Study on Diels–Alder reaction of Spilanthol.

Rodrigo Barrón Velázquez[1], Mariana Macías Alonso[1], Edgar Juárez Robles[1] and Joaquín González Marrero[1,*].

[A1] National Polytechnic Institute – UPIIG, Av. Mineral de Valencia No. 200, Col. Fracc. Industrial Puerto Interior, Silao de la Victoria, Guanajuato, 36275, Mexico.

*Correspondence: **jgonzalezm@ipn.mx**

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INTRODUCTION.

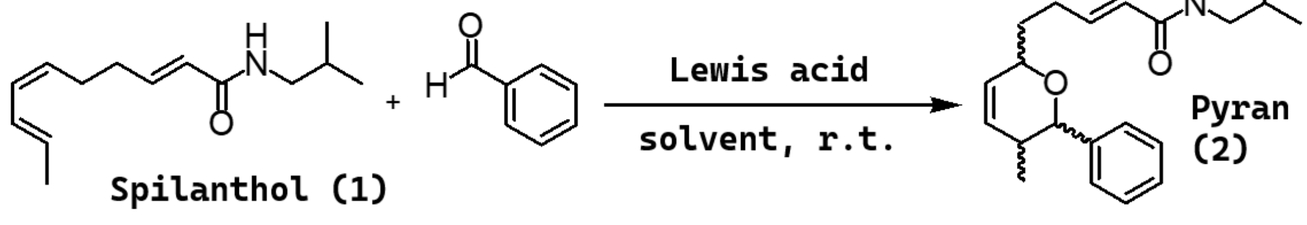
Spilanthol (1), or (2E,6Z,8E)-N-isobutyl-2,6,8-decatrienamide, is a naturally occurring N-alkylamide found in various medicinal plants, notably Heliopsis longipes, widely used in traditional remedies across the globe [1]. Structurally, spilanthol features an unsaturated amide and a conjugated diene system, rendering it an intriguing compound for Diels–Alder cycloaddition reactions. Its use as a renewable scaffold opens a sustainable route for the synthesis of structurally diverse, potentially bioactive heterocycles, contributing to the advancement of green synthetic methodologies.

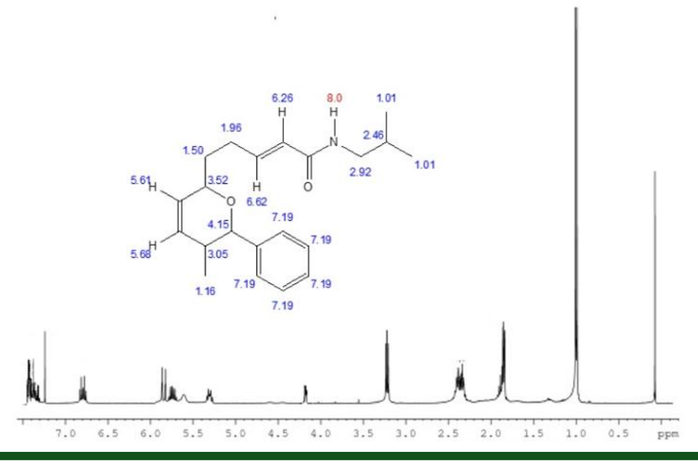
MATERIALS AND METHODS.

Spilanthol (1) was extracted from dried roots of H. longipes via ethanol maceration and purified by column chromatography. Cycloaddition reactions were performed using various dienophiles (1.2 equiv) in suitable solvents (0.2 mM concentration). A range of Brønsted and Lewis acids was evaluated as catalysts. TLC monitored reaction progress, and the crude products were purified by flash chromatography.

RESULTS AND DISCUSSION.

Among the dienophiles evaluated, p-anisaldehyde, in combination with the Lewis acid $BF_3 \cdot OEt_2$, effectively promoted the formation of the desired [4+2] cycloadduct [2]. Neither thermal conditions nor other Lewis acids yielded the product, often resulting in decomposition or no reaction. The use of $BF_3 \cdot OEt_2$ led to a pyran derivative (2) [3] with an isolated yield of 9% for the endo isomer and 23% for the exo isomer. The structure of both products was confirmed by NMR spectroscopy.





CONCLUSIONS.

This work highlights spilanthol (1) as a promising, bio-based diene for Diels–Alder chemistry. The use of $BF_3 \cdot OEt_2$ as a promoter enables efficient, one step access to heterocyclic scaffolds from renewable plant resources. These findings underscore the potential of natural alkamides in green synthetic strategies and their relevance in the development of novel pharmacophores from biomass-derived starting materials.

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