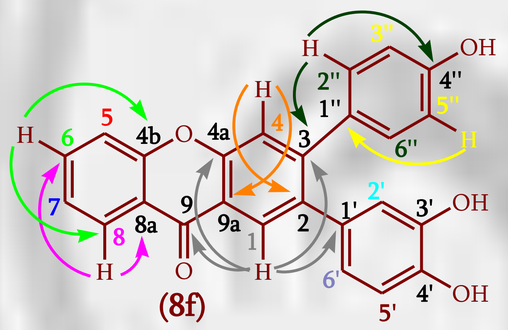
STRUCTURAL ELUCIDATION



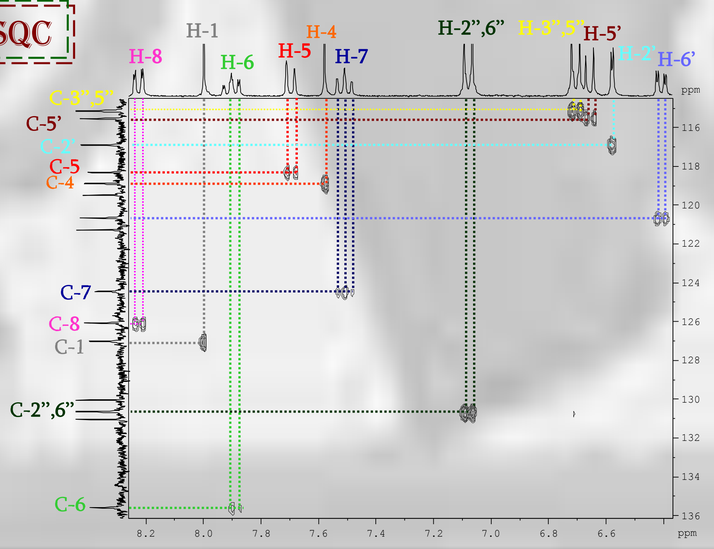


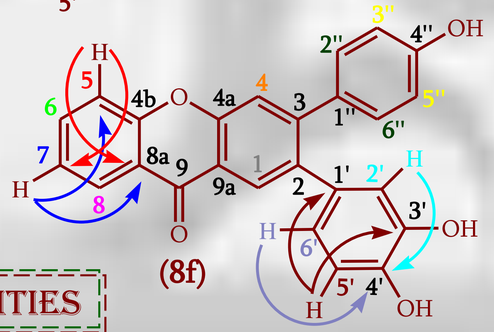
^{1}H NMR





HSQC





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