Understanding the influence of the trifluoromethyl group on the chemo-, regio-, and stereoselectivity of [3+2]-cycloadditions of thiocarbonyl S-methanides with α,β-unsaturated ketones. A molecular electron density theory study

Lakhdar Benhamed[1], Sidi Mohamed Mekelleche[1], Wafaa Benchouk[1], Imad Eddine Charif[1], Mar Ríos-Gutiérrez[2], and Luis Domingo[3]

[1]Abou Bakr Belkaid University Tlemcen Faculty of Sciences
[2]Universitat de Valencia Facultat de Quimica
[3]Universidad de Valencia

July 21, 2020

Abstract

Experimentally (G. Mlostoń et al., J. Fluor. Chem. 190 (2016) 56–60), it has been found that the type of the obtained cycloadduct of the [3+2] cycloaddition (32CA) reaction of thiocarbonyl S-methanides with α,β-unsaturated ketones depends strongly on the location of the trifluoromethyl group. In the case of enones containing the CF3CH=CH moiety, the 32CA reaction occurs chemo- and regioselectively onto the C=C double bond giving trifluoromethylated tetrahydrothiophene derivatives. On the other hand, enones containing the CF3–C=O fragment react as carbonyl heteroethylenes leading to trifluoromethylated 1,3-oxathiolanes also in a chemo- and regioselective manner. Our aim in the present work is to perform a theoretical study of the all chemo-, regio-, and stereo-isomeric reaction paths of these 32CA reactions within the Molecular Electron Density Theory. Activation Gibbs free energies, calculated at the B3LYP/6-311G(d,p) level in tetrahydrofurane at -40°C, show that the ortho/endo reaction path giving the trifluoromethylated tetrahydrothiophene is more favoured, while the meta/endo reaction path leading to trifluoromethylated 1,3-oxathiolanes is more preferred in total agreement with experimental findings. The low activation barriers in combination of the Electron Localization Function topological analysis of the most relevant points along the Intrinsic Reaction Coordinate reveals the pseudomonoradical character of the studied 32CA reactions.

Hosted file

`main-document-IJQC-final.docx` available at https://authorea.com/users/344899/articles/471261-understanding-the-influence-of-the-trifluoromethyl-group-on-the-chemo-regio-and-stereoselectivity-of-3-2-cycloadditions-of-thiocarbonyl-s-methanides-with-%CE%B1-%CE%B2-unsaturated-ketones-a-molecular-electron-density-theory-study

Hosted file

`Tables_IJQC_21July.doc` available at https://authorea.com/users/344899/articles/471261-understanding-the-influence-of-the-trifluoromethyl-group-on-the-chemo-regio-and-stereoselectivity-of-3-2-cycloadditions-of-thiocarbonyl-s-methanides-with-%CE%B1-%CE%B2-unsaturated-ketones-a-molecular-electron-density-theory-study