Synthesis of Biologically Relevant Heterocycles Mediated by Porphyrin-based Catalysts

E. Gallo,* M. Cavalleri and C. Damiano
Department of Chemistry, University of Milan, Via Golgi, 19 – 20136 Milan (Italy)
emma.gallo@unimi.it

The formation of C-N bonds is a reaction of great synthetic interest because of the biological and pharmaceutical relevance of aza-derivatives. The insertion of an aza-fragment into an organic skeleton is efficiently performed by using organic azides (RN₃) as nitrene ('RN') sources in the presence of low-toxic and chemical stable metal porphyrin catalysts. The sustainability of the synthetic procedure is related to the formation of benign N₂ as the only stoichiometric side-product.

Herein we report the use of metal porphyrins to promote the synthesis of biologically interesting compounds such as: a) \(\beta\)-amino ester by amination of benzylic C-H bonds. The methodology was effective in synthesizing derivatives of methyl L-3-phenyllactate in order to convert them into corresponding \(\beta\)-lactams;\(^1\) b) dihydrophenanthridines and phenanthridines,\(^2\) important core structures of pharmaceutical compounds, through the intramolecular amination of several 2-azido biaryls; c) C₃-functionalized indoles\(^3\) by an intermolecular reaction of aryl azides with alkynes. Several derivatives were synthesized with yields up to 95%, high regioselectivities and without requiring either the time consuming pre-functionalization of reagents or the addition of oxidants/additives. d) \(N\)-substituted oxazolidinones,\(^4\) antitumor and antibacterial agents, by the 100% atom efficient cycloaddition of CO₂ to aziridines. In addition, a catalytic tandem reaction, in which aziridines were first synthesized and then reacted with CO₂ without being isolated nor purified, was also investigated.

\(^1\) P. Zardi, A. Caselli, P. Macchi, F. Ferretti, E. Gallo Organometallics 2014, 33, 2210-2218
\(^2\) D. Intrieri, M. Mariani, A. Caselli, F. Ragaini, E. Gallo Chem. Eur. J. 2012, 18, 10487-10490