Tetramic acids, new synthetic approach and their medicinal functionalization/derivatization towards therapeutic compounds

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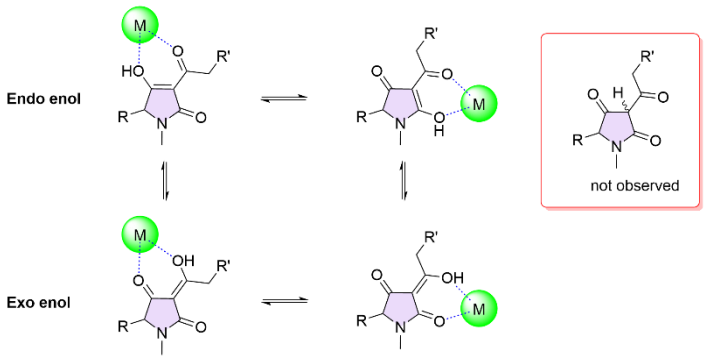
Natural products have always played an important role in medicinal chemistry but their laborious diversification for optimization of pharmacological properties and investigation of structure−activity relationships (SARs) still remains challenging. Since drug discovery requires shorter synthetic routes to provide a number of effective compounds.[1] Such examples constitute marine derived natural compounds like simple 3-acyl-tetramic acids (e.g. Penicillenol A1) and 3-Decalinoyltetramic acids (e.g. Equisetin). These chemical entities bear the N-methyl tetramic acid ring with 3-acyl and 5-alkyl substitutions present. All of which are considered natural metal binders and their mechanism of action include metalloproteins of Zn^{2+} or Fe^{3+} following the illustration below.[2]



Herein we will present a new synthetic methodology for the construction of functionalized tetramic acid molecules with putative anti-inflammatory activity aiming lipoxygenase (LOX). An important non heme Fe^{3+} containing protein associated with the production of pro-inflammatory mediators that it's being implicated with many infections, autoimmune diseases, tumors, neurodegeneration, cardiovascular diseases, diabetes and other chronic conditions.

References

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2. Zaghouani, M., & Nay, B., 3-Acylated tetramic and tetronic acids as natural metal binders: myth or reality?. *Natural product report*s, 2016, 33(4), 540-8.