

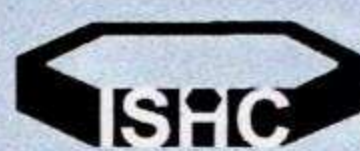
# **4<sup>th</sup>** Eurasian Meeting on Heterocyclic Chemistry



**Book of Abstracts**

**August 27 - August 31, 2006**

**Thessaloniki, GREECE**



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## SYNTHESIS OF POLYHYDROXY-2,3-DIARYLXANTHONES WITH POTENCIAL ANTIOXIDANT ACTIVITY

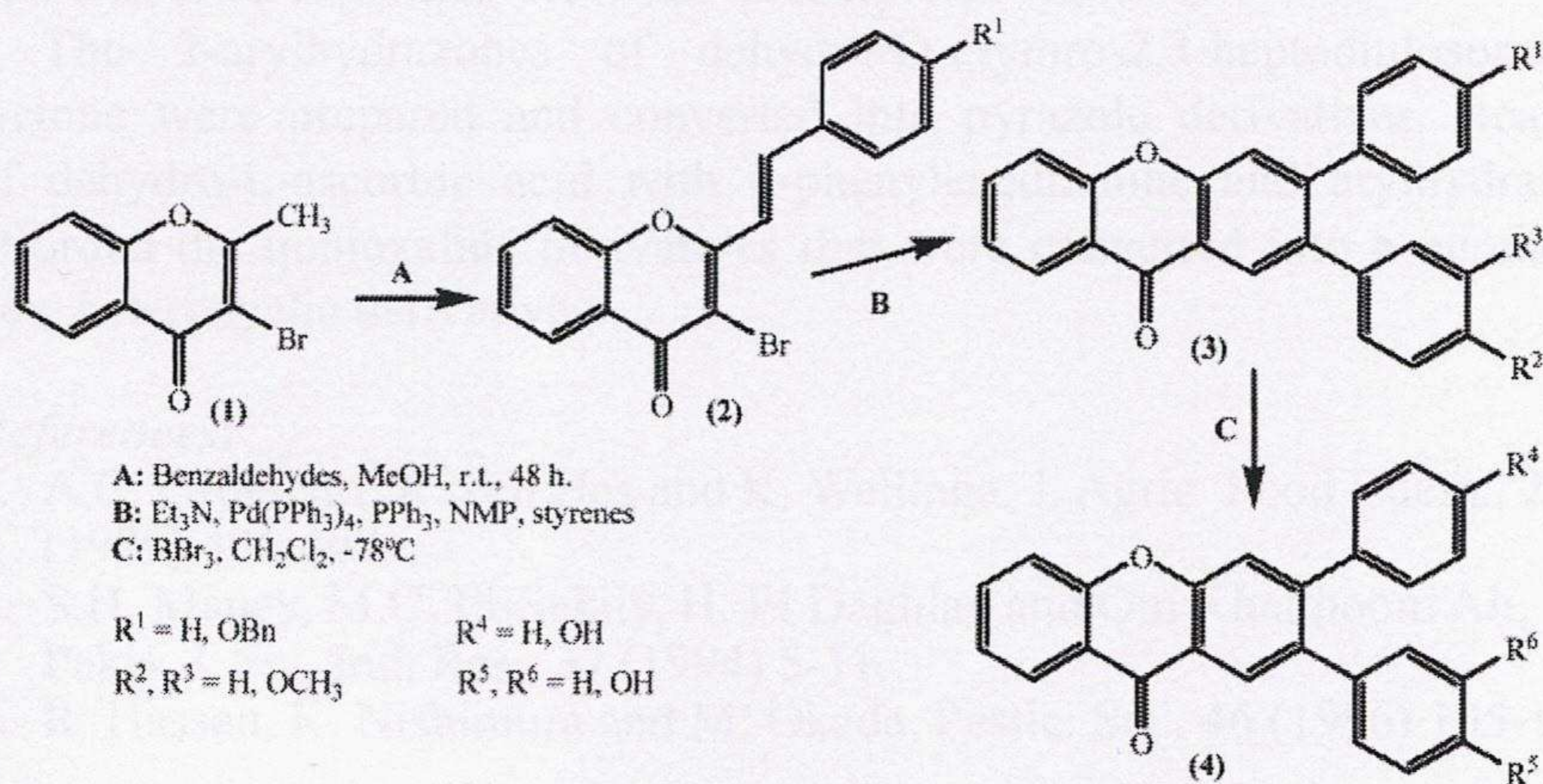
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Xanthenes are a well-studied class of heterocyclic compounds [1] and over the years these substances have been extensively studied due to their biological properties. Both natural and synthetic derivatives have shown important antimicrobial, anti-tumour, anti-inflammatory as well as antioxidant activities [2]. Several structure/activity studies of polyphenolic compounds revealed that the presence of hydroxyl substituents in certain positions of their skeleton is of great importance for a high antioxidant activity [3].

Taking this knowledge into consideration, we report the synthesis of new polyhydroxy-2,3-diarylxanthenes, starting from the 3-bromo-2-methylchromone **1**. Aldol condensation of **1** with benzaldehydes leads to the formation of 3-bromo-2-styrylchromones **2** followed of Heck reaction with styrenes to give the 2,3-arylxanthenes **3** [4]. The final step consists in the cleavage of protective groups to obtain the desired polyhydroxy-2,3-diarylxanthenes **4**. The experimental procedures and the characterization of the new compounds will be presented and discussed.



*Acknowledgements:* Thanks are due to the University of Aveiro, FCT and FEDER for funding the Organic Chemistry Research Unit and the project POCI/QUI/58835/2004. One of us (C.M.M. Santos) is also grateful to PRODEP 5.3 for financial support.

[1] K. Hostettman, M. Hostettman, in *Methods in Plant Biochemistry*, Vol. 1 – Plant Phenolics, Ed. P. M. Dey, J. B. Harbone, Academic Press, **1989**, pp. 493. [2] (e.g.) G. J. Bennett, H.-H. Lee, *Phytochemistry*, **1989**, 28, 967; H. Minami, M. Kinoshita, Y. Fukuyama, M. Komoda, T. Yoshizawa, M. Sugiura, K. Nakagawa, H. Tago, *Phytochemistry*, **1994**, 36, 501; A. Abdel-Lateff, C. Klemke, G. M. König, A. D. Wright, *J. Nat. Prod.*, **2003**, 66, 706; Y.-M. Chiang, Y.-H. Kuo, S. Oota, Y. Fukuyama, *J. Nat. Prod.*, **2003**, 66, 1070. [3] (e.g.) E. Fernandes, F. Carvalho, A. M. S. Silva, C. M. M. Santos, D. C. G. A. Pinto, J. A. S. Cavaleiro, M. L. Bastos, *J. Enz. Inhib.*, **2002**, 17, 45; P. Filipe, A. M. S. Silva, P. Morlière, C. M. Brito, L. K. Patterson, G. L. Hug, J. N. Silva, J. A. S. Cavaleiro, J.-C Mazière, J. P. Freitas, R. Santus, *Biochem. Pharmacol.*, **2004**, 67, 2207. [4] C.M. M. Santos, A. M. S. Silva, J. A. S. Cavaleiro, *Synlett*, **2005**, 3095.



# SYNTHESIS OF POLYHYDROXY-2,3-DIARYLXANTHONES WITH POTENCIAL ANTIOXIDANT ACTIVITY

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4<sup>th</sup> Eurasium Meeting on Heterocyclic Chemistry, Tessaloniki, Greece 4<sup>th</sup> Eurasium Meeting on Heterocyclic Chemistry, Tessaloniki, Greece 4<sup>th</sup> Eurasium Meeting on Heterocyclic Chemistry, Tessaloniki, Greece

## INTRODUCTION

Xanthenes are a well-studied class of heterocyclic compounds [1] and over the years these substances have been extensively studied due to their biological properties. Both natural and synthetic derivatives have shown important anti-microbial, anti-tumour, anti-inflammatory as well as antioxidant activities [2]. Several structure/activity studies of polyphenolic compounds revealed that the presence of hydroxyl substituents in certain positions of their skeleton is of great importance for a high antioxidant activity [3].

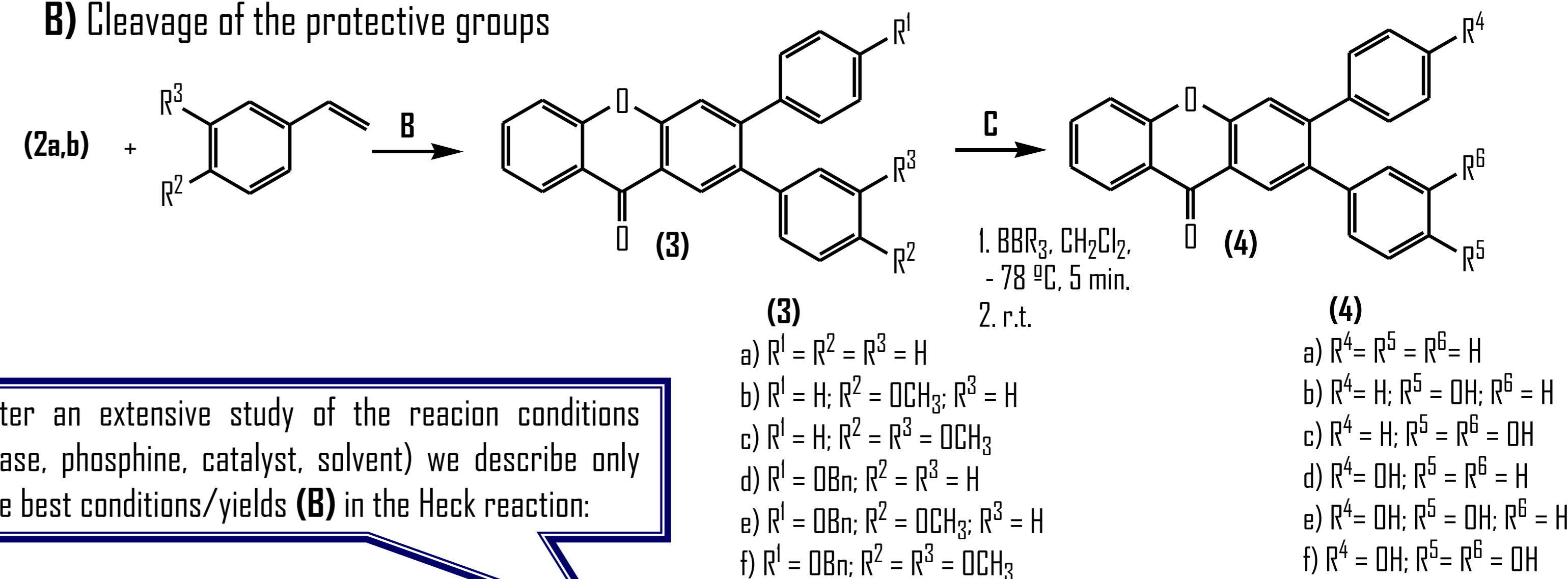
Taking this knowledge into consideration, we report the synthesis of new polyhydroxy-2,3-diarylxanthenes, starting from the 3-bromo-2-methylchromone 1. Aldol condensation of 1 with benzaldehydes leads to the formation of 3-bromo-2-styrylchromones 2 followed by Heck reaction with styrenes to give the 2,3-arylxanthenes 3 [4]. The final step consists in the cleavage of protective groups to obtain the desired polyhydroxy-2,3-diarylxanthenes 4.

## 3. SYNTHESIS OF POLYHYDROXY-2,3-DIARYLXANTHONES (4)

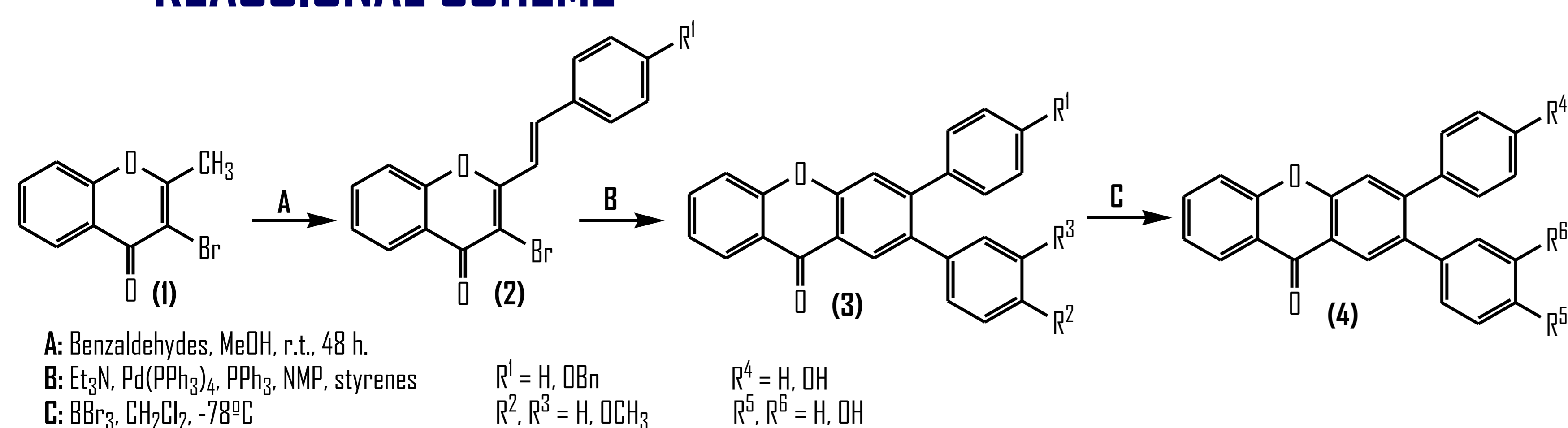
The synthesis of polyhydroxy-2,3-diarylxanthenes (4) involves also two steps:

A) Heck reaction of 3-bromo-2-styrylchromone 2 with styrenes

B) Cleavage of the protective groups



## REACTIONAL SCHEME



## GENERAL PROCEDURE

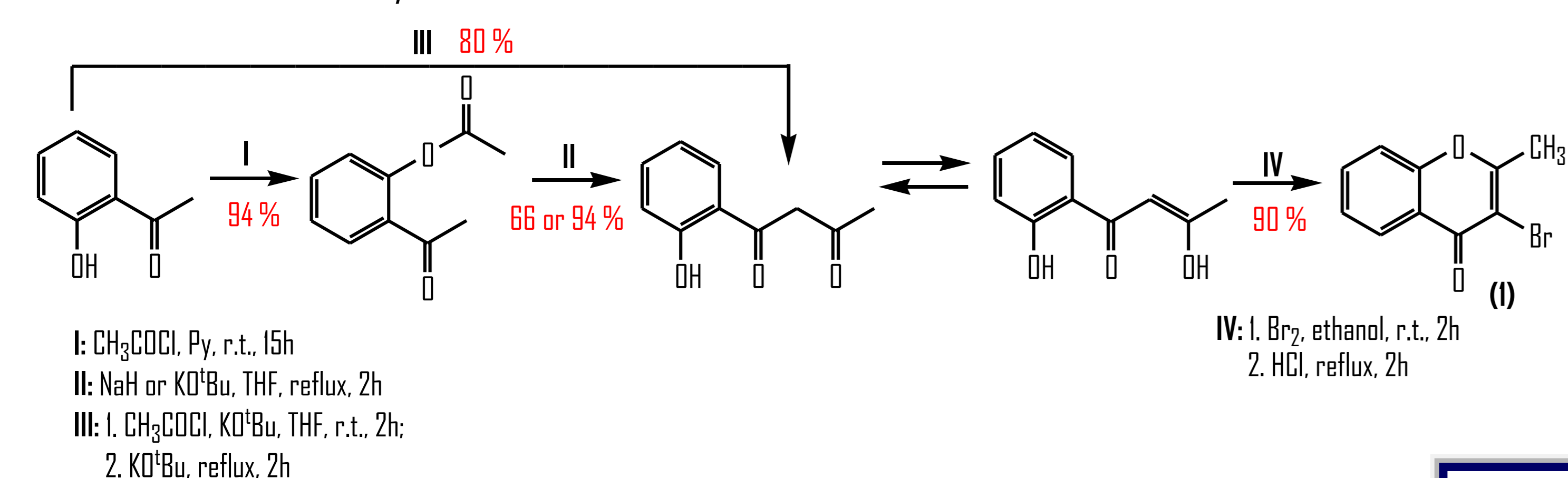
### 1. PREPARATION OF 3-BROMO-2-METHYLCHROMONE (1)

The preparation of 3-bromo-2-methylchromone (1) involves 3 steps:

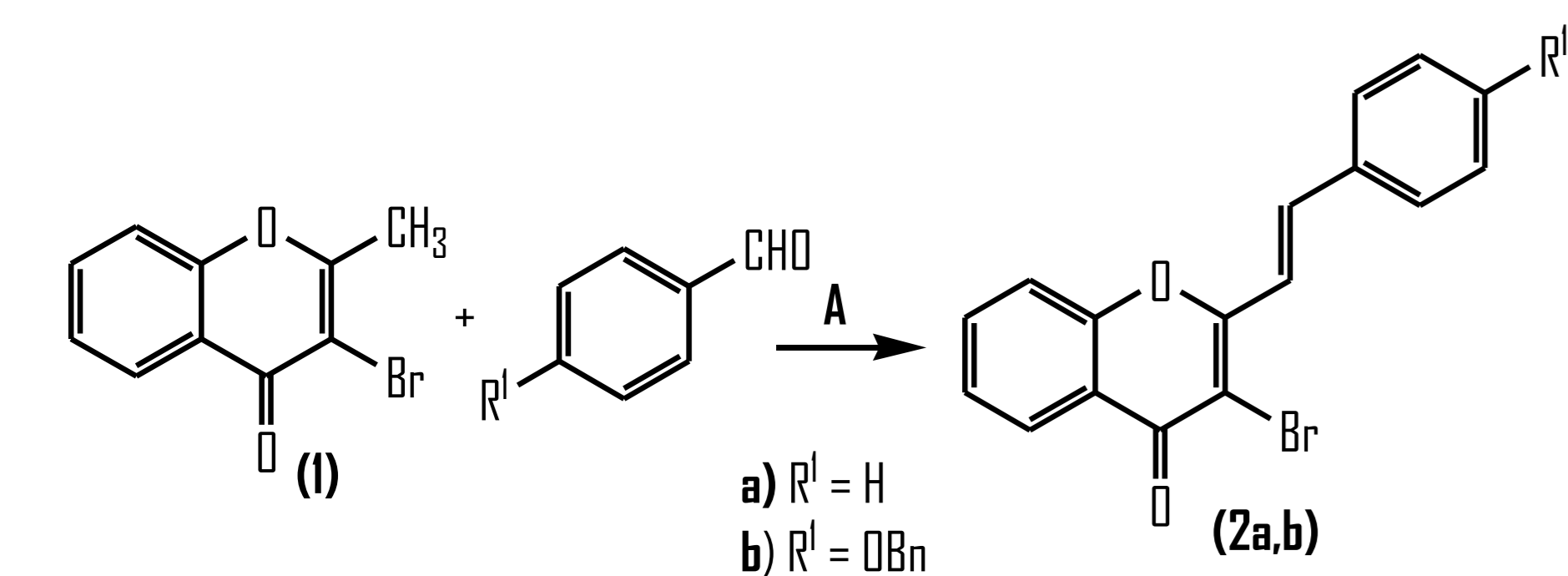
A) Acetylation of 2'-hydroxyacetophenone

B) Transposition of the acetyl group

C) Bromination and cyclization



### 2. SYNTHESIS OF 3-BROMO-2-STYRYLCHROMONES (2)



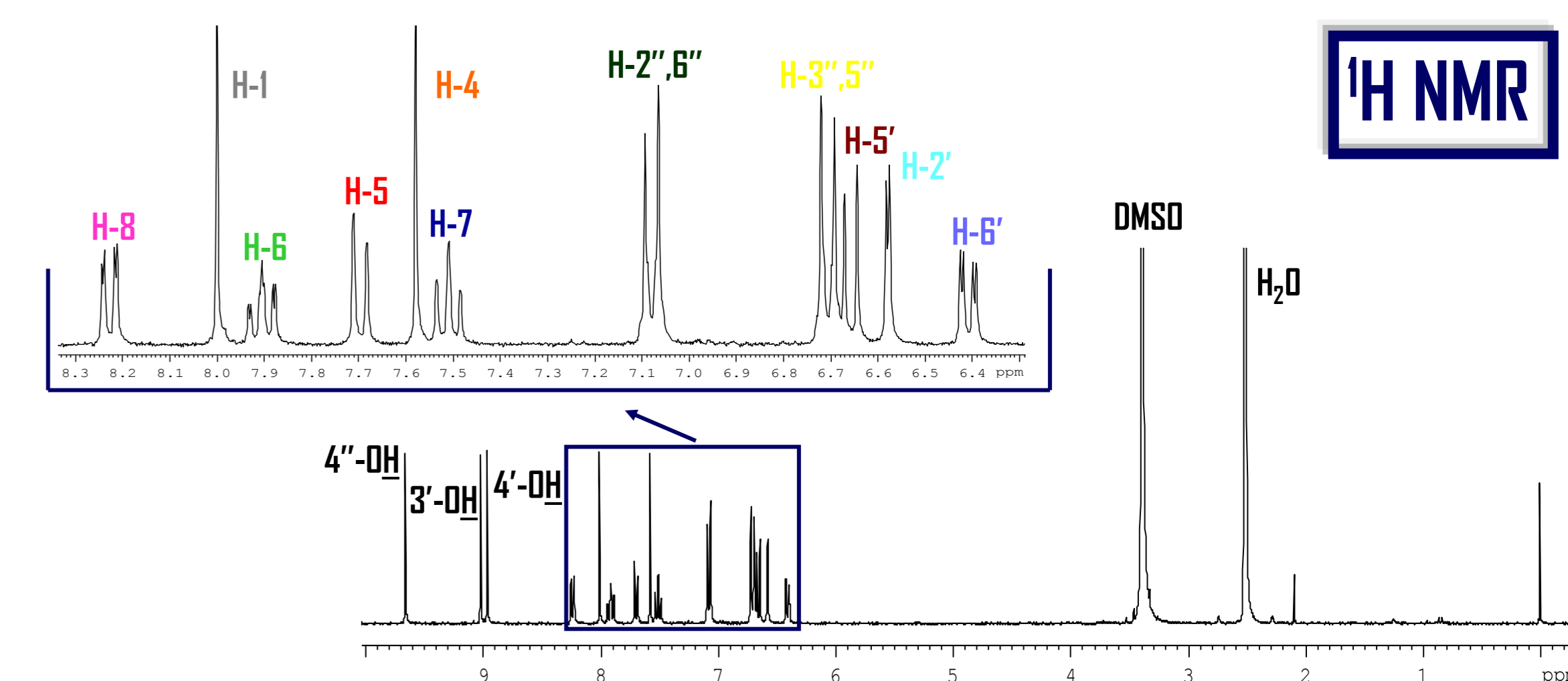
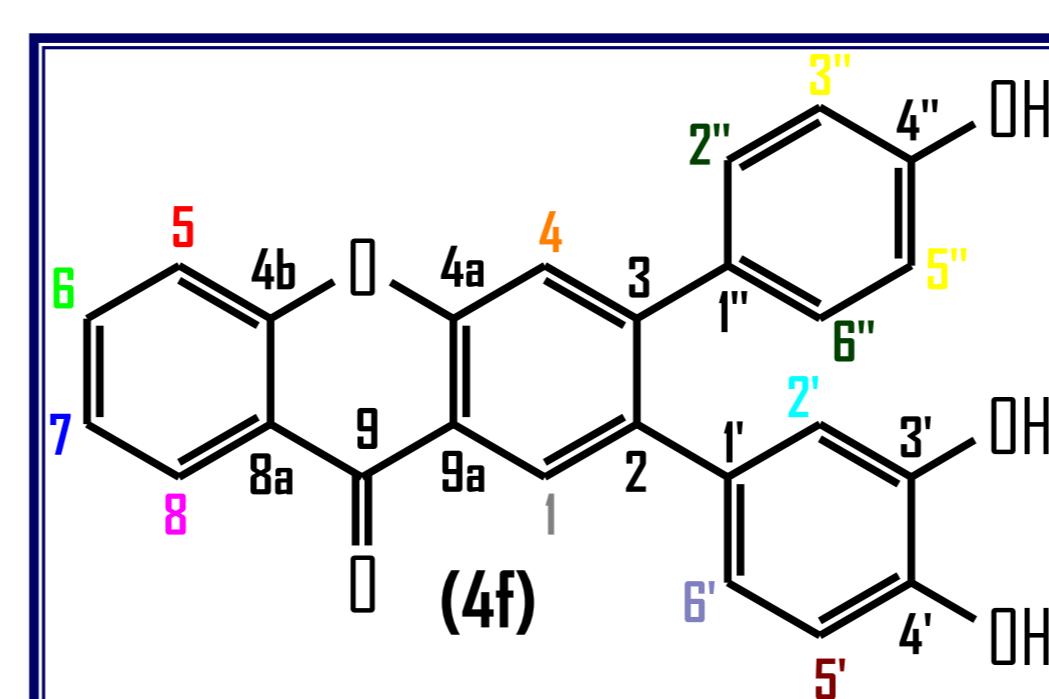
The hydroxyl group of 4-hydroxybenzaldehyde must be protected. In this case, we used benzyl chloride, K<sub>2</sub>CO<sub>3</sub>, DMF.

Base (eq.)	Time (h)	2a (%)	2b (%)
4	2	55	52
4	12	56	52
4	24	61	53
<b>4</b>	<b>48</b>	<b>87</b>	<b>68</b>
4	72	49	49

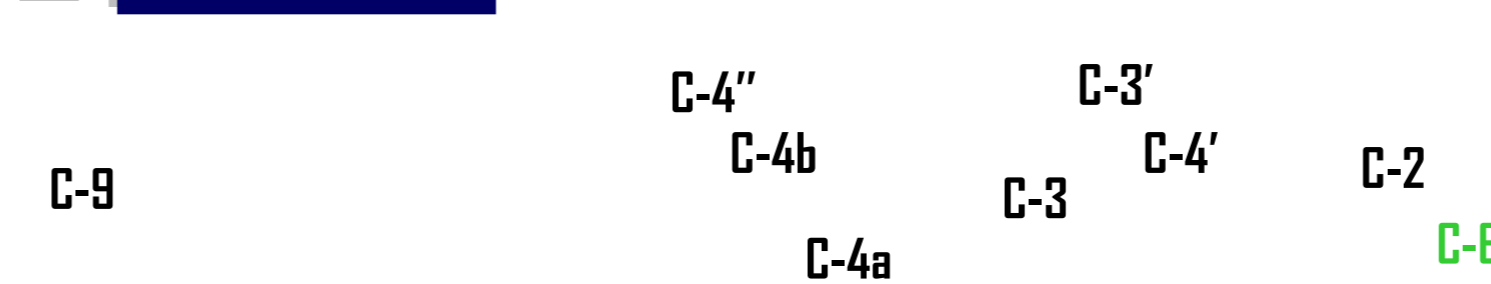
## REFERENCES

- [1] K. Hostettman, M. Hostettman, in *Methods in Plant Biochemistry*, Vol. 1 – Plant Phenolics, Ed. P. M. Dey, J. B. Harbone, Academic Press, 1989, pp. 493.  
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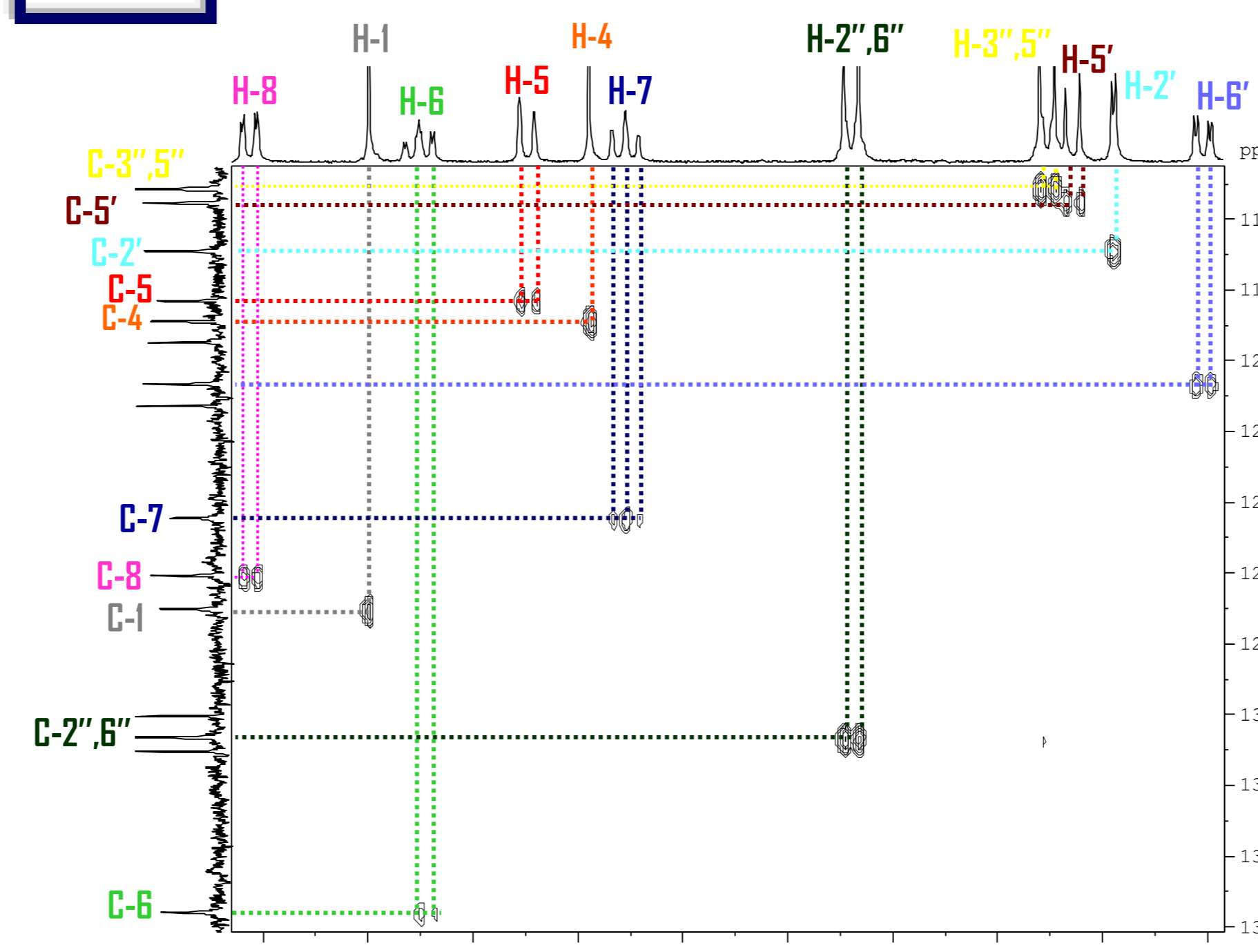
## STRUCTURAL ELUCIDATION OF 3',4',4''-TRI-HYDROXY-2,3-DIPHENYLXANTHONE (4f)



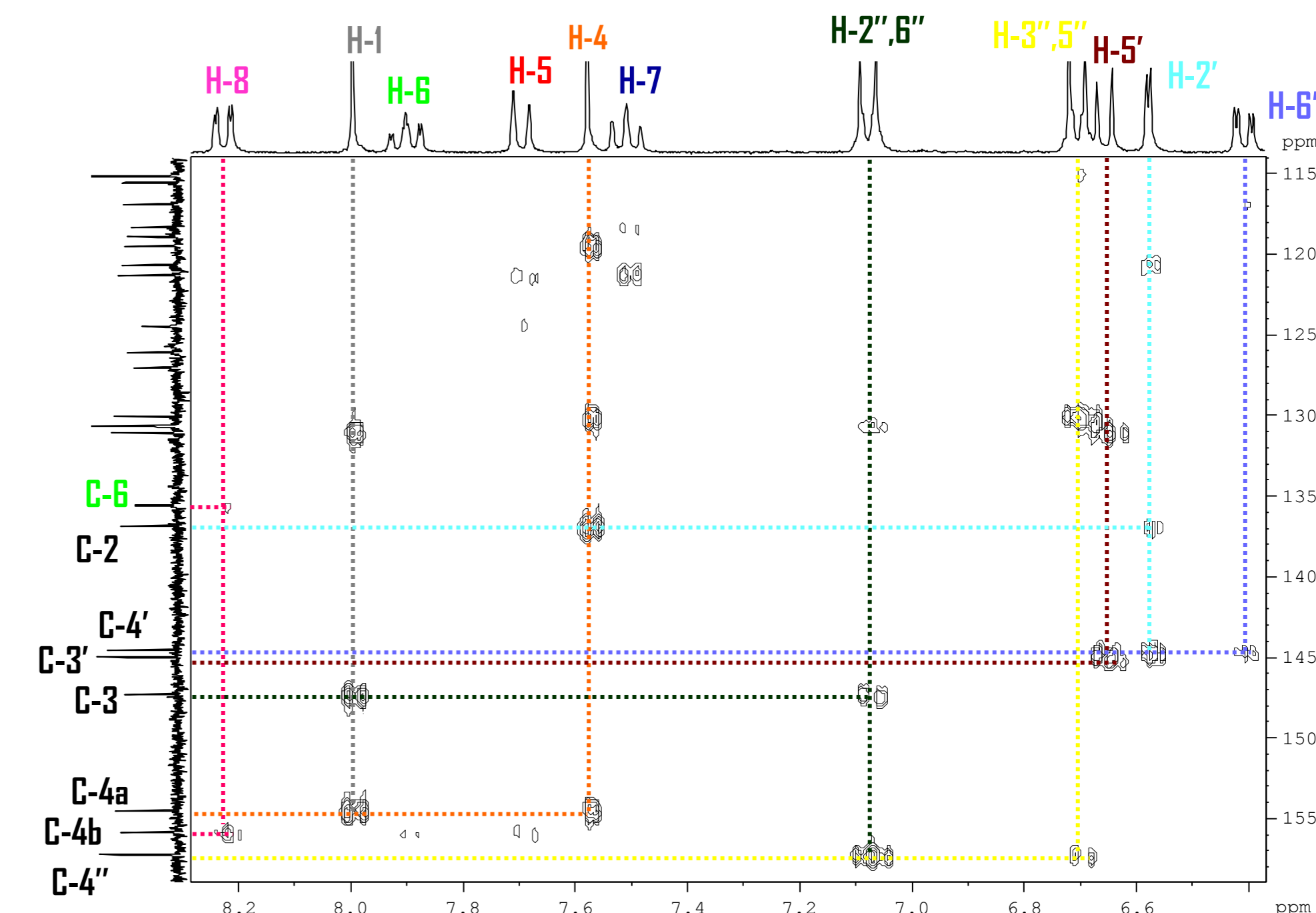
### 13C NMR



### HSQC



### HMBC



## ACKNOWLEDGEMENTS

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