# Total Synthesis of Alkenyle and Enediol Dihomo-Isofurans as Biomarkers of the Oxidative Stress

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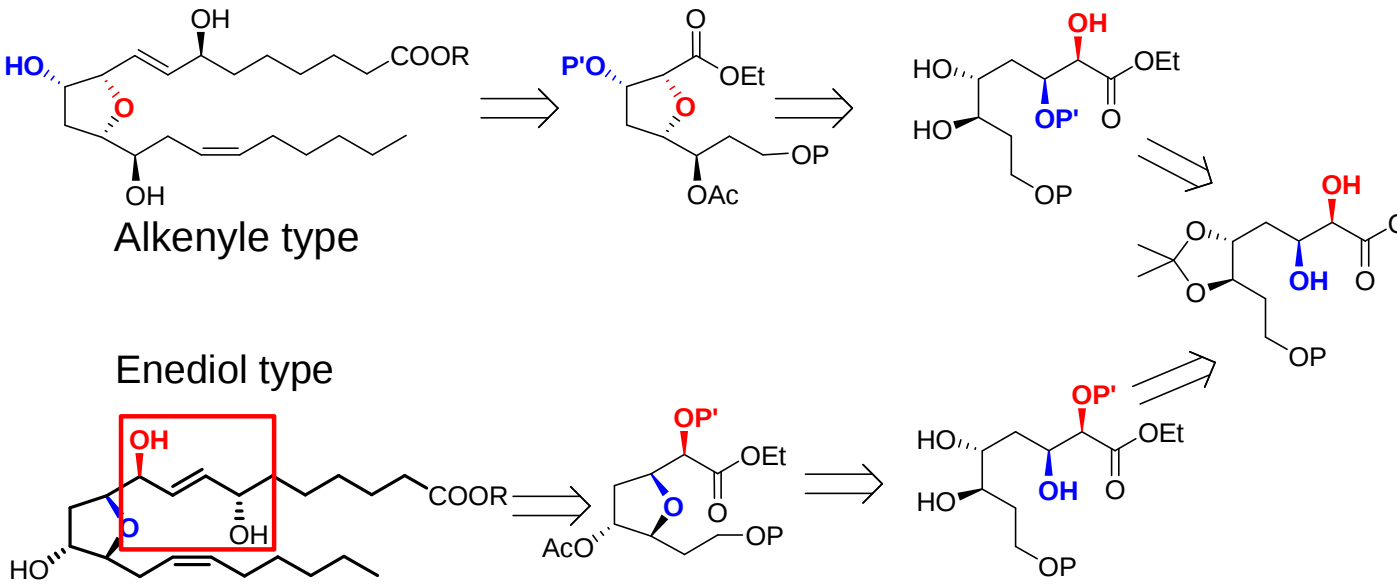
Oxidative stress (OS) is a biological phenomenon involved in many pathologies, specially neurodegenerative diseases. This phenomenon has an impact on polyunsaturated fatty acids (PUFAs) through a non enzymatic radical pathway to form oxygenated metabolites. Those metabolites can be quantified in the biological fluids to evaluate the OS. Thus, adrenic acid (AdA, C22:4 n-6), the most abundant PUFA in the brain's white matter, is metabolized into compounds known as dihomo-Isofurans, recently discovered by our team and highlighted in pig brains.[1] Therefore those compounds could be great biomarkers of myelin-related diseases, such as the Rett syndrome.

The whole of these compounds being a huge family (256 isomers), it seems interesting to develop a flexible strategy which would allow us to access a good part of those isomers. These compounds have a common tetrahydrofuranic core bearing one hydroxyl function and two lateral chains of diverse structures, which can be classified in two categories: alkenyle and enediol (**Scheme 1**). Our strategy is based on the late introduction of the lateral chains from two cyclic intermediates obtained through the cyclization of a 1,2,5-triol and a 1,2,4-triol to access the alkenyle and enediol structures respectively. These triols are obtained by regioselective monoprotection of a common diol intermediate synthesized in 7 steps starting from commercial *trans*-β-muconic acid.




**Scheme 1**: Divergent strategy for the total synthesis of Isofuran-like compounds

[1] A. de la Torre, Y. Y. Lee, C. Oger, P. T. Sangild, T. Durand, J. C-Y. Lee, J-M. Galano, **2014**, *Submitted*