

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

Recent developments in the synthesis of 1-aryl-9H-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

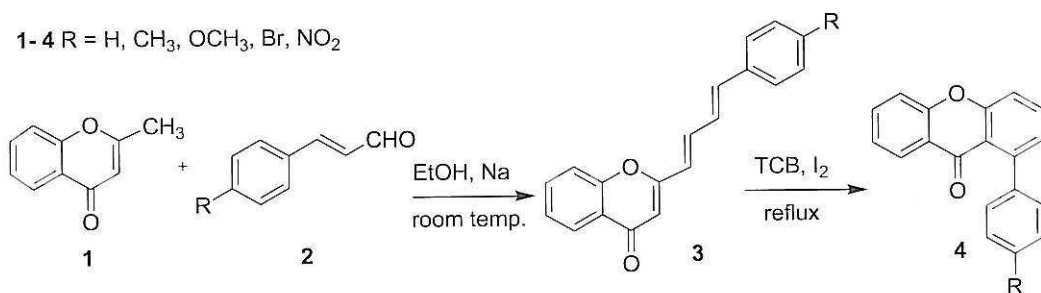
^aDepartment of Chemistry & QOPNA, University of Aveiro, 3810-193 Aveiro, Portugal

^bDepartment of Vegetal Production and Technology, Escola Superior Agrária de Bragança, 5301-855 Bragança, Portugal

Xanthenes or 9H-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 xanthenes 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-9H-xanthen-9-ones **4a-e**. The methodology involves the condensation of 2-methyl-4H-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)-4H-chromen-4-ones **3a-e**.⁴ The final step consists in the electrocyclization and oxidation reactions giving rise to the desired xanthenes **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.



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.
- (3) Brase S., Encinas A., Keck J., Nising C. F. *Chem. Rev.* **2009**, *109*, 3960.
- (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-9H-xanthen-9-ones", *2PYChem*, Universidade de Aveiro, **2010**.



Universidade de Aveiro

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

Cátia I. C. Esteves^a, Clementina M. M. Santos^{a,b}, Cristela M. Brito^a, Artur M. S. Silva^a, José A. S. Cavaleiro^a

^aDepartment of Chemistry & QOPNA, University of Aveiro, 3810-193 Aveiro, Portugal

^bDepartment of Vegetal Production and Technology, Escola Superior Agrária de Bragança, 5301-855 Bragança, Portugal

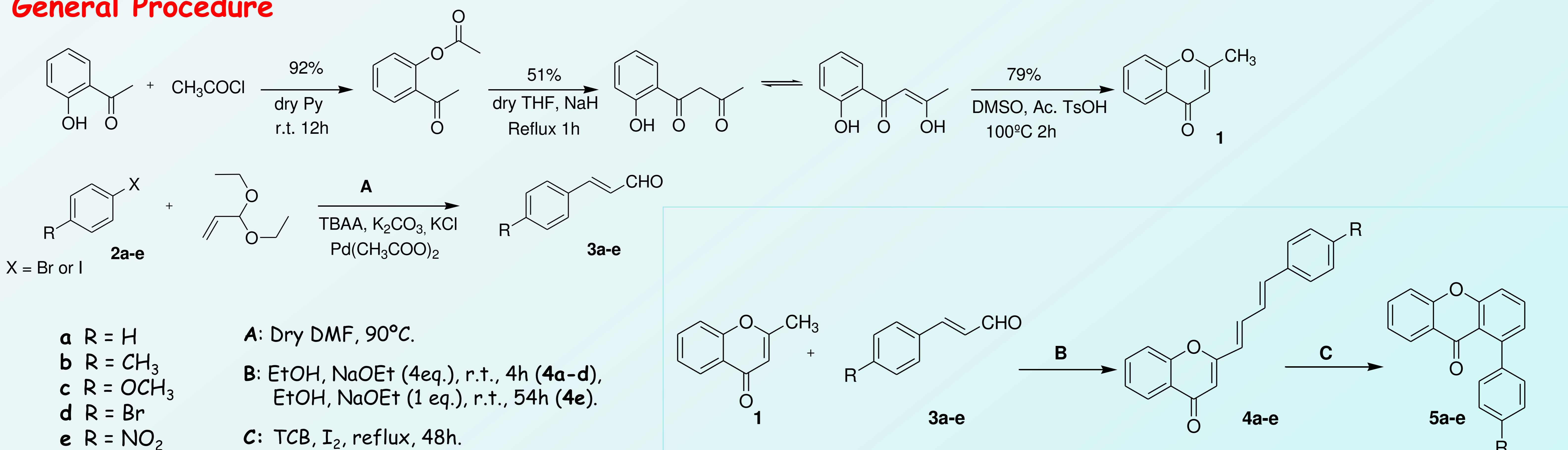
Introduction

Xanthenes or 9H-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 xanthenes 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-9H-xanthen-9-ones **5a-e**. The methodology involves the condensation of 2-methyl-4H-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)-4H-chromen-4-ones **4a-e**.⁴ The final step consists in the electrocyclization and oxidation reactions giving rise to the desired xanthenes **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



Reaction A

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

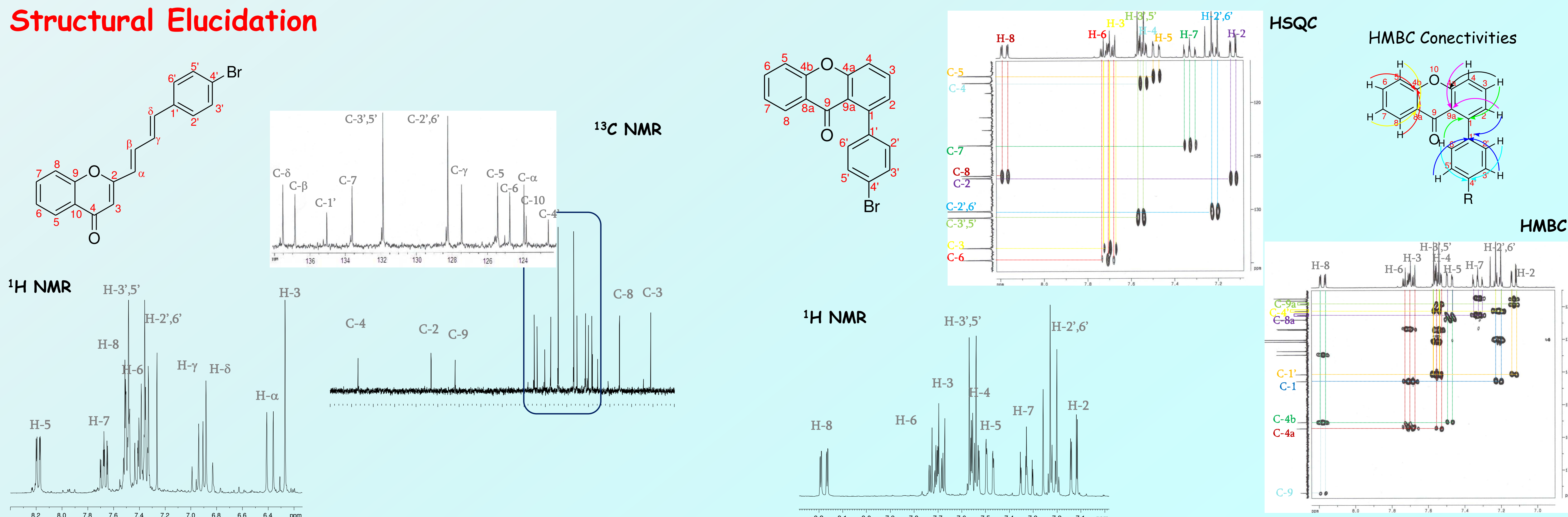
Reaction B

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



Acknowledgements

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 for the financial support through project SFRH/BI/51098/2010.

References

- (1) Franklin G., Conceição L. F. R., Kombrink E., Dias A. C. P. *Phytochem.* **2009**, *70*, 60.
- (2) Ngoupayo J., Tabopda T. K., Ali M. S., *Bioorg. Med. Chem.* **2009**, *17*, 5688.
- (3) Brase S., Encinas A., Keck J., Nising C. F. *Chem. Rev.* **2009**, *109*, 3960.
- (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-9H-xanthen-9-ones", 2PYChem, Universidade de Aveiro, **2010**.