

6º ENCONTRO NACIONAL DE QUÍMICA ORGÂNICA

LIVRO DE RESUMOS

Universidade do Minho, Braga, Portugal

20 a 22 de Julho de 2005

Synthesis of 2,3-Distyrylchromones

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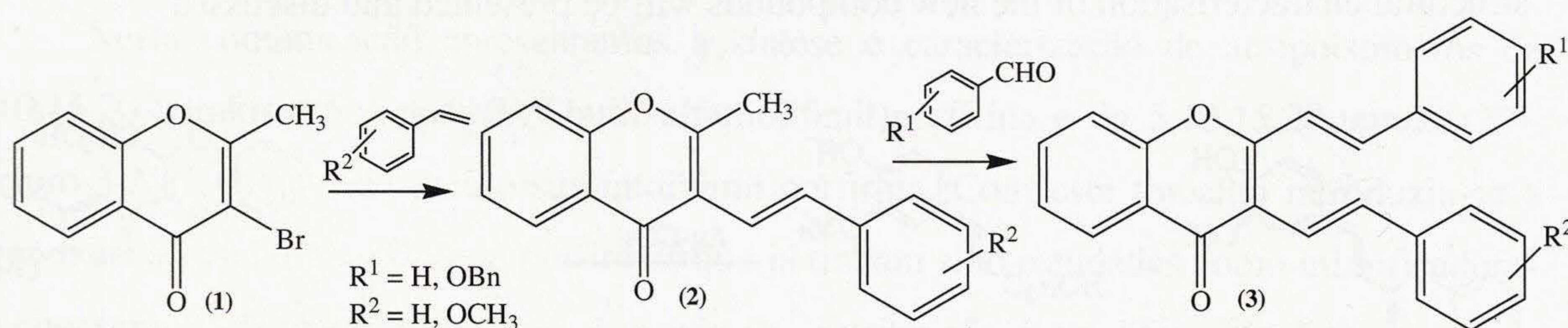
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Styrylchromones are a small group of naturally occurring chromones, which presented significant cytotoxic activity.¹ In the past decades, many of 2-styrylchromone derivatives have been synthesized and object of several studies, revealing important pharmacological, biocidal and mainly antioxidant activities.²

However, the studies on the chemistry of 3-styrylchromones are scarce; only a small number of synthetic routes and chemical transformations have been reported.¹

Following our interest on the synthesis of 2- and 3-styrylchromones, we developed a new synthesis of 2,3-distyrylchromones for further evaluation of the corresponding antioxidant activity. The first approach is the preparation of 3-bromo-2-methylchromone **1**, followed of Heck reaction with styrenes to give the 3-styrylchromones **2**. Finally the Aldol condensation gives the desired 2,3-distyrylchromones **3** (Scheme 1). Experimental procedures and spectroscopic characterization of all compounds will be presented and



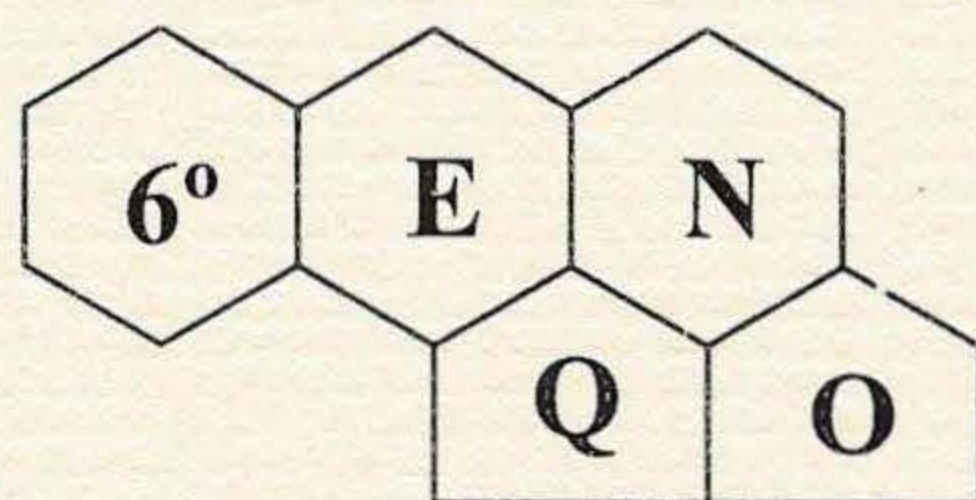
discussed.

Scheme 1

Acknowledgements: Thanks are due to the University of Aveiro, FCT and FEDER for funding the Organic Chemistry Research Unit and the project POCTI/QUI/38394/2001. One of us (C.M.M. Santos) is also grateful to PRODEP 5.3 for financial support.

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² a) 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*, 45-48. b) F. Peixoto, A. I. R. N. A. Barros, A. M. S. Silva, *J. Biochem. & Mol. Toxicol.* **2003**, *16*, 209-219. c) E. Fernandes, M. Carvalho, F. Carvalho, A. M. S. Silva, C. M. M. Santos, D. C. G. A. Pinto, J. A. S. Cavaleiro, M. L. Bastos, *Arch. Toxicol.* **2003**, *77*, 500-505.



Certificado de Participação

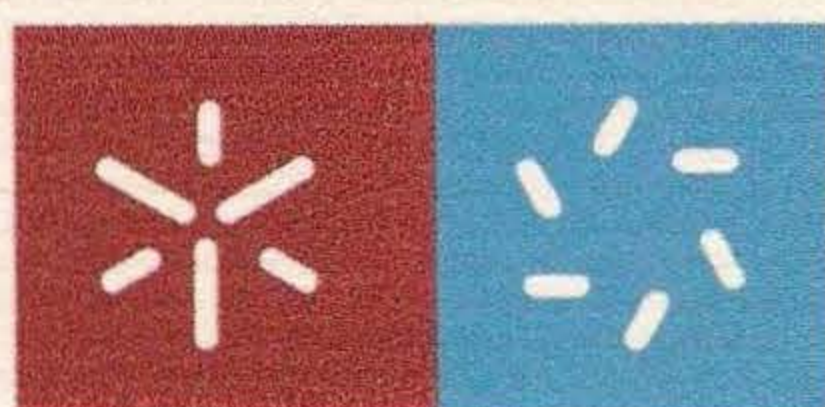
CLEMENTINA MARIA MOREIRA SANTOS

Participou no 6º Encontro Nacional de Química Orgânica,
realizado na Universidade do Minho, de 20 a 22 de Julho
de 2005.

Braga, 20 de Julho de 2005

A Comissão Organizadora,

Ana Paula Campos



Universidade do Minho

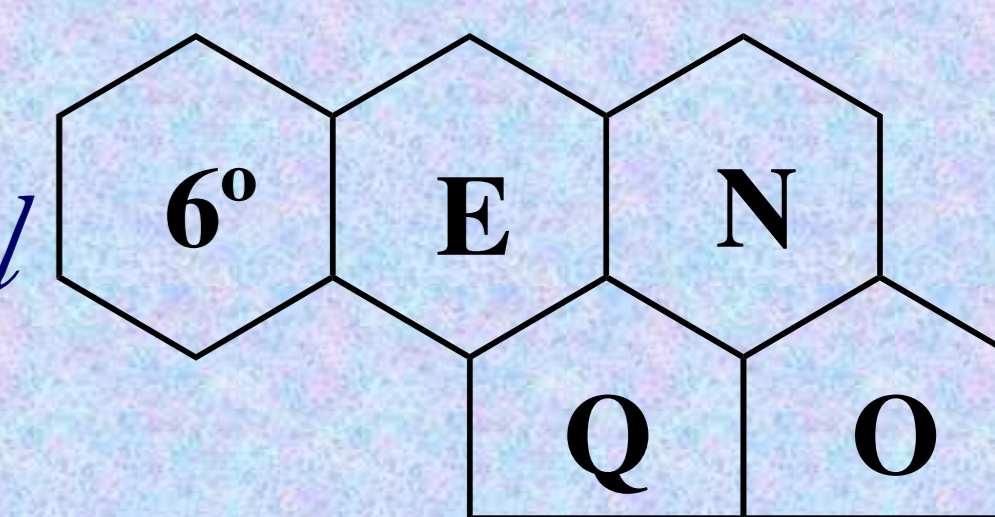


SYNTHESIS OF 2,3-DISTYRYLCHROMONES

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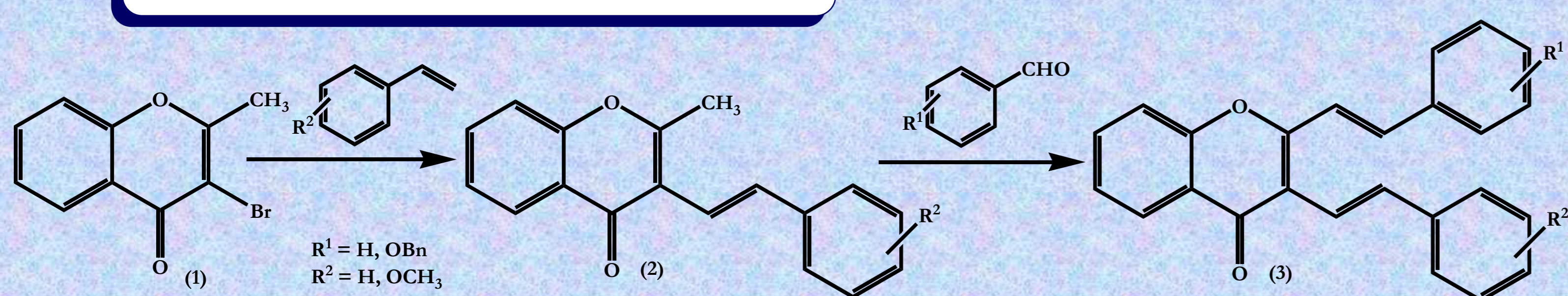
INTRODUCTION

Styrylchromones are a small group of naturally occurring chromones, which presented significant cytotoxic activity.¹ In the past decades, many of 2-styrylchromone derivatives have been synthesized and object of several studies, revealing important pharmacological, biocidal and mainly antioxidant activities.²

However, the studies on the chemistry of 3-styrylchromones are scarce; only a small number of synthetic routes and chemical transformations have been reported.¹

Following our interest on the synthesis of 2- and 3-styrylchromones, we developed a new synthesis of 2,3-distyrylchromones for further evaluation the corresponding antioxidant activity. The first approach is the preparation of 3-bromo-2-methylchromone **1**, followed of Heck reaction with styrenes to give the 3-styrylchromones **2**. Finally the Aldol condensation gives the desired 2,3-distyrylchromones **3** (Scheme 1).

REACTIONAL SCHEME

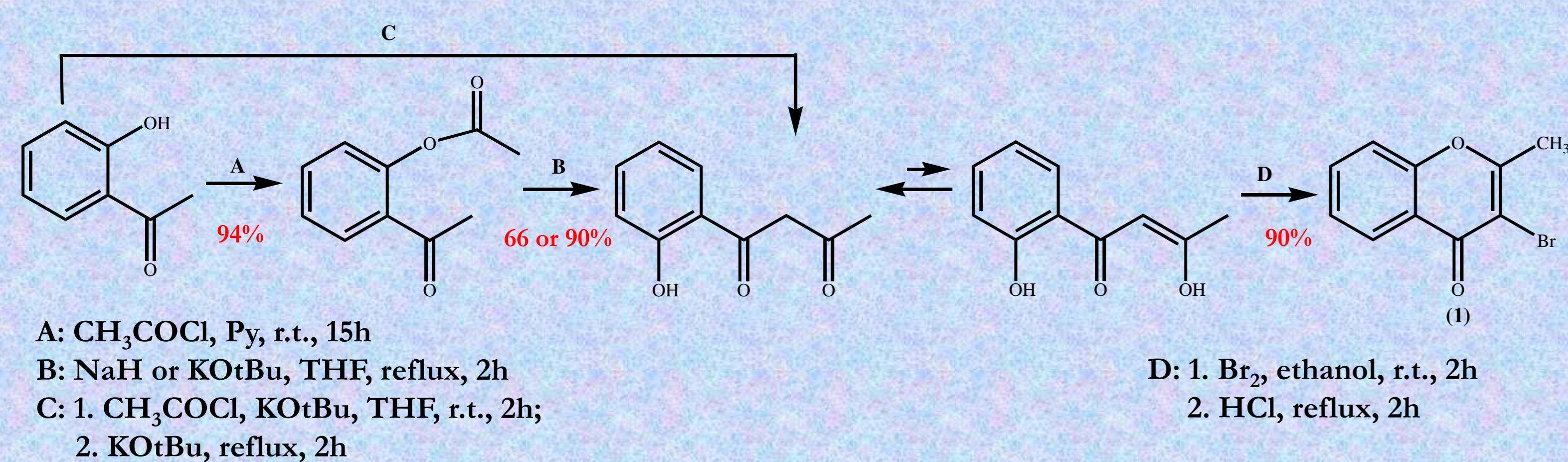


Scheme 1

GENERAL PROCEDURE

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

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



2. PREPARATION OF 2-METHYL-3-STYRYLCHROMONES (2a-c)

In order to prepare 2-methyl-3-styrylchromones (2a-c), we developed a study of reactivity of 3-bromo-2-methylchromone (1) in Heck reaction with styrene. Table 1 presents some of the experiences carried out to find the better experimental conditions.

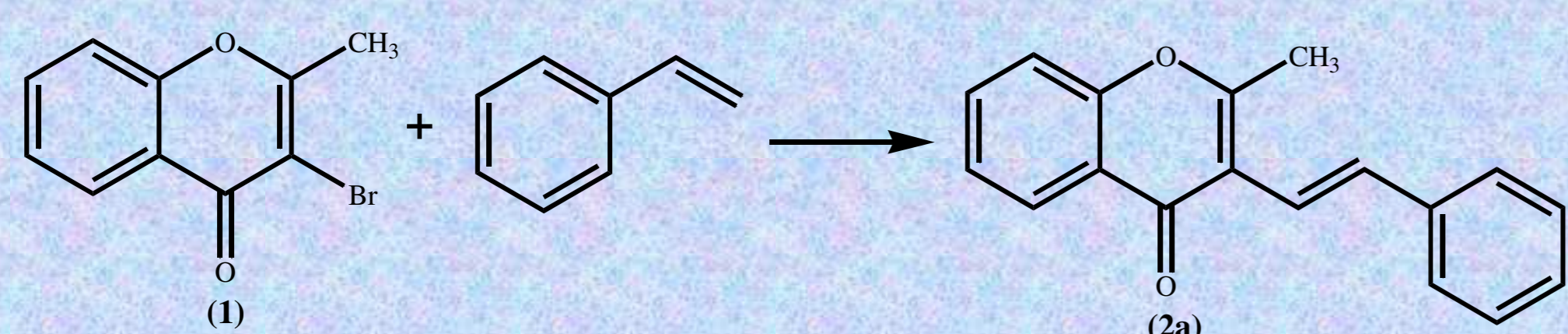


Table 1

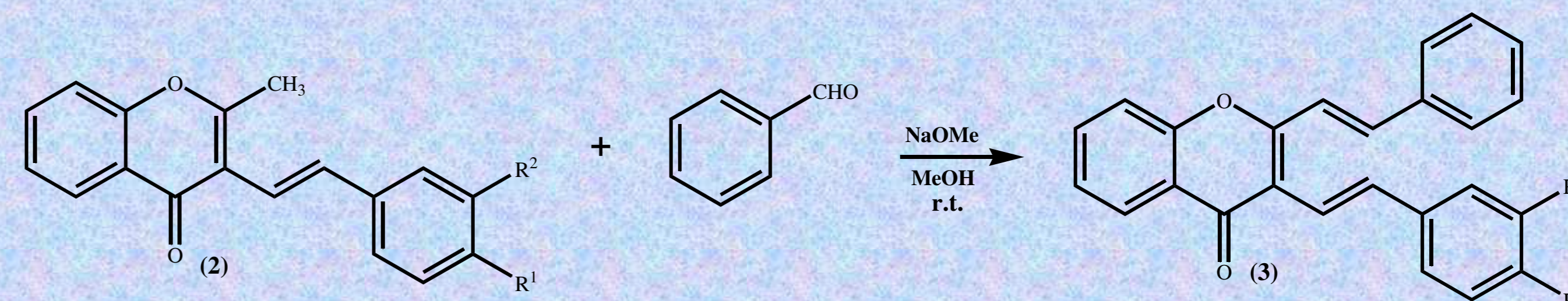
Entry	Et ₃ N (eq.)	PPh ₃ (eq.)	Catalyst (eq.)	Styrene (eq.)	Temperature (°C)	Time (h)	2a (%)
1	1	0.1	Pd(PPh ₃) ₄ - 0.02	2.66	100	24	0.0
2	1	0.1	Pd(PPh ₃) ₄ - 0.02	2.66	160	24	9.1
3	1	0.1	Pd(PPh ₃) ₄ - 0.05	2.66	160	24	21.1
4	1	0.1	Pd(PPh ₃) ₄ - 0.02	2.66	reflux	24	10.6
5	1	0.1	Pd(PPh ₃) ₄ - 0.05	5.00	160	24	9.2
6	1	0.1	Pd(PPh ₃) ₄ - 0.05	5.00	160	12	9.0
7	1	0.1	Pd(PPh ₃) ₄ - 0.05	5.00	160	9	47.9
8	1	0.1	Pd(PPh ₃) ₄ - 0.05	5.00	160	6	36.3
9	1	0.1	Pd(PPh ₃) ₄ - 0.05	5.00	160	3	26.9
10	1	0.1	Pd(OAc) ₂ - 0.05	5.00	160	9	46.2
11	1	0.1	Pd(PPh ₃)Cl ₂ - 0.05	5.00	160	9	38.8
12	1	0.1	PdCl ₂ - 0.05	5.00	160	9	48.4

☉ The best conditions/yield obtained are marked in red.

Taking in consideration the best yields obtained (entry 12), we applied the conditions to the other 2-methyl-3-styrylchromones (2b-c).

3. SYNTHESIS OF 2,3-DISTYRYLCHROMONES (3a-c)

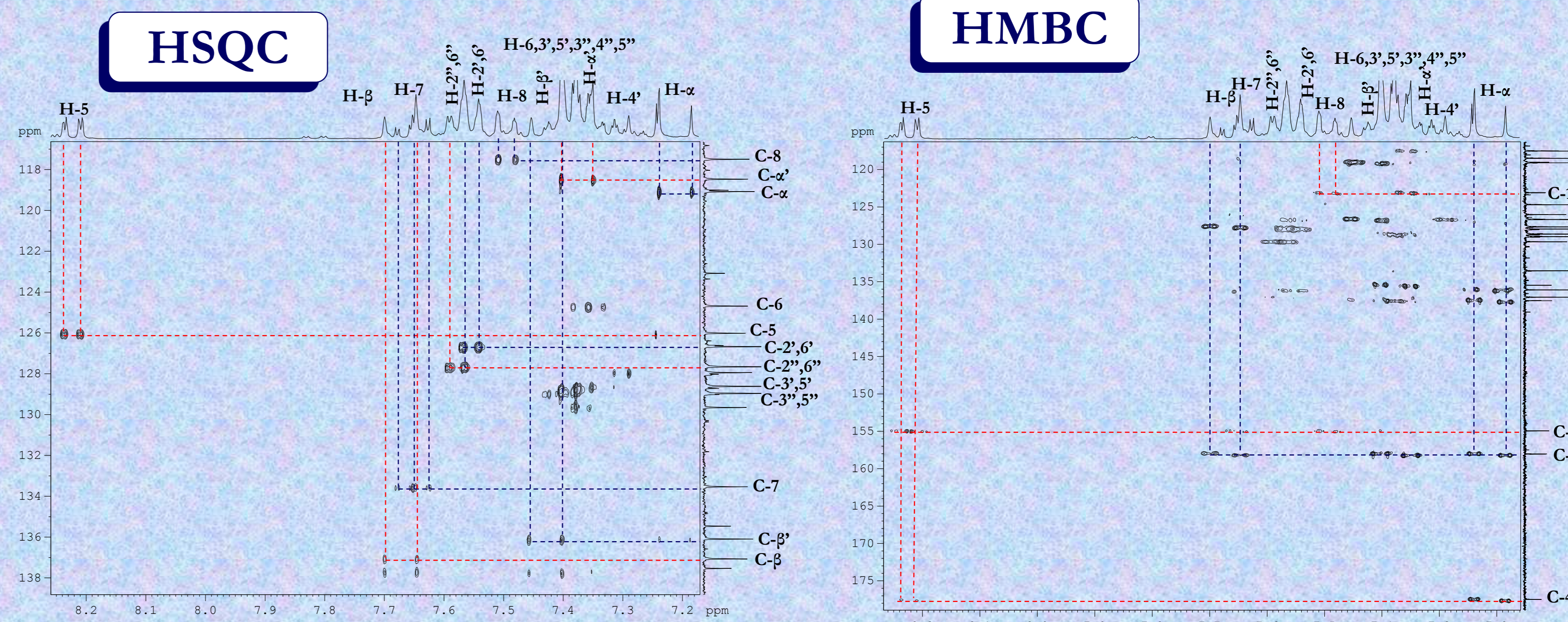
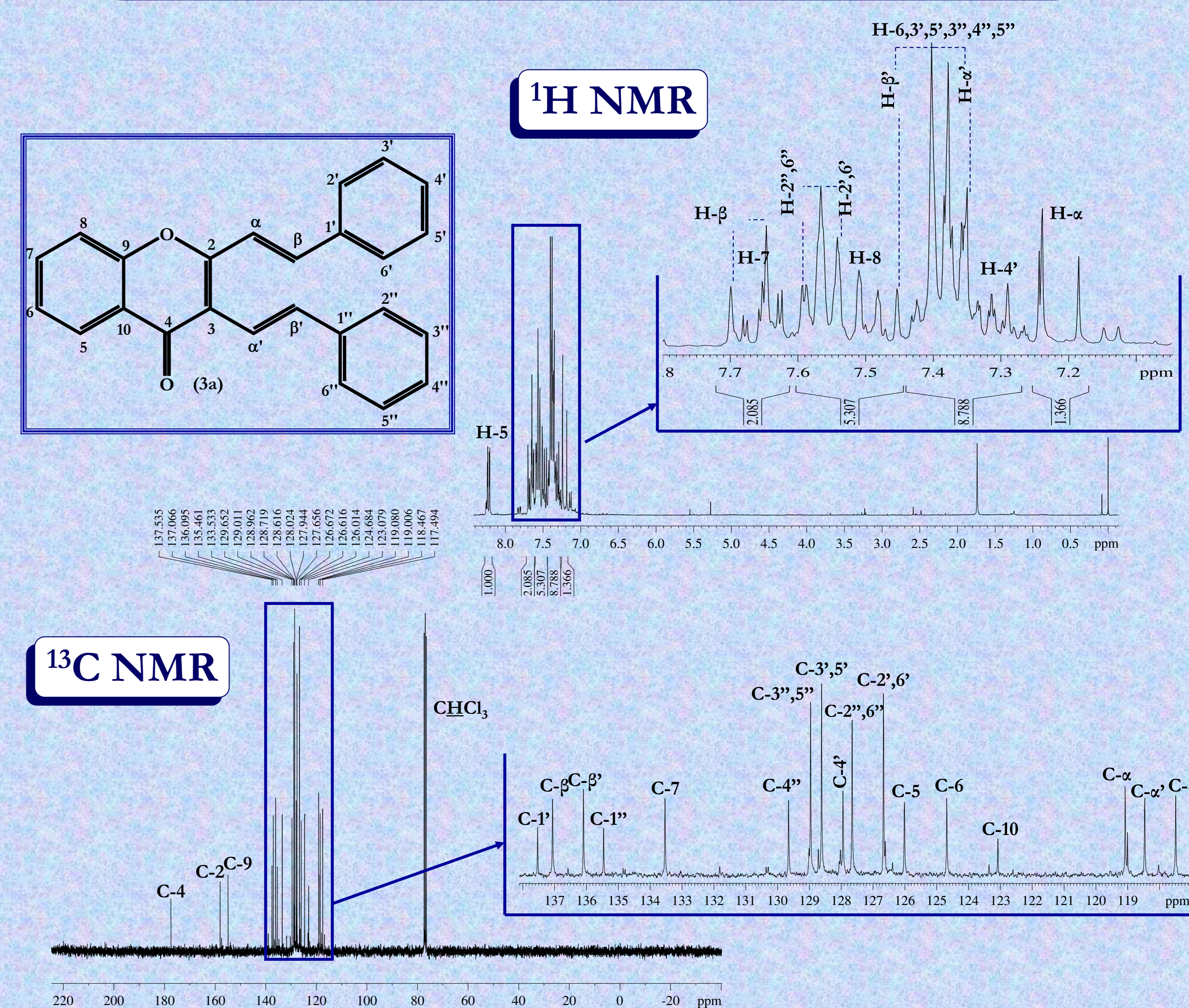
We synthesized the 2-methyl-3-styrylchromone 2a-c according to the conditions in entry 7 and then, the Aldol condensation with benzaldehyde, at room temperature during 48 h gives the desired 2,3-distyrylchromones 3a-c.



Compound	R ¹	R ²	Yield (%)
2a	H	H	47.9
2b	OCH ₃	H	49.1
2c	OCH ₃	OCH ₃	51.5

Compound	R ¹	R ²	Yield (%)
3a	H	H	52.9
3b	OCH ₃	H	57.6
3c	OCH ₃	OCH ₃	67.1

STRUCTURAL ELUCIDATION OF 2,3-DISTYRYLCHROMONE (3a)



ACKNOWLEDGEMENTS

Thanks are due to the University of Aveiro, FCT and FEDER for funding the Organic Chemistry Research Unit and the project POCTI/QUI/38394/2001. One of us (C.M.M. Santos) is also grateful to PRODEP 5.3 for financial support.

REFERENCES

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