Synthesis of isobenzofuranones by Diels-Alder reaction

Milena G. Teixeira1, Elson S. Alvarenga1, Antonio J. Demuner1, Célia R. A. Maltha1, Luiz Claudio A. Barbosa2

1LASA, Departamento de Química, Universidade Federal de Viçosa, UFV, Viçosa, MG, 36571-000
2Departamento de Química, Universidade Federal de Minas Gerais, UFMG, Belo Horizonte, MG

Keywords: γ-lactones, Diels-Alder and phthalides.

INTRODUCTION

Phthalides or isobenzofuranones are fused γ-lactones with an aromatic ring which have attracted the attention of many research groups because of their wide spectrum of activity as antifungal, antibacterial, antiviral, etc1. The α,β-unsaturated lactones are found as structural subunits in a wide variety of natural products possessing diverse biological activities2. Furthermore, simple lactones have been used as intermediates for the synthesis of biologically active compounds. In the present work we have synthesized 9-carbon lactones with structures similar to natural phthalides through Diels-Alder (DA) reaction. For this goal, furan-2(5H)-one has acted as an excellent dienophile in cycloaddition reactions with cyclopentadiene.

RESULTS AND DISCUSSION

Initial studies focused on a reaction between cyclopentadiene with furan-2(5H)-one (1) (Scheme 1). In a typical procedure, addition of 10.0 equivalents of cyclopentadiene to a solution of (1) in dry toluene were heated (72 h, 100°C).

Scheme 1. Diels-Alder reaction of furan-2(5H)-one with cyclopentadiene.

The relative stereochemistry of (1a) and (1b) was determined using the NOEDIFF experiments (Figure 1 and Figure 2).

Figure 2. Representation of positive NOE interactions for compounds (1a) and (1b).

Following our synthetic route, the adducts (1a) and (1b) were subjected to hydrogenation, halogenation and epoxidation reactions as Scheme 2. Structures of the products were determined by 1H NMR, 13C NMR, HETCOR, NOEDIFF, IR and mass spectra.

CONCLUSION

Were prepared ten analogues of phthalides using as main tool the Diels-Alder reaction, which allowed obtaining highly functionalized bicyclic compounds.

ACKNOWLEDGEMENTS

FAPEMIG, CAPES, CNPq and UFV.

REFERENCES