XVI Encontro Luso-Galego de Química

Aveiro 10 a 12 de Novembro de 2010

Sociedade Portuguesa de Química

Universidade de Aveiro

Asociación de Químicos de Galicia

Colegio Oficial de Químicos de Galicia

CP-35

Recent developments in the synthesis of 1-aryl-9*H*-xanthen-9-ones

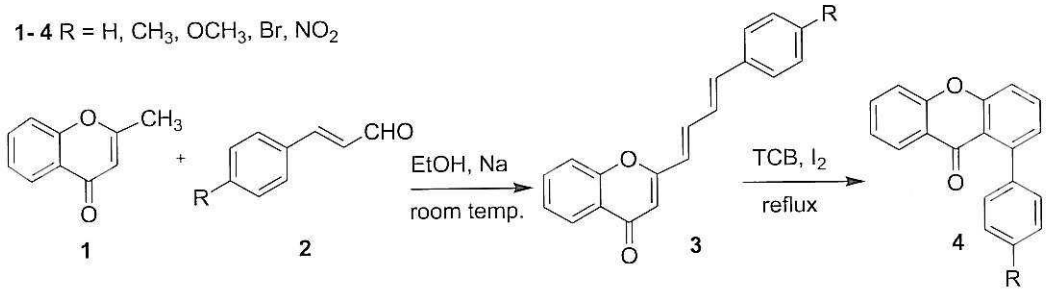
Cátia I. C. Esteves,[a] Clementina M. M. Santos,[a,b] Cristela M. Brito,[a] Artur M. S. Silva[a] and José A. S. Cavaleiro[a]

[a]*Department of Chemistry & QOPNA, University of Aveiro, 3810-193 Aveiro, Portugal*
[b]*Department of Vegetal Production and Technology, Escola Superior Agrária de Bragança, 5301-855 Bragança, Portugal*

Xanthones or 9*H*-xanthen-9-one (dibenzo-γ-pirone) are a class of natural oxygen heterocyclic compounds with a large diversity of functional groups.[1] In recent years, several studies have been reported on both natural and synthetic derivatives of this class of compounds due to their wide range of biological and pharmacological properties (including anti-inflammatory, cancer chemopreventive, antibacterial, antimalarial, radical scavenging, cytotoxicity, inhibition of cyclooxygenase, and prostaglandin E2 activities).[1-3] Some xanthones even surpass the antimicrobial activity of traditional antibiotics.[1]

These promising applications have motivated the search for new derivatives and as a part of an ongoing study we present here the latest developments and improvements on the synthesis of 1-aryl-9*H*-xanthen-9-ones **4a-e**. The methodology involves the condensation of 2-methyl-4*H*-chromen-4-one **1** with cinnamaldehydes **2a-e** (**2a** commercially available and **2b-e** prepared from the corresponding halobenzenes), to afford the (*E,E*)-2-(4-arylbuta-1,3-dien-1-yl)-4*H*-chromen-4-ones **3a-e**.[4] The final step consists in the electrocyclization and oxidation reactions giving rise to the desired xanthones **4a-e**. It was performed by refluxing chromones **3a-e** in trichlorobenzene with a catalytic amount of iodine (Scheme 1).

Details on the synthesis and structural characterization of compounds **3** and **4** will be presented and discussed.



Scheme 1

Acknowledgments
Thanks are due to University of Aveiro, FCT and FEDER for funding the Organic Chemistry Research Unit. One of us (C. I. C. Esteves) is also grateful to FCT for her fellowship (SFRH/BI/51098/2010).

References

(1) Franklin G., Conceição L. F. R., Kombrink E., Dias A. C. P. *Phytochemistry* **2009**, *70*, 60.
(2) Ngoupayo J., Tabopda T. K., Ali M. S., *Bioorg. Med. Chem.* **2009**, *17*, 5688.
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(4) The results reported here are an improvement of those already reported by Brito C. M., Master Thesis, Universidade de Aveiro, **2009**; Brito C. M., Silva A. M. S., Cavaleiro J. A. S., "New routes to the synthesis of 1-aryl-9*H*-xanthen-9-ones", 2PYChem, Universidade de Aveiro, **2010**.

Encontro Luso-Galego de Química
10 - 12 November 2010, Aveiro, Portugal

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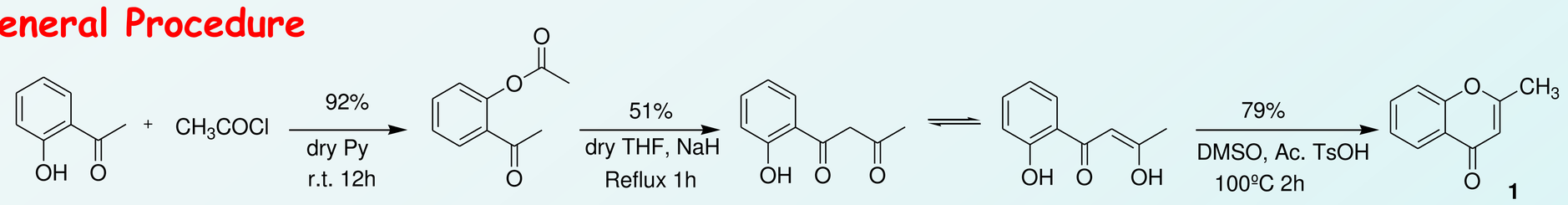
Introduction

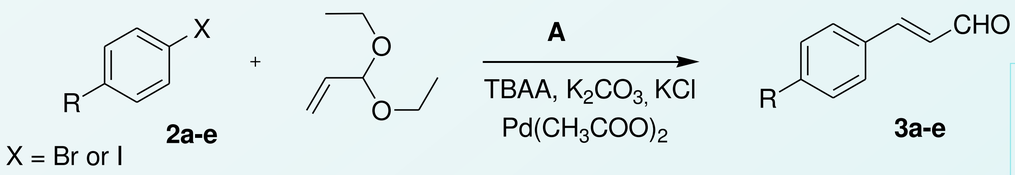
Xanthones or 9*H*-xanthen-9-one (dibenzo-γ-pirone) are a class of natural oxygenated heterocyclic compounds with a large diversity of functional groups.[1] In recent years, several studies have been reported on both natural and synthetic derivatives of this class of compounds due to their wide range of biological and pharmacological properties (include anti-inflammatory, cancerchemopreventive, antibacterial, antimalarial, radical scavenging, cytotoxicity, inhibition of cyclooxygenase, and prostaglandin E2 activities).[1-3] Some xanthones even surpass the antimicrobial activity of traditional antibiotics.[1]

These promising applications have motivated the search for new derivatives and as a part of an ongoing study we present here the latest developments on the synthesis of 1-aryl-9*H*-xanthen-9-ones **5a-e**. The methodology involves the condensation of 2-methyl-4*H*-chromen-4-one **1** with cinnamaldehydes **3a-e** (**3a** commercially available and **3b-e** prepared from the corresponding halobenzenes), to afford the (*E,E*)-2-(4-arylbuta-1,3-dien-1-yl)-4*H*-chromen-4-ones **4a-e**.[4] The final step consists in the electrocyclization and oxidation reactions giving rise to the desired xanthones **5a-e**. It was performed by refluxing chromones **4a-e** in trichlorobenzene with a catalytic amount of iodine.

Details on the synthesis and structural characterization of compounds **4** and **5** are presented and discussed.

General Procedure



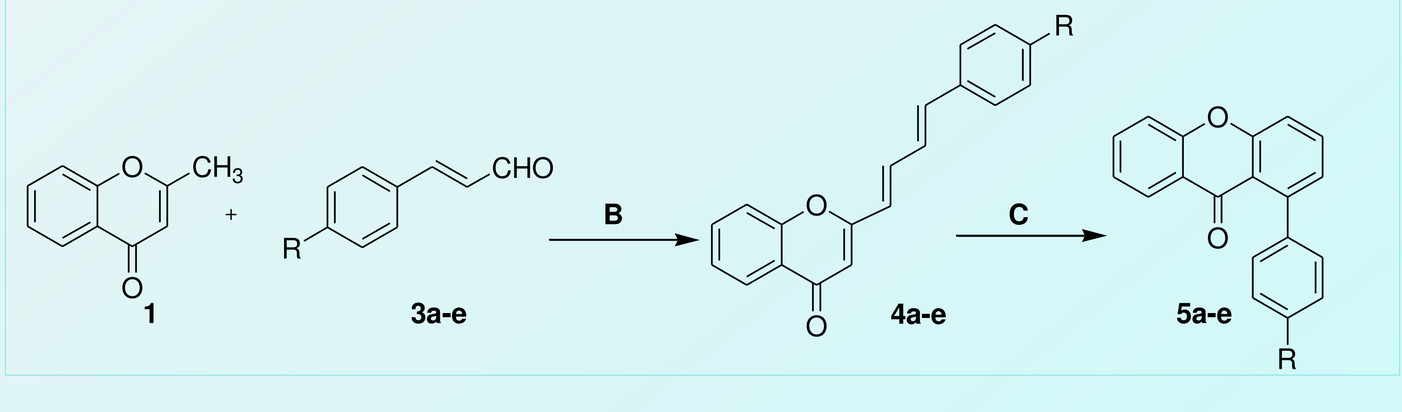


a R = H
b R = CH_3
c R = OCH_3
d R = Br
e R = NO_2

A: Dry DMF, 90ºC.

B: EtOH, NaOEt (4eq.), r.t., 4h (**4a-d**), EtOH, NaOEt (1 eq.), r.t., 54h (**4e**).

C: TCB, I_2, reflux, 48h.



Reaction A

Benzene derivative	Product	η (%)
2b	3b	63
2c	3c	68
2d	3d	33
2e	3e	69

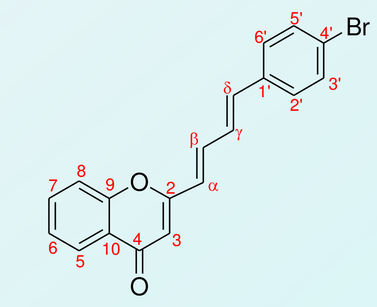
Reaction B

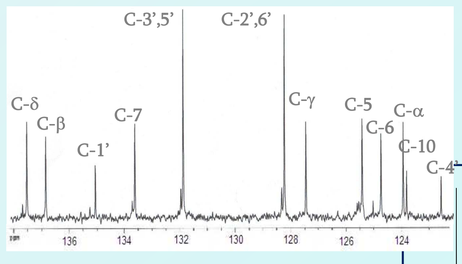
Cinnamaldehyde	Product	η (%)
3a	4a	80
3b	4b	77
3c	4c	83
3d	4d	70
3e	4e	68

Reaction C

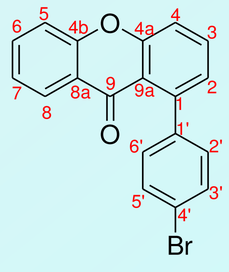
Chromone	Product	η (%)
4a	5a	30
4b	5b	26
4c	5c	70
4d	5d	56
4e	5e	50

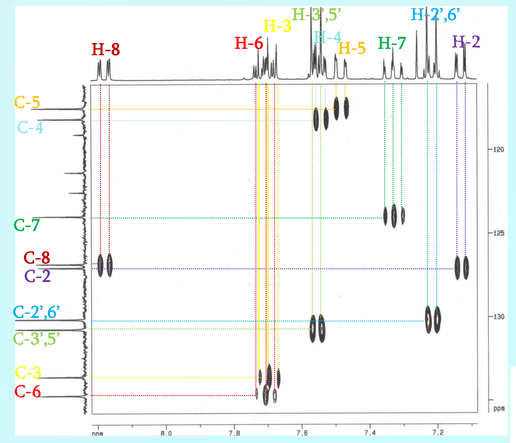
Structural Elucidation





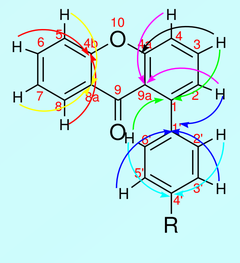
^{13}C NMR



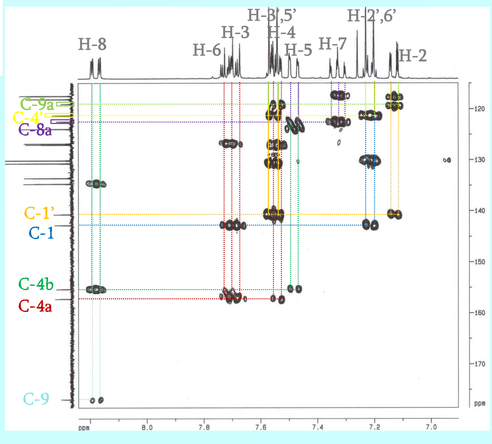


HSQC

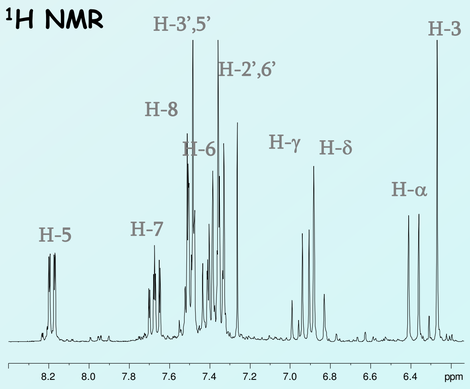
HMBC Conectivities

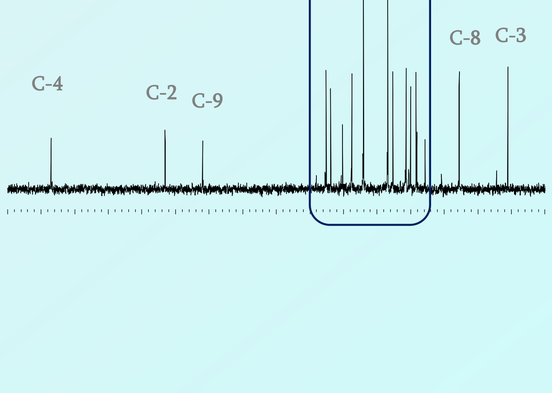


HMBC

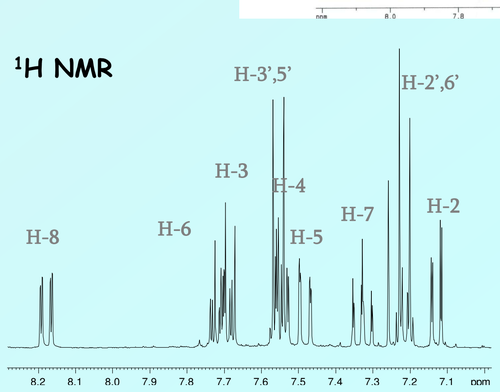


^{1}H NMR





^{1}H NMR



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