S_NAr reactivity of thiophene derivatives investigated using conceptual DFT

POUZENS Jean-Thomas[a], SOUISSI Salma[b], INGROSSO Francesca[c], BOUBAKER Taoufik[d], HIERSO Jean-Cyrille[a], FLEURAT-LESSARD Paul[a]

[a] *Institut de Chimie Moléculaire de l'Université de Bourgogne (ICMUB, UMR-CNRS 6302), Université de Bourgogne, 9 Avenue Alain Savary, 21000 Dijon, France*

[b] *Laboratoire de Chimie Théorique, Sorbonne Université (LCT, UMR-CNRS 7614-8233)*

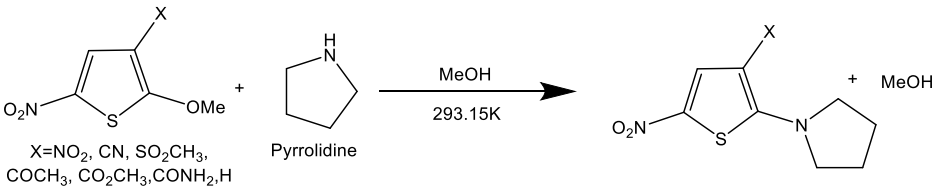
[c] *Laboratoire de Chimie et Physique Théoriques (LPCT, UMR-CNRS 7019), Université de Lorraine, 1 Rue Grandville, 54000 Nancy, France*

[d] *Université de Monastir, Faculté des Sciences, Laboratoire de Chimie Hétérocyclique, Produits Naturels et Réactivité (LR11S39), Avenue de l'Environnement, 5019 Monastir, Tunisie.*

Jean-Thomas.Pouzens@u-bourgogne.fr

Thiophenes are heterocycles of industrial interest which have attracted considerable attention due to their versatility in different applications. For instance, substituted thiophenes are used to synthetize materials with photophysical properties and electrochemical systems and they are increasingly being employed in therapeutical applications.[1], [2] The formation of amino substituted thiophenes through aromatic nucleophilic substitution (S_NAr) have been extensively studied experimentally.[3], [4] To gain more insights on the substituent effects, the electrophilicities of numerous thiophenes derivatives have been provided using Mayr's electrophilicity scale.[5] However, further analysis of such properties and computational efforts to achieve a description of the reaction mechanism are rare.[6]

In this work, we performed quantum chemistry calculations to investigate the mechanism of the S_NAr reaction of pyrrolidine with seven substituted thiophenes.



Scheme of the studied S_NAr reaction.

We then used conceptual DFT and Topological approaches [7] to rationalize the evolution of the computed activation energies by means of quantum descriptors, such as Parr's electrophilicity and the LUMO energy. We showed that, though the relative reactivity of different thiophene sites is hard to model, the reactivity of the thiophene derivatives nicely correlates with global descriptors.

References

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