Synthesis of isobenzofuranones by Diels-Alder reaction

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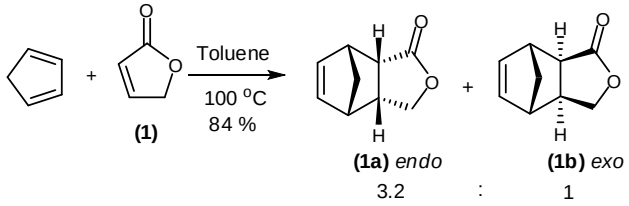
Keywords: γ-lactones, Diels-Alder and phthalides.

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, etc[1]. The *α*,*β*-unsaturated lactones are found as structural subunits in a wide variety of natural products possessing diverse biological activities[2]. 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.

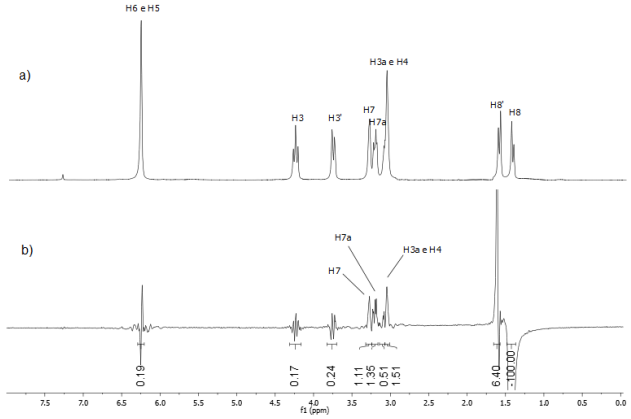


Figure 1. a) ^{1}H NMR spectra of **(1a)**; b) Representative NOEDIFF by irradiating H8 of **(1a)**.

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

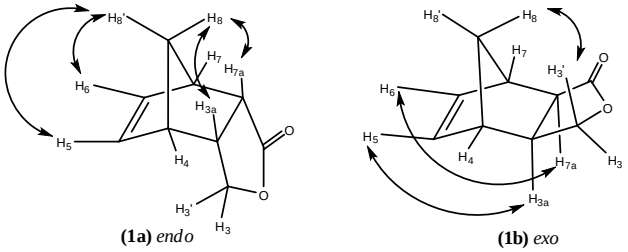
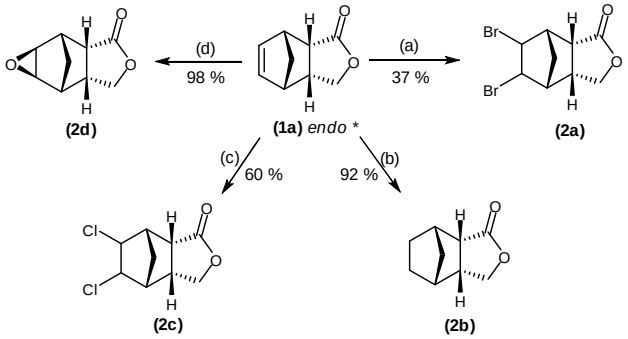


Figure 2. Representation of positive NOE interactions for compounds **(1a)** and **(1b)**.

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 ^{1}H NMR, ^{13}C NMR, HETCOR, NOEDIFF, IR and mass spectra.



* The adduct **(1b)** was submitted the same reactions as compound **(1a)**.

Scheme 2. (a) Br_2, CH_2Cl_2; (b) H_2, Pd/C (10%), EtOH; (c) Cl_2, CH_2Cl_2; (d) MCPBA, CH_2Cl_2.

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.

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