Towards the development of a simple procedure for the synthesis of α- and β-pyranonaphthoquinone derivatives through microwave-assisted reactions.

Milena O. Macedo[1] (IC); Ruan C. B. Ribeiro[2] (PG); Pone K. Boniface[1] (PQ); Fernando de C. da Silva[2] (PQ); Carlos R. Kaiser[1] (PQ); Vitor F. Ferreira[2*] (PQ); Sabrina B. Ferreira[1*] (PQ); sabrinab@iq.ufrj.br

[1]Universidade Federal do Rio de Janeiro, Instituto de Química, Departamento de Química Orgânica, LaSOPB, 21949-900, Rio de Janeiro, Brasil; [2]Universidade Federal Fluminense, Instituto de Química, Departamento de Química Orgânica, 24020150, Niterói, Brasil.

Palavras Chave: *pyranonaphthoquinones; microwave; synthesis; o-quinone methide*

Abstract

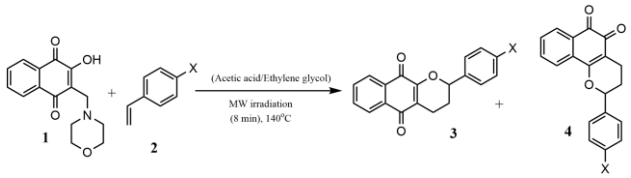
We have demonstrated a new route for the synthesis of α- and β-pyranonaphthoquinone derivatives from intermediate *o*-quinone methide (*o*-QM).

Introduction

Naphthoquinone is a class of organic compounds derived from naphthalene. Pyranonaphthoquinone and their derivatives have been reported to possess a wide range of biological activities that are of importance for drug development, including anticancer and antibacterial activity.[1] Consequently, the synthesis of pyranonaphthoquinones with different substitution patterns and with very simple, timesaving and convenient method has drawn much research interest. The present study aim to develop a novel route for the synthesis of pyranonaphthoquinones (α and β) and their derivatives through microwave assisted organic synthesis by using 2-hydroxy-3-(morpholinomethyl)-2,3-dihydronaphthalene-1,4-dione (**1**) as precursor along with acetic acid, ethylene glycol and some substituted styrenes.

Results and Discussion

First, 2-hydroxy-3-(morpholinomethyl)naphthalene-1,4-dione (**1**) was obtained from the reaction of lawsone, morpholine, ethanol and paraformaldehyde according to previously described protocol[2] with minor modifications. The obtained compound (**1**) was further subjected to microwave irradiation conditions (140 ^{o}C, 8 min.) alongside acetic acid, ethylene glycol and some substituted styrenes (Scheme 1). Under these reaction conditions, the yields of the β isomers of the pyranonaphthoquinones were found to be increased as compared to the results reported previously by Silva *et al.* (2009)[3] in which the α isomers of pyranonaphthoquinones were predominant. In these experiments, the formation of the by-product benzoxanthene (reaction that take place between the intermediate isoforms when the time of the reaction is lengthy) was negligible under microwave irradiation situations.



Scheme 1. Synthesis of α- and β-pyranonaphthoquinones

Table 1. Table showing the yields of the reactions under microwave irradiation conditions

Substituted styrenes	Yields of β- isomer	Yields of α-isomer
Stryrene	43%	26%
4- chlorostyrene	43%	36%
4-bromostyrene	29%	33%
4-methylstyrene	61%	56%
2,4-dimethylstyrene	47%	43%
4-Fluorostyrene	28%	8%
4-methoxystyrene	72%	12%

Conclusion

In summary, we have demonstrated a rapid and direct method that offers a simple and efficient route for the synthesis of biologically important pyranonaphthoquinones with excellent yields of the β isomers. The present findings showed a new route for the synthesis of α- and β-pyranonaphthoquinone derivatives from intermediate (3*H*)-naphthalenetrione-3-(4-morpholinylmethyl) produced from 2-hydroxy-3-(morpholinomethyl)naphthalene-1,4-dione (**1**). Particularly, valuable features of this method included operational simplicity, minimal environment impact, high yields, increased safety for small scale as well as short reaction time.

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