Synthesis of fluorescein derivatives by Multicomponent Friedel-Crafts reaction using Niobium pentachloride as Lewis acid

Bruno Henrique Sacoman Torquato da Silva, Lucas Michelão Martins, Luiz Carlos da Silva Filho

UNESP (Universidade Paulista “Júlio de Mesquita Filho”), São Paulo, Brazil

The fluorescein derivatives are an important class of heterocyclic compounds and has been attracting a large interest in the scientific community, taking several photochemistry and biochemical applications, such as: dyes in solar cells and other organic devices, and probes for use as cell biomarkers.[1] The Friedel-Crafts reaction is one of the most important reactions to formation of carbon-carbon bonds, leading to formation of aromatic ketones and alkylated rings.[2] Therefore, in this work we study the synthesis of fluorescein derivatives through Friedel-Crafts reaction using the niobium pentachloride as Lewis acid.

For the obtainment of fluorescein derivatives (1), the reactions were realized between 2,0 mmols of phenol derivatives (2) (substituted in meta or para position) and 1,0 mmol of phthalic anhydride (3), under inert atmosphere of N₂ and heating of 90 °C, using methanesulfonic acid as solvent and 0.25 eq. of NbCl₅. The adducts of fluorescein were obtained in reaction times ranging from 50 to 180 minutes and in yields ranging from 76 to 85% depending of the phenol derivative utilized. The results obtained, showed that the presence of electron-donating groups in the phenolic derivative favor the formation of the fluorescein derivative (1), while in the presence of electron-withdrawing groups wasn't observed the formation of products, with recovery of starting materials.

\[
\begin{align*}
\text{OH} & \quad \text{O} \\
\text{O} & \quad \text{R} \\
\text{R} & \quad \text{O} \\
\text{R} & \quad \text{OH, OMe, Me, Cl, Br, NO₂.}
\end{align*}
\]

Acknowledgments: this work was supported by FAPESP, CAPES, CNPq and CBMM.
