

Synthesis of New N,O-Acetals 2-Amino-1,4-naphthoquinones Derivatives Under Microwave Irradiation

Alessandro K. Jordão,^a David R. da Rocha,^a Vitor F. Ferreira^{*a}

^aUniversidade Federal Fluminense, Instituto de Química, Departamento de Química Orgânica, 24020-141 Niterói, Rio de Janeiro, Brazil

ceguito@vm.uff.br

Keywords: Naphthoquinones, N,O-Acetals, Microwave in organic synthesis

INTRODUCTION

Naphthoquinones are important natural substances that are widely distributed in different families of plants, fungi and some animals.¹ The introduction of amino substituents onto the quinone moiety can exert influence on its redox properties, inducing oxidative stress in cells and alkylation of DNA. The aminoquinones are found in important bioactive compounds such as antitumor² (1) and antimalarial³ (2) agents.

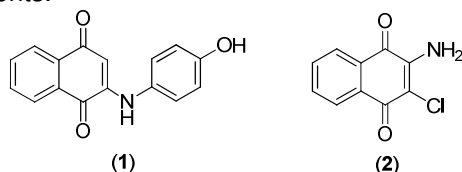
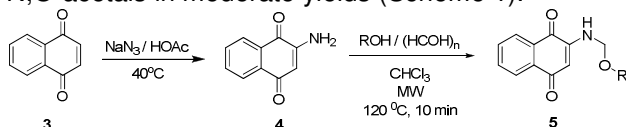


Figure 1. Examples of bioactive aminonaphthoquinones.

RESULTS AND DISCUSSION

The aim of this work is the synthesis of a new series of N,O-acetals 2-amino-1,4-naphthoquinone derivatives to evaluate biological activity. N,O-acetals are related by Barluenga and co-workers⁴ as compounds unstable at room temperature that need to be stored at -18°C to avoid decomposition. Herein we describe a methodology employing microwave irradiation to obtain in satisfactory yields stabiles N,O-acetals. In the first step 1,4-naphthoquinone (3) was used as the starting material, which was reacted with sodium azide in acetic acid to produce 2-amino-1,4-naphthoquinone (4).⁵ Addition Reaction of 4 with paraformaldehyde in the presence of alcohols under microwave irradiation formed the N,O-acetals in moderate yields (Scheme 1).



Scheme 1. Synthesis of N,O-acetals of 2-amino-1,4-naphthoquinones 5a-e.

Exploring this reaction, it was possible to prepare in moderate to good yields N,O-acetals 2-amino-1,4-naphthoquinones derivatives (5a-e), which are shown in the Table 1.

The reactions were performed in a closed glass vessel in chloroform. These compounds were characterized by spectroscopic methods such as ¹H and ¹³C NMR. This is the first example of stabiles N,O-acetals naphthoquinones and the compounds synthesized are very promising for biological activity screenings.

Table 1. Yields of the N,O-acetals of 2-amino-1,4-naphthoquinones 5a-e

| Product | R | Yield (%) |
|---------|--|-----------|
| 5a | -CH ₃ | 74 |
| 5b | -CH ₂ CH ₃ | 47 |
| 5c | -CH ₂ C ₆ H ₅ | 45 |
| 5d | -C≡CH | 21 |
| 5e | (Methyl-5'-deoxy-2',3'-O-isopropylidene-β-D-ribofuranosid-5'-yl) | 35 |

CONCLUSION

In summary, we reported herein the synthesis of a novel series of N,O-acetals 2-amino-1,4-naphthoquinones derivatives under microwave irradiation.

ACKNOWLEDGEMENTS

CNPq, FAPERJ-PRONEX, FINEP e CAPES-PNPD

REFERENCES

- 1 Franco, C. F. J.; Jordão, A. K.; Ferreira, V. F.; Pinto, A. C.; de Souza, M. C. B. V.; Resende, J. A. L. C.; Cunha, A. C. *J. Braz. Chem. Soc.* **2011**, 22, 187.
- 2 Benites, J.; Valderrama, J. A.; Bettega, K.; Pedrosa, R. C.; Calderon, P. B.; Verrax, J. *Eur. J. Med. Chem.* **2010**, 45, 6052.
- 3 Kapadia, G. J.; Azuine, M. A.; Balasubramanian, V.; Sridhar, R. *Pharmacol. Res.* **2001**, 43, 363.
- 4 Barluenga, J.; Bayón, A. M.; Campos, P.; Asensio, G.; Gonzalez-Nuñez, E.; Molina, Y. J. *J. Chem. Soc. Perkin. Trans. I* **1988**, 1631.
- 5 Fieser, L. F.; Hartwell, J. L. *J. Am. Chem. Soc.* **1935**, 57, 1482.