THE DOMINO CHEMISTRY APPROACH TO MOLECULAR DIVERSITY: COMPETING DOMINO PROCESSES MODULATED BY THE SUBSTITUTION PATTERN

Isabel Castellote,¹ Susana Porcel,¹ Talbi Kaoudi,¹ Nicolas Birlirakis,¹ Loïc Toupet² and Siméon Arseniyadis¹*

¹Institut de Chimie des Substances Naturelles, CNRS, F-91198 Gif-sur-Yvette (FRANCE)
²GMCM-UMR 6626, Université de Rennes I, Campus de Beaulieu, 35042 Rennes (FRANCE)

We describe our findings on the effect of angular substitution on product distribution of Pb(OAc)₄ mediated domino reactions. Potential mechanistic pathways for these reactions are discussed based on product distributions and spectroscopic results.

The olefin, due to its energy content serves as a source of diversity permitting the domino process to occur while lead tetraacetate as a good electrophile, possessing a high oxidation potential and a high coordination number Pb(OAc)₄ serves as the oxidant for the oxidative cleavage and as the Lewis acid promoter for the ring expansion. The key step (metal addition on the olefin, as portrayed in Scheme 1) is responsible for the course of the domino process and reaction conditions can be tailored to fit a particular type of transformation.

Scheme 1: The process can be modulated by the substitution pattern; facial selectivity controls the efficiency of orbital overlap.

The results obtained for Pb(OAc)₄ induced domino transformations show that there is a dual pathway to high diversity. Stereoelectronic factors control the orbital alignment so that either ring expanded 2 or fused/bridged tricyclic 3 type products are formed from 1.

Scheme 2: We can alter diversity using the appropriate substitution pattern

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