

# ***N,N*-Diethyl-1-Tosyl-3-Indoleglyoxylamide as a Dienophile in Diels-Alder Reactions. Hyperbaric vs. Thermal Conditions**

**B. Biolatto, M. Kneeteman and P.M. Mancini**

Laboratorio Fester, Dpto. de Química, Facultad de Ingeniería Química, Universidad Nacional del Litoral, Santiago del Estero 2829, 3000, Santa Fe, Argentina

E-mail: pmancini@fiquis.unl.edu.ar

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**Abstract:** Under high pressure conditions, the Diels-Alder reaction involving *N,N*-diethyl-1-tosyl-3-indoleglyoxylamide and 1-(*N*-acetyl-*N*-propylamino)-1,3-butadiene produces a highly functionalized intermediate for the synthesis of Indole Alkaloids, in shorter times and higher yields than under thermal conditions.

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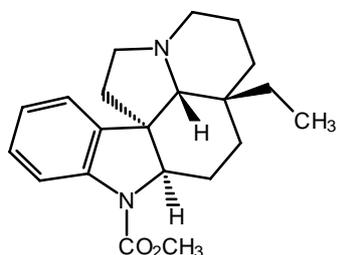
## **Introduction**

From the limited number of heteroaromatic compounds which can act as dienophiles in normal Diels-Alder (D-A) reactions [1], 1-tosyl-3-nitroindole proves to be the most reactive, leading to high yields in dihydrocarbazoles with nitrous acid extrusion in the reactions involving isoprene (155°C, 26 hours), 1-(*N*-acetyl-*N*-propylamino)-1,3-butadiene (90°C, 96 hours) and 1-(*N*-benzoyl-*N*-benzylamino)-1,3-butadiene (130°C, 96 hours) [1,2]. The reactions with Danishefsky diene (65°C, 24 hours) produces adducts that keep the original functionality [3]. Under hyperbar conditions (12 kbar, room temperature), the named reactions offer products keeping the nitro-substitution, except with the dienamides, where the dihydrocarbazole is still the main product [3]. The *N,N*-diethyl-1-tosyl-3-indoleglyoxylamide **1** is, between the acyl-substituted indoles, the one that produces the highest yields reacting with isopren [1], constituting therefore a potentially suitable substrate for the comparative study of the D-A reactions with 1-(*N*-acetyl-*N*-propylamino)-1,3-butadiene **2** under hyperbar and thermal conditions. Complementary, it would allow to synthesise properly substituted intermediates for the advanced synthesis of Indole Alkaloids, such as (-)-*Aspidospermine* (Scheme 1).

## **Experimental**

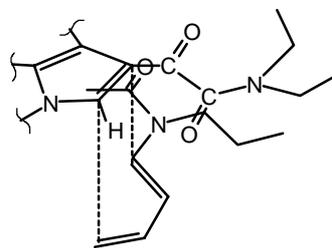
The thermal reaction between the indoleglyoxamide **1** and the dienamide **2** should be carried out at high temperatures in order to induce the dienophilic character of **1**. The maximum limit of temperature is set in 130°C, due to the thermal instability of the dienamide **2**. Under thermal conditions (120°C, 96 hours) the reaction leads to two diastereomeric adducts (total regioselectivity) in very low yields (ca.

9%). Under hyperbar conditions (11.5 kbar, 40°C, 48 hours), the reaction leads to 50% of a single isomer **3** (Scheme 3), which arises from the *exo* addition (Scheme 2). This experimental condition allows to recover ca. 48% of the unreacted dienophile.



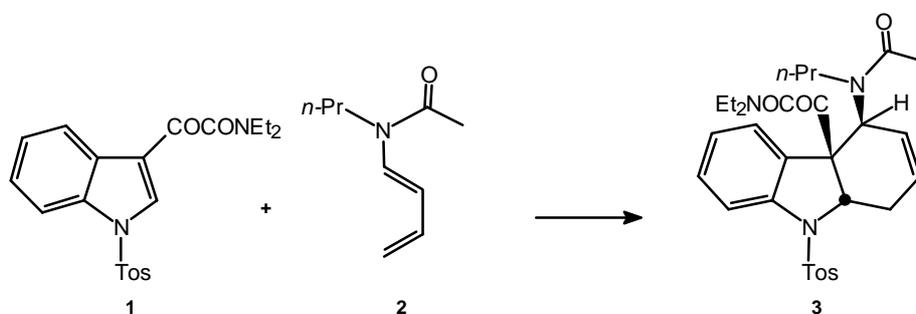
(-)-Aspidospermine

Scheme 1.



Exo addition

Scheme 2.



Scheme 3.

## Results and Discussions

The D-A reaction between *N,N*-diethyl-1-tosyl-3-indoleglyoxamide and 1-(*N*-acetyl-*N*-propylamino)-1,3-butadiene, carried out under hyperbar conditions, is clean, fast and leads to higher yields compared to thermal conditions, since it allows to produce a single adduct which holds the basic skeleton and appropriate functionality of (-)-*Aspidospermine* and related *Plumerane* alkaloids.

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**References and Notes**

1. Wenkert, E.; Moeller, P. D. R.; Piettre, S. *J. Am. Chem. Soc.* **1988**, *110*, 7188.
2. Biolatto, B.; Kneeteman, M.; Mancini, P. *Tetrahedron Lett.* **1999**, *40*, 3343.
3. Biolatto, B.; Kneeteman, M.; Gonzalez Sierra, M.; Mancini, P. M. *Unpublished results.*