Reactivity of nitrated quinolinic systems in reactions with isoprene

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Introduction
We have recently demonstrated that naphthalene substituted with a nitro group in 1- or 2-positions can react via C1-C2 bond by a $[4\pi + 2\pi]$ cycloaddition when the used diene is sufficiently nucleophilic, such as trans-1-methoxy-3-trimethylsilyloxy-1,3-butadiene (diene of Danishefsky) (Paredes et al., 2000). The tricyclic adduct obtained at temperatures from 80 to 150°C suffers extrusion of nitrous acid and methanol to form the hydroxyphenantrenic derivative (Fig. 1). However, the use of poor or moderately activated dienes, such as isoprene and 1-methoxy-1,3-butadiene, leads to the corresponding N-naphthylpyrroles (Fig. 1), obtained by heterocycloaddition and later thermal rearrangement (Della Rosa et al., 2004; Paredes et al., 2003).

Figure 1

In view of the above findings, our interest has been to extend this study to a series of nitroquinolines and nitroisoquinolines, and their reactions with isoprene as diene partner.

Taking into account that it has been demonstrated for Diels-Alder reactions that the classification of the diene/dienophile pair on a single electrophilicity scale is a tool for predicting the feasibility of a cycloaddition process (Domingo, 2002; Domingo and Aurell, 2002; Domingo et al., 2002 a,b), theoretical studies were performed in order to predict the reactivity of the forementioned systems based on the Density Functional Theory.

Methodology

* Experimental

Conditions: Experiences were carried out in closed ampules using benzene as solvent. The reaction time was 96 h and the temperature was 150°C. The work-up of the reaction was performed by silicagel column chromatography using hexane-ethyl acetate as eluent. Products were identified by spectroscopic techniques (NMR, IR and MS).

Dienophiles are shown in Fig. 2.
**Computational details**

Geometry optimizations were carried out for the series of dienes and dienophiles under study, using the B3LYP/6-31G(d) theory level implemented in GAUSSIAN 98 program (Frisch et al., 1998). The global electrophilicity index was evaluated using the following equation (Parr et al., 1999):

\[
\mu \approx \frac{\varepsilon_{HOMO} + \varepsilon_{LUMO}}{2} \\
\eta \approx \varepsilon_{LUMO} - \varepsilon_{HOMO}
\]

Chemical potential and chemical hardness were approached from the energies of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) in the ground state of the molecule (Parr and Yang, 1989).

**Results and Discussion**

All dienophilic substrates against isoprene, a diene of low nucleophilicity, do not suffer normal Diels-Alder reaction, but show the adduct product of the hetero Diels-Alder reaction, resulting in the respective quinolinic and isoquinolinic derivatives substituted by methylpyrrole (Fig. 3).
Theoretical calculations are displayed in Table 1. According to these results we can draw as conclusion that the studied dienophiles are strong electrophiles since they show high $\omega$ values (Domingo et al., 2002a).

**Table 1.** Global properties of some reagents involved in D-A reactions.

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Global Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\mu$ (a.u.)</td>
</tr>
<tr>
<td>4-Nitroquinoline N-oxide</td>
<td>-0.17538</td>
</tr>
<tr>
<td>4-Nitroquinoline</td>
<td>-0.18168</td>
</tr>
<tr>
<td>4-Nitroisoquinoline</td>
<td>-0.17912</td>
</tr>
<tr>
<td>1-Nitroisoquinoline</td>
<td>-0.17536</td>
</tr>
<tr>
<td>Isoprene</td>
<td>-0.12085</td>
</tr>
</tbody>
</table>

**Conclusions**

Dienophiles under study have a reactive behaviour similar to that of mononitronaphthalenes in the reactions with isoprene, since in all instances heterocycloaddition products were observed.

Quinolines seem to be more reactive than isoquinolines, which is justified by the index increase, thus reflecting a higher electrophilic nature.

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**References**