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NEW SYNTHESSES OF NOVEL ARYLXANTHONES

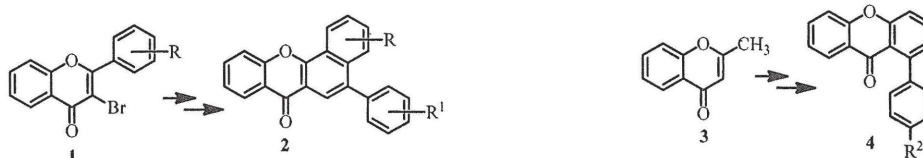
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Xanthenes represent an outstanding class of oxygenated heterocycles widespread in nature, commonly distributed in several higher plant families, such as *Gentianaceae*, *Guttiferae* and *Polygalaceae* and in a few families of fungi and lichens [1]. Both natural and synthetic derivatives often endowed with interesting pharmacological properties (e.g. anti-inflammatory, antitumour and antioxidant activities [1,2]). Naturally-occurring xanthenes present different types of substituents (e.g. hydroxyl, methoxyl and prenyl groups, among others) in different positions of their scaffold leading to a large variety of analogues [2]. The presence of an aryl ring attached to the xanthone core has only been reported in some synthetic derivatives [3,4].

We have dedicated our previous work to the development of novel methodologies for the synthesis of xanthenes bearing a 2,3-diaryl substitution pattern [4]. Herein, we report the latest advances in the synthesis of novel 5-arylbenzo[*c*]xanthenes **2** and 1-aryl-9*H*-xanthen-9-ones **4** [5]. 5-Arylbenzo[*c*]xanthenes **2** are obtained by the Heck reaction of 3-bromoflavones **1** with styrene derivatives, leading to (*E*)-3-styrylflavones, followed by an one-pot photoinduced electrocycloisatation and *in situ* oxidation of cycloadducts. The condensation of 2-methylchromone **3** with cinammaldehydes led to (*E,E*)-2-(4-arylbuta-1,3-dien-1-yl)-4*H*-chromen-4-ones, which after an one-pot electrocycloisatation and *in situ* oxidation of cycloadducts gave the desired 1-aryl-9*H*-xanthen-9-ones **4**.



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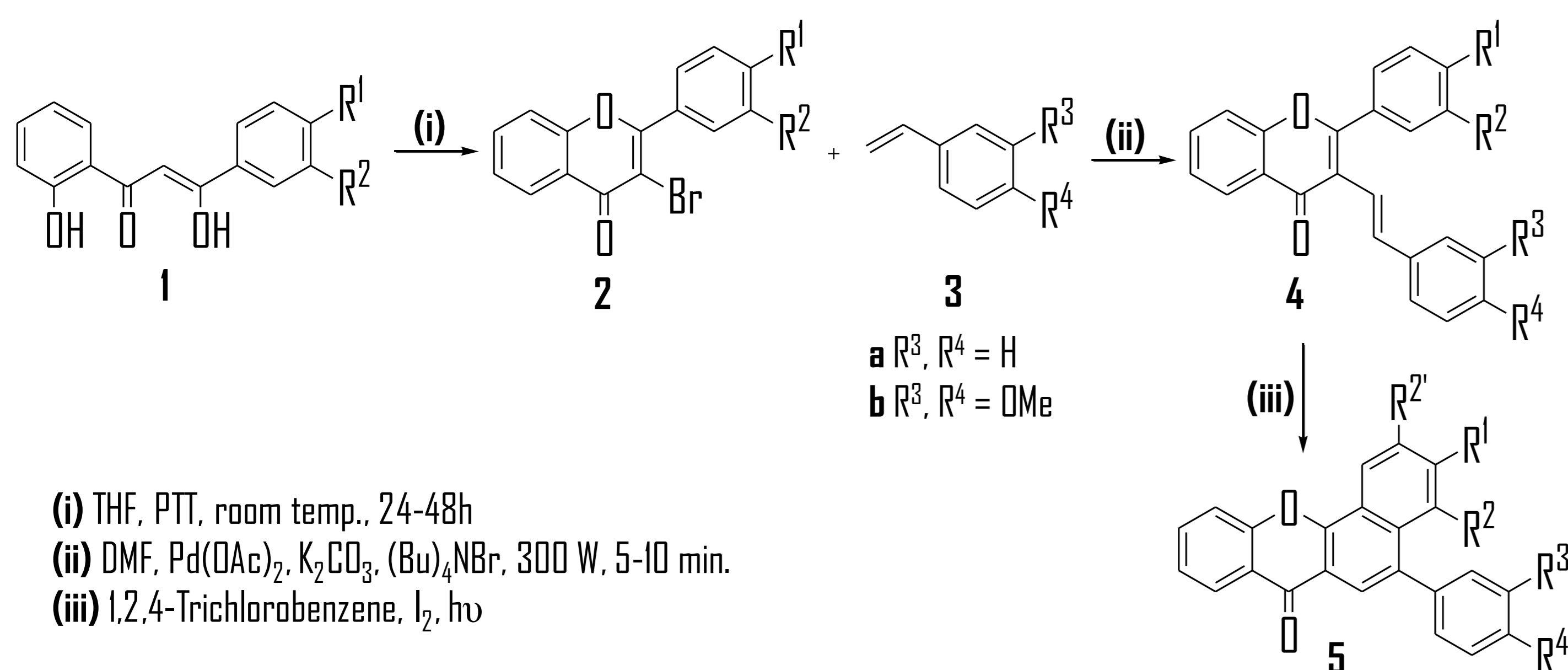
- [1] a) Gales, L.; Damas, A.M. *Curr. Med. Chem.* **2005**, *12*, 2499. b) Vieira, L.M.M.; Kijjoo, A. *Curr. Med. Chem.* **2005**, *12*, 2413.
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INTRODUCTION

- Xanthenes represent an outstanding class of oxygenated heterocycles widespread in nature, commonly distributed in several higher plant families, such as *Gentianaceae*, *Guttiferae* and *Polygalaceae* and in a few families of fungi and lichens [1]. Both natural and synthetic derivatives often endowed with interesting pharmacological properties (e.g. anti-inflammatory, antitumour and antioxidant activities) [1,2].
- Naturally-occurring xanthenes present different types of substituents (e.g. hydroxyl, methoxyl and prenyl groups, among others) in different positions of their scaffold leading to a large variety of analogues [2]. The presence of an aryl ring attached to the xanthere scaffold has only been reported in some synthetic derivatives [3,4].
- We have dedicated our previous work to the development of novel methodologies for the synthesis of xanthenes bearing a 2,3-diaryl substitution pattern [4]. Herein, we report the latest advances in the synthesis of novel 5-arylbenzo[*c*]xanthenes **5** and 1-aryl-9*H*-xanthen-9-ones **9** [5].

SYNTHESIS OF 5-ARYLBENZO[*c*]XANTHONES 5

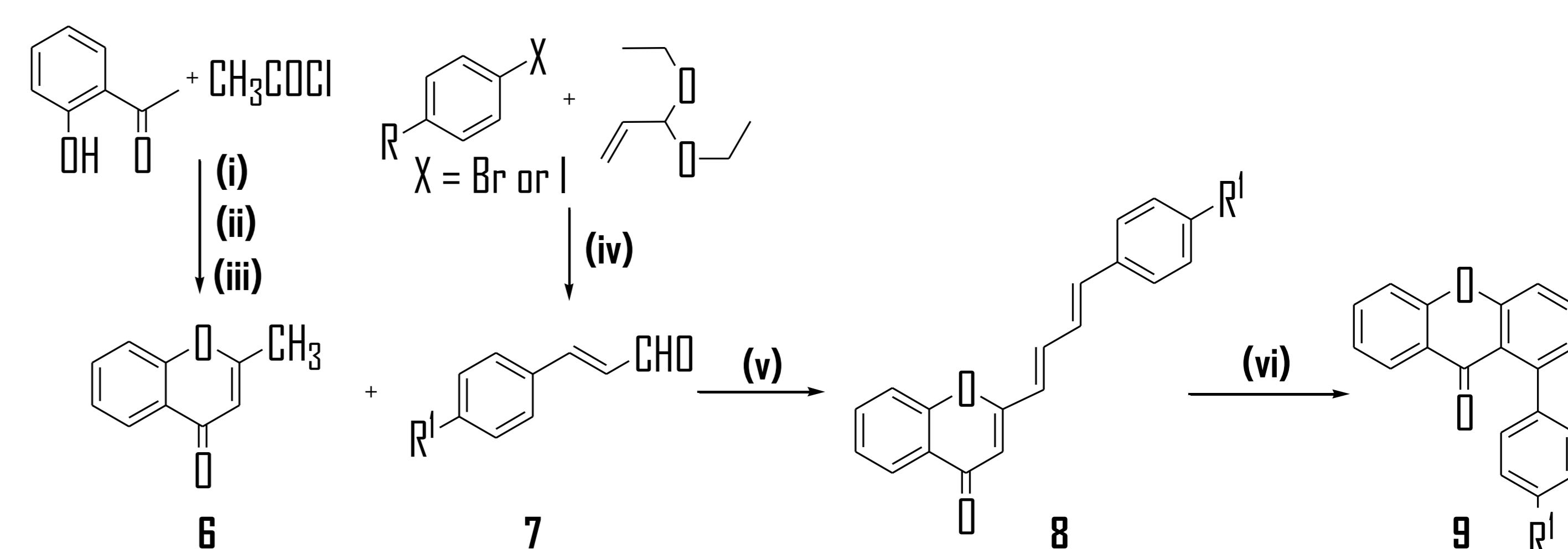
5-Arylbenzo[*c*]xanthenes **5** are obtained by the Heck reaction of 3-bromoflavones **2** with styrene derivatives **3**, leading to (*Z*)-3-styrylflavones **4**, followed by an one-pot photoinduced electrocycloisalisation and *in situ* oxidation of the formed cycloadducts.



3-Bromoflavones 2 η (%)	3-Styrylflavones 4 η (%)	Benzo[xanthenes 5 η (%)
a R ¹ , R ² = H	R ¹ , R ² = H	R ³ , R ⁴ = H
b R ¹ = Me, R ² = H	R ¹ = Me, R ² = H	R ³ , R ⁴ = H
c R ¹ = OMe, R ² = H	R ¹ = OMe, R ² = H	R ³ , R ⁴ = H
d R ¹ = Cl, R ² = H	R ¹ = Cl, R ² = H	R ³ , R ⁴ = H
e R ¹ = NO ₂ , R ² = H	R ¹ = NO ₂ , R ² = H	R ³ , R ⁴ = H
f R ¹ , R ² = OMe	R ¹ , R ² = OMe	R ³ , R ⁴ = H
g ---	R ¹ , R ² = OMe	R ³ , R ⁴ = OMe
h ---	---	---

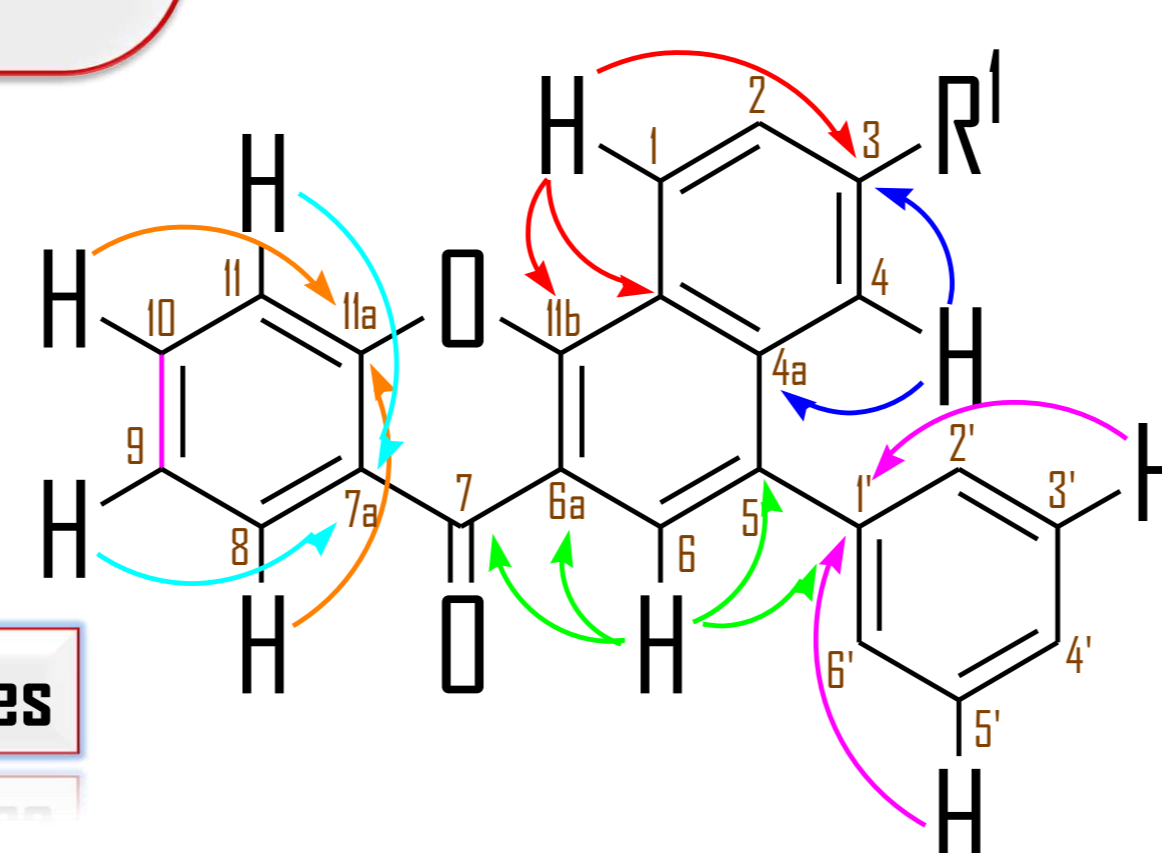
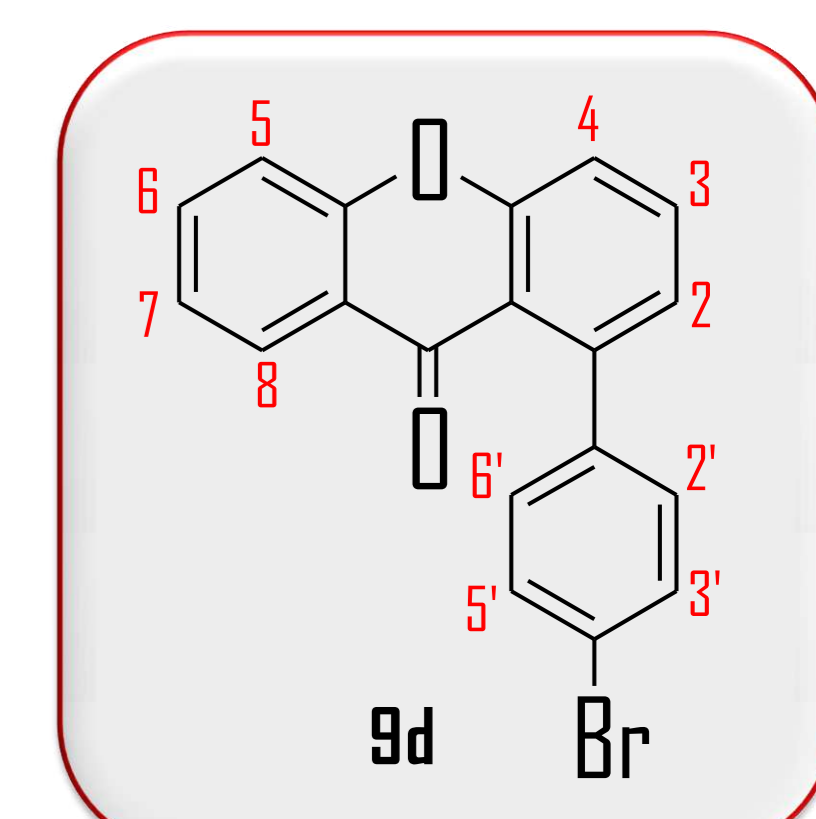
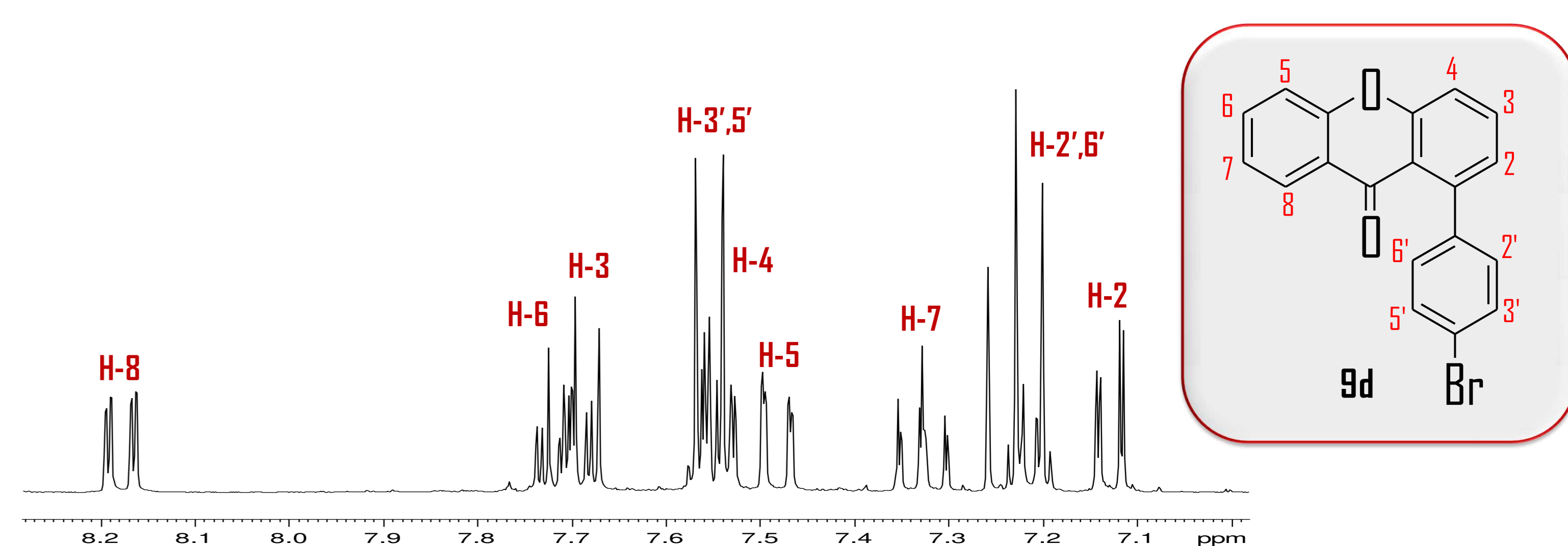
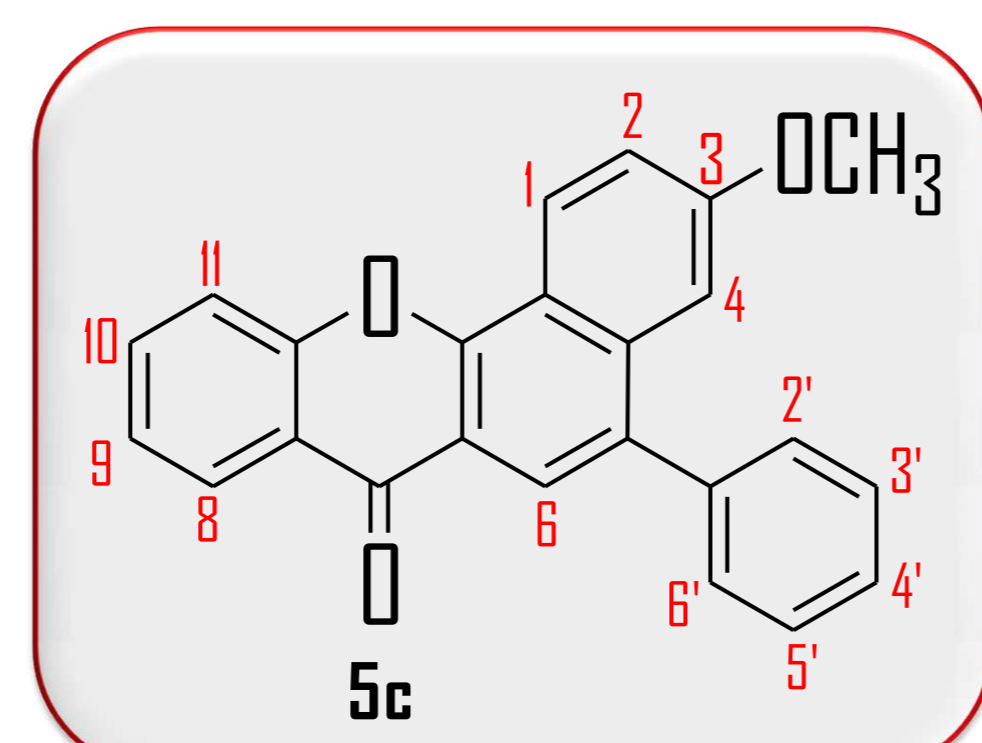
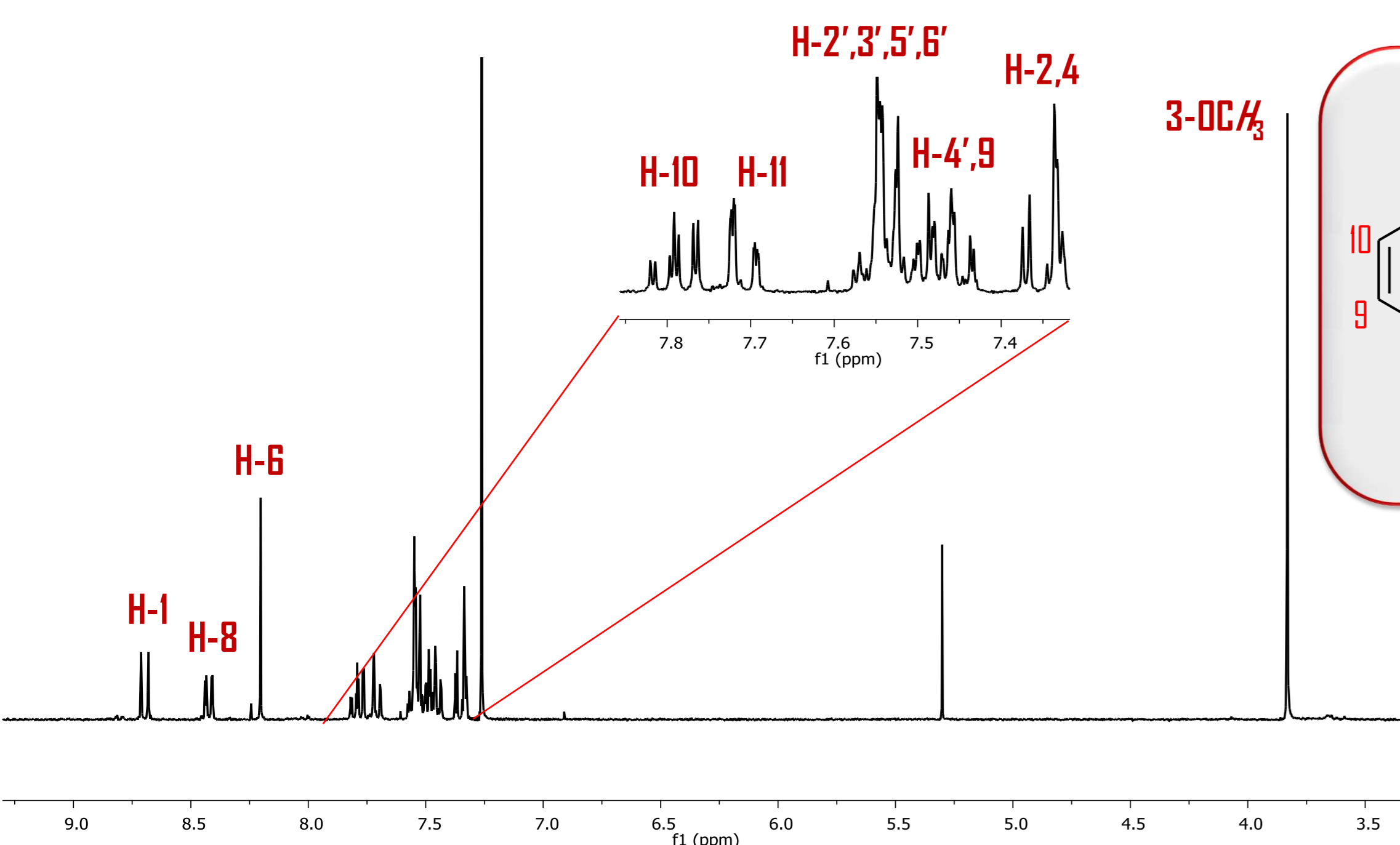
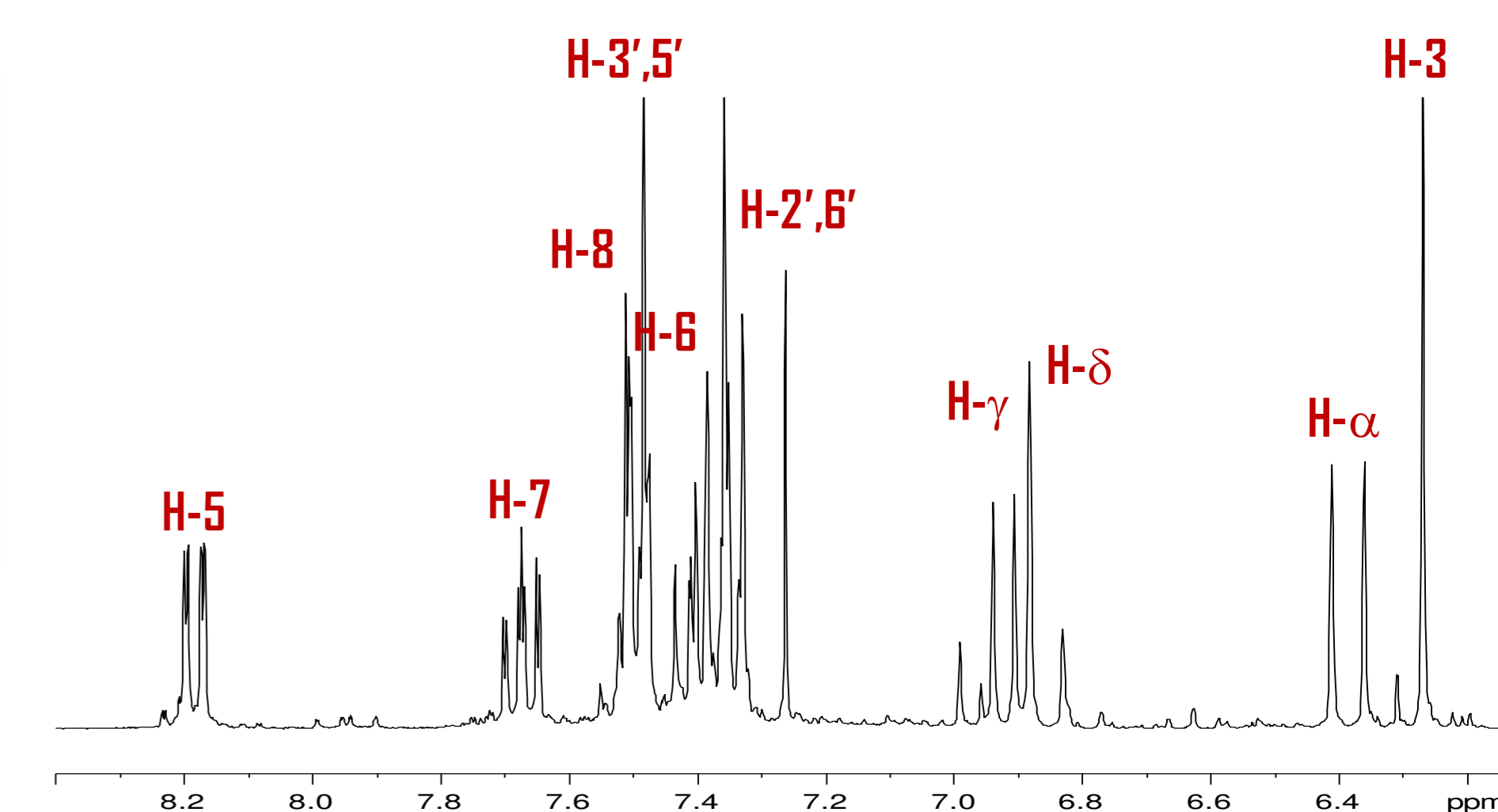
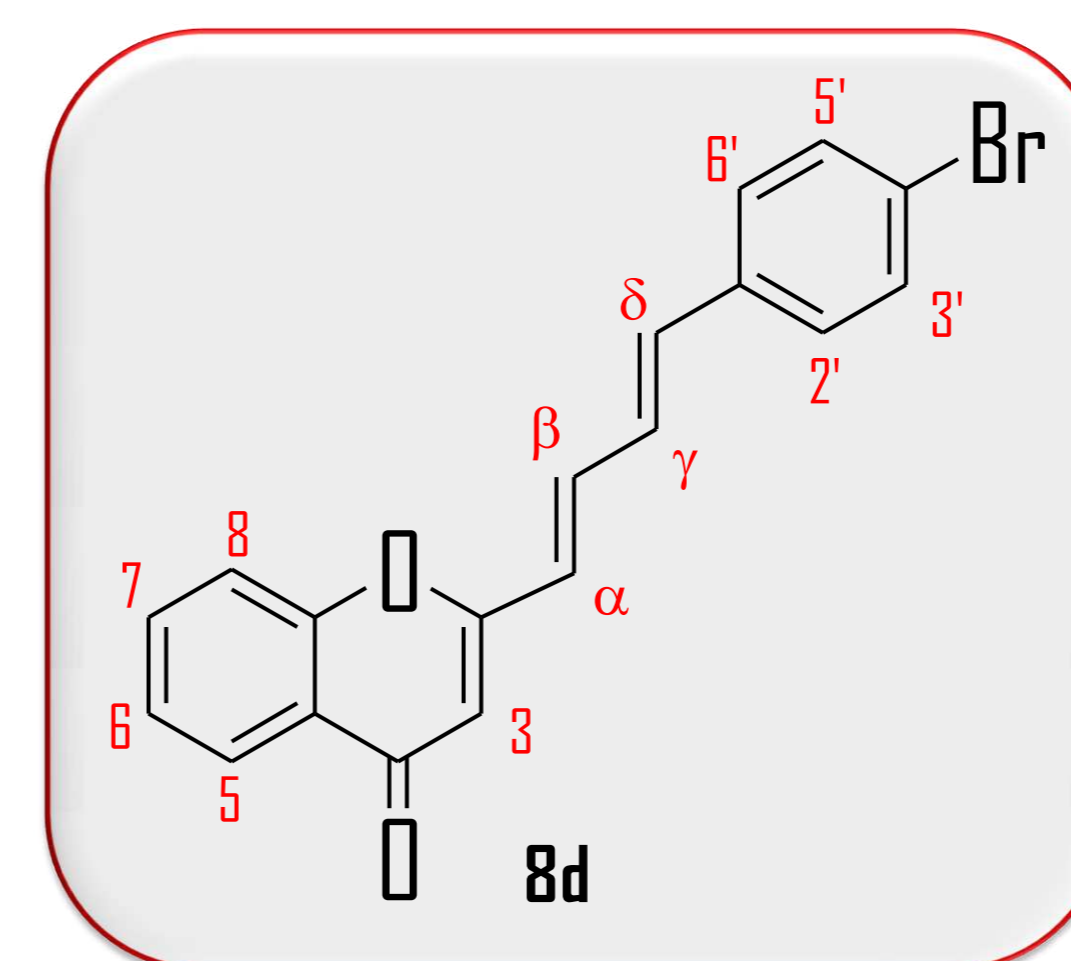
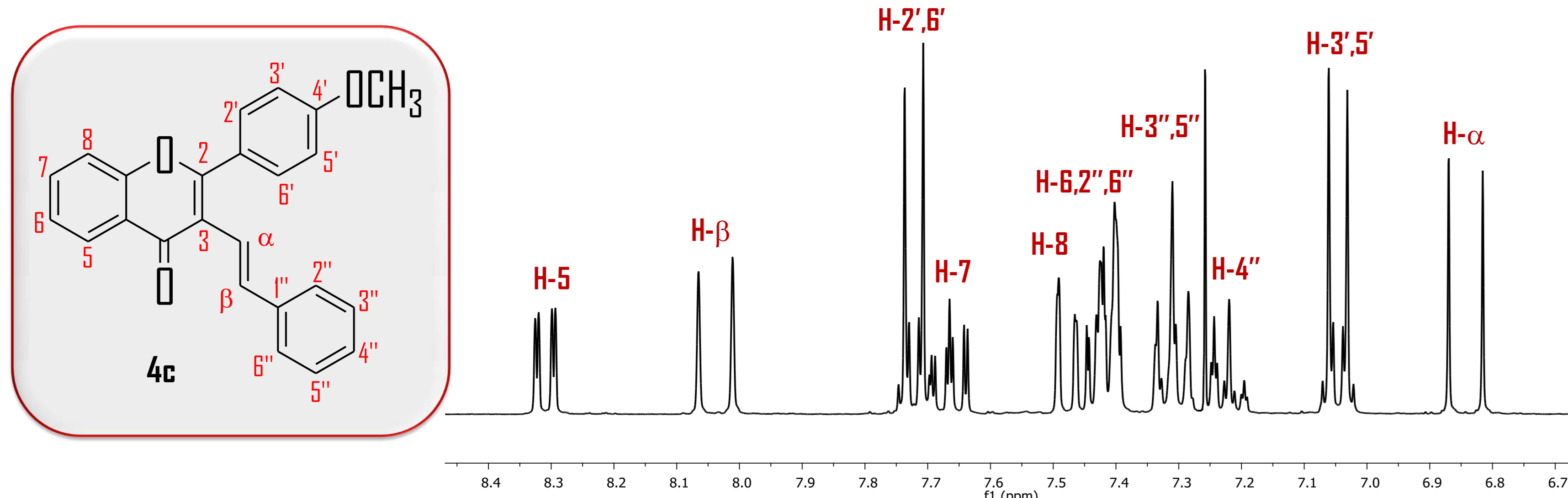
SYNTHESIS OF 1-ARYL-9*H*-XANTHEN-9-ONES 9

The condensation of 2-methylchromone **6** with cinnamaldehydes **7** led to (*E*)-2-(4-arylbuta-1,3-dien-1-yl)-4*H*-chromen-4-ones **8**, which after an one-pot electrocycloisalisation and *in situ* oxidation of the formed cycloadducts gave the desired 1-aryl-9*H*-xanthen-9-ones **9**.

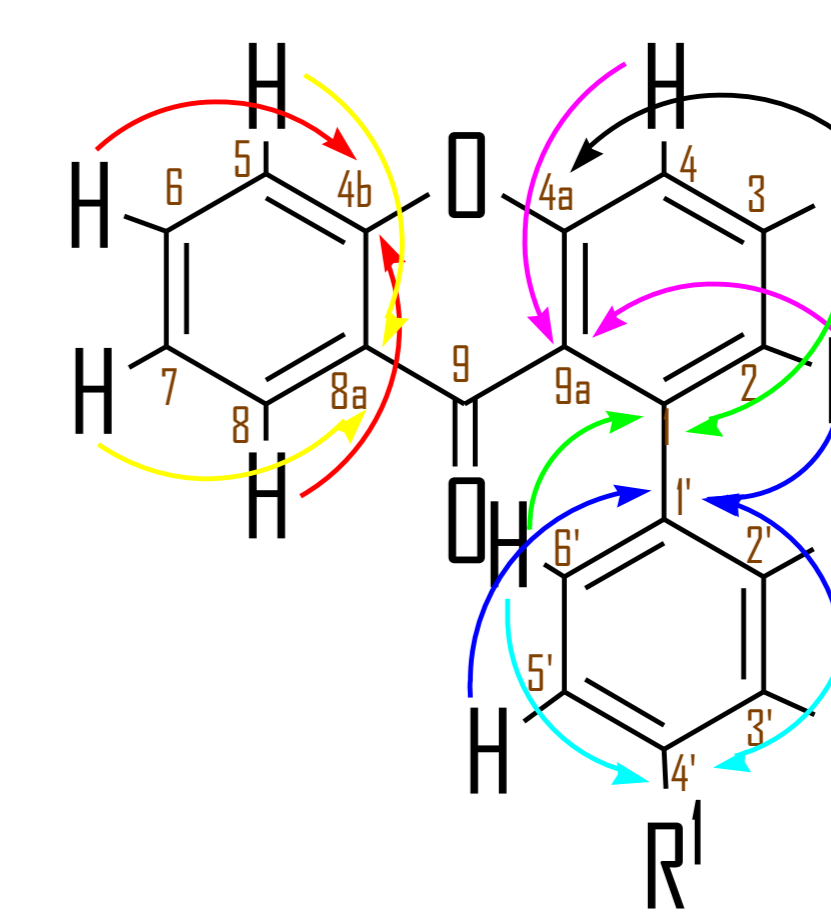


- (i)** Dry Py, room temp., 12h
(ii) Dry THF, NaH, reflux, 1 h
(iii) DMSO, TsOH ac., 100 °C, 2 h
(iv) Dry DMF, Pd(OAc)₂, K₂CO₃, (Bu)₄NOAc, KCl, 90 °C
(v) EtOH, NaOEt, room temp.
(vi) 1,2,4-Trichlorobenzene, I₂, reflux, 48h

	Cinnamaldehydes 7 η (%)	Chromones 8 η (%)	Xanthenes 9 η (%)
a R ¹ = H	-	80	30
b R ¹ = Me	63	77	26
c R ¹ = OMe	68	83	70
d R ¹ = Br	33	70	56
e R ¹ = NO ₂	69	68	50



HMBC connectivities



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