Synthesis of fused chromene-1,4-naphthoquionones under acid catalysis and microwave irradiation

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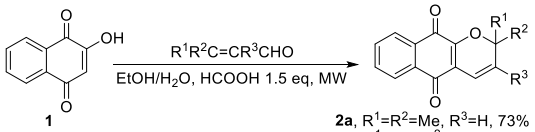
INTRODUCTION

The moiety 2*H*-chromene are often found in different natural products, which exhibit different biological activities.[1] Among them, an important family are chromenes coupled with *ortho*-and *para*-quinones that have been isolated from many types of plants, fungi and insects.[2] The wide range of important biological activities of these molecules has stimulated further research into the synthesis of natural and synthetic benzochromenes coupled with *ortho*- and *para*-quinone derivatives.
In this work we developed the synthesis of fused chromene-1,4-naphthoquionones.

RESULTS AND DISCUSSION

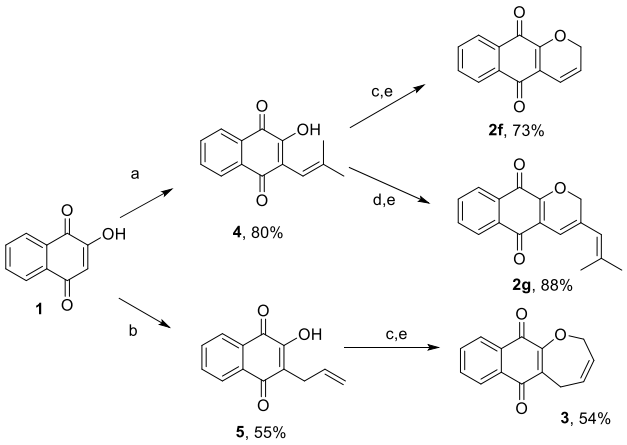
As previously mentioned, chromenes are substances of great importance in chemistry, but there are few methods to synthesize these compounds. The methodology used herein apply formic acid for the Knoevenagel condensation between lawsone (**1**) and α,β-unsaturated aldehydes to generate the ortho-quinone methide (*o*-QMS) intermediates; this was followed by 6π-electrocyclization to yield the α-xiloidone analogues **2a-e**. (Scheme 1)



2a, R^1=R^2=Me, R^3=H, 73%
2b, R^1=Me; R^2=CH_2-Prenyl, R^3=H, 70%
2c, R^1=R^2=H, R^3=Me, 70%
2d, R^1=Me, R^2=R^3=H, 54%
2e, R^1=R^3=H, R_2=Pr, 46%

Scheme 1. Synthesis of xiloidones by electrocyclization

Given the difficulty of synthesizing other xyloidone derivatives, we attempted another synthetic method involving the *O*- and *C*-alkylation of lawsone followed by cyclization using ring-closing metathesis (RCM), yielding compounds **2f-g** and **3**. (Scheme 2)



Three Steps (a or b, c or d then e)
a) $(CH_3)_2CH_2CHO$, TsOH, $PhCH_3$, reflux or b) Allyl Bromide, DMF, K_2CO_3, MW.
c) Allyl Bromide, Acetone, K_2CO_3
d) Propargyl Bromide, Acetone, K_2CO_3
e) CH_2Cl_2, Grubbs catalyst, reflux

Scheme 2. Synthetic xyloidone derivatives obtained using ring-closing metathesis

CONCLUSION

The methodologies explored herein for synthesis of fused chromene-1,4-naphthoquinones, applying Knoevenagel-electroncyclization reaction or ring close metathesis (RCM) led successfully to several α and β-xiloidones in moderate to good yields .

ACKNOWLEDGEMENTS

CAPES CNPq FAPERJ PRONEX FAPERJ

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[2] Curtis, M. D.; Shiu, K.; Butler, W. M. e Huffmann, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 3335.