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Combined experimental and computational studies devoted to the synthesis of 1,4-lactones

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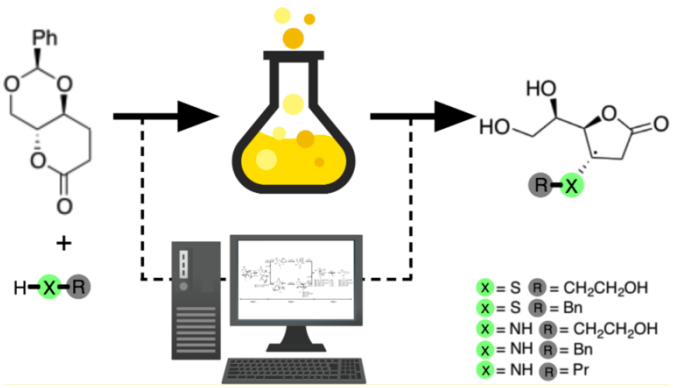
Graphical Abstract



Abstract.

Lactones are important biological molecules that offer a new molecular scaffold to develop new and more selective inhibitors targeting glycosidases [1]. The chemical routes that can speed up their synthesis in a *stereo*- and *regio*-selective way have become a major demand. A new derivative of 2,4-O-alkylidene-D-erythrose, enclosing a C=C moiety into a 1,5-lactone ring, was found to induce a complete facial selectivity in 1,3-dipolar cycloadditions [2]. This new D-erythrosyl 1,5-lactone was studied as a Michael acceptor with sulfur and nitrogen nucleophiles and from which a complete facial selectivity was demonstrated in all reactions [3]. Sulfides attack exclusively at C-4, but primary amines and hydrazine attack both at C-2 and C-4. The sulfur adducts formed are 1 (D-erythrose derivative):1 (nucleophile), and the nitrogen adducts are 1:2. The theoretical and computational results clearly explain the origin of the *stereo*-selectivity, and the energetic course of the reactions, starting

	with nitrogen and sulfide nucleophiles. Considering that the 1,4-lactones obtained in this work offer a new molecular scaffold for organic synthesis, these new results provide a solid theoretical platform that can be used to speed up synthesis of other derivatives in a *stereo*- and *regio*-selective way.

References *(mandatory)*

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[2] Sousa, C. E.; Ribeiro, A. M.; Gil Fortes, A.; Cerqueira, N. M.; Alves, M. J. Total Facial Discrimination of 1,3-Dipolar Cycloadditions in a d-Erythrose 1,3-Dioxane Template: Computational Studies of a Concerted Mechanism. J. Org. Chem. 2017, 82 (2), 982−991.

[3] Rocha, J. F.; Freitas, D. S.; Noro, J.; Teixeira, C. S. S.; Sousa, C. E.; Alves, M. J.; Cerqueira, N. M. F. S. A. Total Stereoselective Michael Addition of N- and S- Nucleophiles to a d-Erythrosyl 1,5-Lactone Derivative. Experimental and Theoretical Studies Devoted to the Synthesis of 2,6-Dideoxy-4-functionalized-d-ribono-hexono-1,4-lactone. J. Org. Chem. 2018, 83 (15), 8011-8019 DOI: 10.1021/acs.joc.8b00769.