

# Mechanistic Studies of the Formation of Functionalized Cyclopropanes through Photoisomerization of Tropolone Diels-Alder Adducts

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## INTRODUCTION

Our search for novel chemotherapeutic agents against parasitic diseases has led to a series of bridged hydrazines (**Figure 1, 1a-e**).<sup>1-5</sup> Some of these compounds display promising *in vitro* activities against *Trypanosoma cruzi* and *Leishmania donovani*. To expand the structural diversity of our libraries, and based on results obtained for similar  $\beta,\gamma$ -unsaturated ketone chromophores,<sup>7,8</sup> we studied the photoisomerization these alkyltropolone derivatives. As detailed herein, irradiation of these compounds leads to functionalized cyclopropanes in good yields. Mechanistic studies revealed that the process is stereospecific, proceeds through the formation of allyl radical and ketene intermediates, and involves participation of the solvent.

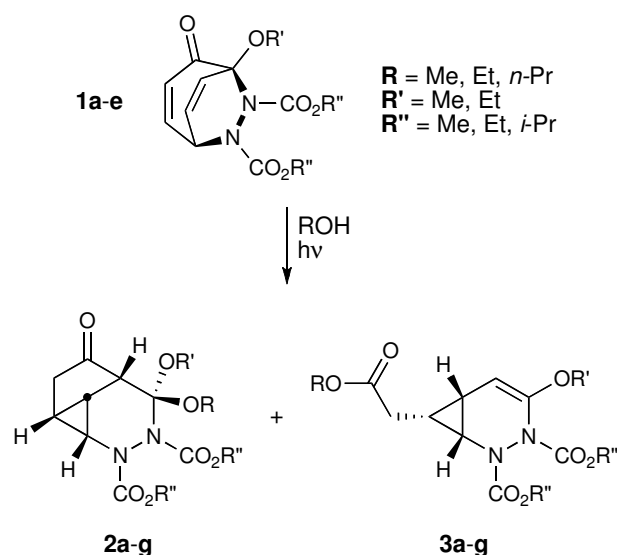
## RESULTS AND DISCUSSION

A survey of reaction conditions indicated that irradiations using alcohols as solvent and a soda-lime glass reactor led in all cases to two isomeric products in high combined yield. Together with HR-MS data, careful interpretation of the 1D and 2D (COSY, HMQC, and HMBC) <sup>1</sup>H and <sup>13</sup>C NMR spectra for both compounds allowed us to elucidate their structures as those shown in **Figure 1 (2a-g and 3a-g)**. Deuterium labeling, in combination with NMR and HR-MS experiments, confirmed the participation of the solvent in the reaction as well as the stereochemical outcome of the process. Based on the results from these studies it was also possible to postulate a detailed reaction mechanism. The stereospecific process is initiated through formation of an allyl radical, which after a 1,3-shift recombines into an unstable intermediate bearing cyclopropane, enolether, and ketene moieties. Attack of the solvent on either the ketene or enolether groups results in the isolated products.

## CONCLUSION

Photoisomerization of tropolone derivatives using alcohols as reaction media leads to novel

substituted cyclopropanes in high yields. The biological evaluation of these and related compounds is currently underway and will be reported in due course.



**Figure 1.** Structure of alkyltropolone Diels-Alder adducts and their photoisomerization products.

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