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## Book of Abstracts

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## Nitromethane conjugate addition to 2-[(1*E*,3*E*)-4-arylbuta-1,3-dien-1-yl]-4*H*-chromen-4-ones

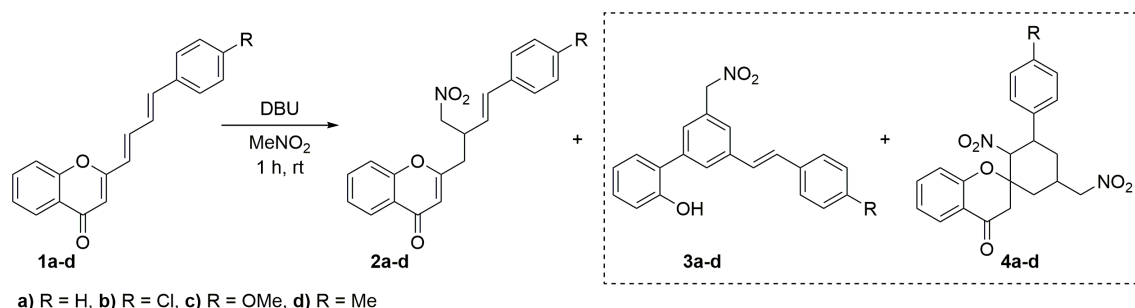
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Chromone are a group of oxygen-containing heterocycles, which are often associated to important biological activities.<sup>1</sup> Chromone derivatives are also seen as interesting scaffolds to input further functionalizations,<sup>2</sup> most of them through chemical transformations such as oxidation, condensation, Diels-Alder or conjugate addition. Conjugate addition of carbon nucleophiles to electron-deficient alkenes is one of the most important methods available for carbon-carbon bond-forming reactions. A wide range of carbon nucleophiles easily undergo conjugate addition with various substrates such as chalcones, cinnamylideneacetophenones or styrylchromones.

Following previous work of our research group involving the 1,6-conjugate addition of nitromethane to (*E*)-2-styrylchromones,<sup>3</sup> herein we report the first reactivity studies in the nitromethane conjugate addition to the extended unsaturated  $\pi$ -system of 2-[(1*E*,3*E*)-4-arylbuta-1,3-dien-1-yl]-4*H*-chromen-4-ones **1** (Scheme 1). The DBU catalyzed nitromethane addition reaction afforded the corresponding  $\beta$ -(nitromethyl)chromones **2** (1,6-conjugate addition) as major products. (*E*)-5'-(Nitromethyl)-3'-styryl-[1,1'-biphenyl]-2-ol **3** and 3'-aryl-2'-nitro-5'-(nitromethyl)spiro [chromane-2,1'-cyclohexan]-4-one **4** derivatives were also isolated as minor products, which result from the addition of two nitromethane molecules, through tandem processes.



Scheme 1: Nitromethane conjugate addition to 2-[(1*E*,3*E*)-4-arylbuta-1,3-dien-1-yl]-4*H*-chromen-4-ones **1**.

Acknowledgements: Thanks are due to University of Aveiro and FCT/MEC for the financial support of the QOPNA research unit (FCT UID/QUI/00062/2013) through national funds and, where applicable, co-financed by the FEDER, within the PT2020 Partnership Agreement, and to the Portuguese NMR Network, as well as to the Polytechnic Institute of Bragança. H.M.T.A. is grateful to FCT for his PhD grant (SFRH/BD/86277/2012).

### References:

1. Gaspar A.; Matos M. J.; Garrido J.; Uriarte E.; Borges F. *Chem. Rev.* **2014**, *114*, 4960.
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# NITROMETHANE CONJUGATE ADDITION TO 2-[(1E,3E)-4-ARYLBUTA-1,3-DIEN-1-YL]-4H-CHROMEN-4-ONES

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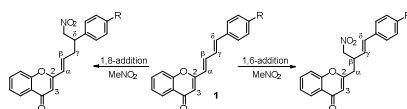
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## Introduction

Following previous work of our research group,<sup>1-3</sup> herein, the reactivity of the extended 3,2:α,β,γ,δ-trisubstituted system of chromones **1** in conjugate addition reactions with nitromethane was addressed. In comparison with 2-styrylchromones, the presence of a third unsaturation extends the π-conjugated system on chromones **1** and allows δ-position to become a novel site for nucleophilic attack (possible 1,8-conjugate addition) (Scheme 1). This feature enables the synthesis of multisubstituted heterocyclic derivatives with new stereocenters.

## Abstract

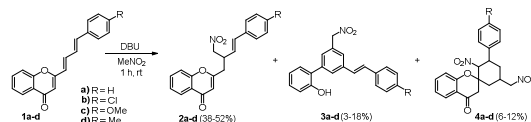
Conjugate addition reaction of nitromethane to the extended π-conjugated system of several chromone derivatives afforded the 1,6-conjugate addition products, together with structure complex oxygen heterocycles through tandem processes.



Scheme 1. Possible sites of conjugate addition to chromones **1**.

## Nitromethane conjugate additions

The DBU-catalyzed addition reaction of nitromethane, under neat conditions, to chromones **1** afforded the β-(nitromethyl)chromones **2** (1,6-conjugate addition) as major products (higher *R<sub>f</sub>*), together with (*E*)-5'-(nitromethyl)-3'-styryl-[1,1'-biphenyl]-2-ol and 3'-aryl-2'-nitro-5'-(nitromethyl)spiro[chromane-2,1'-cyclohexan]-4-one (lower *R<sub>f</sub>*) derivatives **3** and **4**, respectively, as minor products. These byproducts result from the addition of a second molecule of nitromethane, in tandem processes (Scheme 2). The structural elucidation of all compounds was accomplished by NMR (Figures 1-3).



Scheme 2. Nitromethane conjugate addition to chromones **1**.

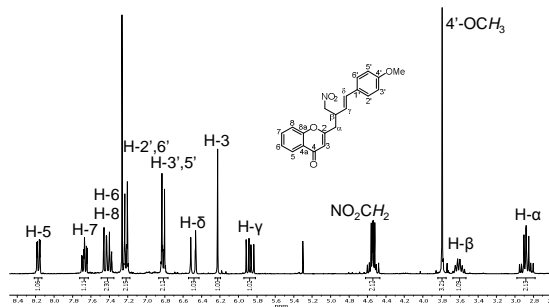
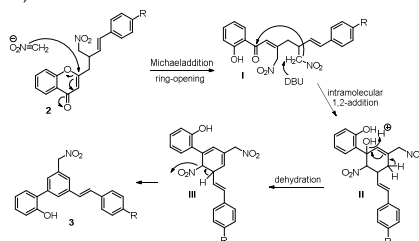


Figure 1. <sup>1</sup>H NMR spectrum of β-(nitromethyl)chromone **2c**.

The formation of derivatives **3** could be explained based on the Michael addition of a nitromethane anion to C-2 of β-(nitromethyl)chromones **2** along with chromone ring opening to give intermediates **I**. A DBU-catalyzed intramolecular 1,2-addition led to intermediates **II**, which upon dehydration affords intermediates **III**, that affords derivatives **3** after HNO<sub>2</sub> elimination (Scheme 3).



Scheme 3. Proposed mechanism towards the formation of compounds **3**.

## Acknowledgements

Thanks are due to FCT/MEC for the financial support of the QOPNA research unit (FCT UID/QUI/00062/2013) through national funds and, where applicable, co-financed by the FEDER, within the PT2020 Partnership Agreement, and to the Portuguese NMR Network. H.M.T.A. is grateful to FCT for his PhD grant (SFRH/BD/86277/2012).

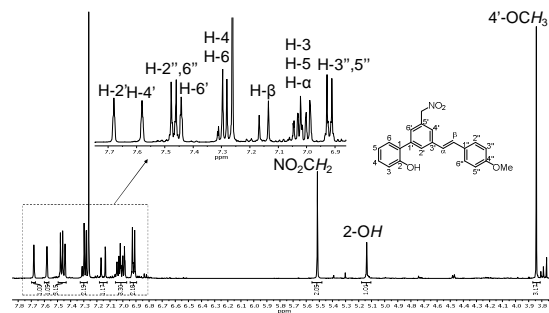
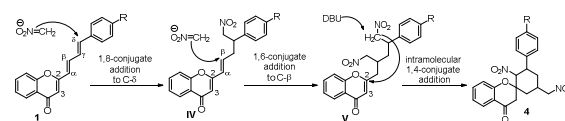


Figure 2. <sup>1</sup>H NMR spectrum of (*E*)-3'-(4-methoxystyryl)-5'-(nitromethyl)-[1,1'-biphenyl]-2-ol (**3c**).

The plausible mechanism for the formation of derivatives **4** involves the 1,8-conjugate addition of a nitromethane anion to C-δ of chromones **1**, affording intermediates **IV**. Then, the 1,6-conjugate addition of another nitromethane anion to C-β of **IV** gives intermediates **V**, which undergoes DBU-catalyzed intramolecular 1,4-conjugate addition to C-2 leading to the formation of the spiro trisubstituted cyclohexanes **4** (Scheme 4).



Scheme 4. Proposed mechanism towards the formation of compounds **4**.

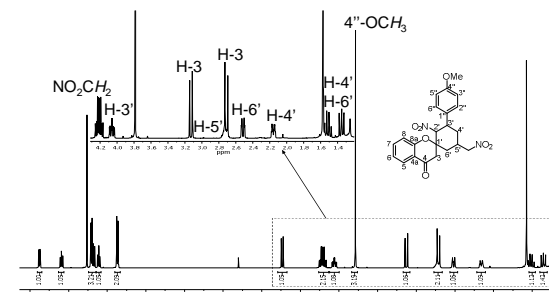


Figure 3. <sup>1</sup>H NMR spectrum of 3'-(4-methoxyphenyl)-2'-nitro-5'-(nitromethyl)spiro[chromane-2,1'-cyclohexan]-4-one (**4c**).

## Conclusion

The conjugate addition reaction of nitromethane to chromones **1** afforded β-(nitromethyl)chromones **2** as major products, as well as compounds **3** and **4** as minor ones, which are formed through tandem processes, due to the competition of 1,6 and 1,8 addition reactions.

## References

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