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Experimental and Computational Studies Addressed to 1,3-Dipolar Cycloadditions of D-Erythrose 1,3-Dioxane 1,5-Lactone with *Regio*- and *Stereo*-selectivity

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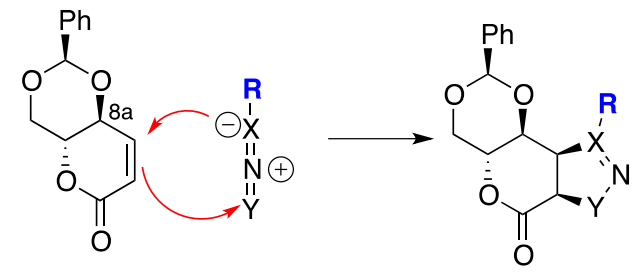
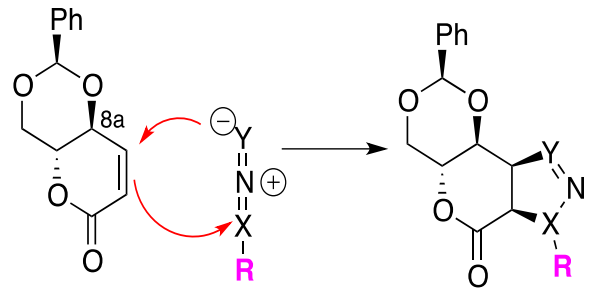
Graphical Abstract



R= Bn, n-Pr, $(CH_2)_3OBn$; X=N; Y=N
R= Ph; X=N Y=H
R= Ph, Me, 2,6-Cl-C_6H_3; X=C; Y=O

isomer A



R= Ph, Me, 2,6-Cl-C_6H_3; X=C; Y=O

isomer B

Abstract

A new D-erythrose 1,3-dioxane 1,5-lactone derivative was synthetized and found to be a highly stereo-selective template as dipolarophile in 1,3-dipolar cycloadditions. Different regio-selectivities were obtained depending on the nature of the 1,3-dipole: complete, with alkyl azides and diazomethylbenzene, inexistent, with nitrile oxides.

To understand the mechanisms of cycloadditions with the three types of 1,3-dipoles, computational studies were performed, giving full agreement with the experimental data.

The computational results showed that all the studied cycloadditions are concerted processes, involving exoenergonic, and small free activation energies. The stereoselectivity of

	the reactions is due to a combination of the steric effect endorsed by hydrogen H-8 and the hyper conjugative effect of the incoming 1,3-dipole with the lactone. The regioselectivity observed in alkyl azides and phenyldiazomethane is mostly dependent on the distortion effect during the cycloaddition process. This distortion effect is however higher in the alkyl azide compounds than in phenyldiazomethane. This distortion effect is absent from nitrile oxides. This study provides a specific example where apparent similar chemistry was found to proceed via different mechanisms, leading to different output results.

References

Sousa, C.E.A.; Ribeiro, A. M. P.; Gil Fortes, A.; N. M. F. S. A. Cerqueira; Alves, M. J. *J. Org. Chem.*, **2017**, *82* (2), pp 982–991.