

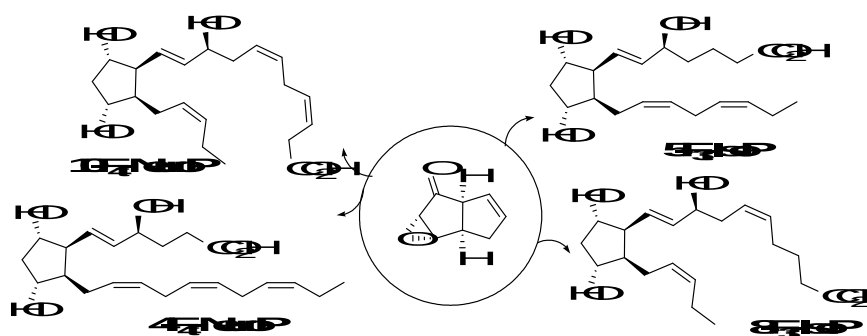
Total Synthesis of Isoprostanes and Neuroprostanes, Non-enzymatic Metabolites of EPA and DHA

Camille Oger, Alexandre Guy, Valérie Bultel-Poncé, Thierry Durand and Jean-Marie Galano, Institut des Biomolécules Max Mousseron, UMR 5247 CNRS-Universités Montpellier 1 & Montpellier 2 - ENSCM, Montpellier, France

Neuroprostanes are molecules that might have paramount applications in medical field, taking into account the specificity of distribution of docosahexaenoic acid (DHA) in the neuronal membrane. In several pathologies, it would be of great utility the availability of a biomarker able to discriminate the damage of gray from that of white brain matter. Moreover, peripheral biological fluids are not universally considered to mirror the biochemical oxidative events occurring in the brain. Nevertheless, our group has repeatedly explored the relevance of changes of plasma levels of F₂-dihomo-isoprostanes in Rett syndrome, a rare genetic cause of autism in girls[1] while other authors have confirmed the importance of monitoring the plasma levels of neuroprostanes in Parkinson's disease.[2]

We then focused our attention on the total synthesis of oxidative stress biomarkers, called F₃-isoprostanes and F₄-neuroprostanes, which are non-enzymatic oxygenated metabolites of omega-3 polyunsaturated fatty acids (PUFAs); EPA (eicosapentaenoic acid) and DHA.

Our retrosynthetic analysis is based on our previously synthesized bicyclic keto-epoxide [3] obtained from 1,3-cyclooctadiene. Two convergent strategies were developed to access different series of F₄-NeuroP and F₃-IsoP.[4][5]



- [1] C. De Felice, C. Signorini, T. Durand, C. Oger, A. Guy, V. Bultel-Poncé, J.-M. Galano, L. Ciccoli, S. Leoncini, M. D'Esposito, et al., *J. Lipid Res.* **2011**, *52*, 2287–2297.
[2] R. C. Seet, C. Y. Lee, E. C. Lim, J. J. Tan, A. M. Quek, W. L. Chong, W. F. Looi, S. H. Huang, H. Wang, Y. H. Chan, et al., *Free Radic Biol Med.* **2010**, *48*, 560–6.
[3] C. Oger, Y. Brinkmann, S. Bouazzaoui, T. Durand, J. M. Galano, *Org. Lett.* **2008**, *10*, 5087–90.
[4] C. Oger, V. Bultel-Poncé, A. Guy, L. Balas, J.-C. Rossi, T. Durand, J.-M. Galano *Chem. Eur. J.* **2010**, *16*, 13976-13980.
[5] A. Guy, C. Oger, J. Heppekaussen, C. Signorini, C. De Felice, A. Fürstner, T. Durand, J.-M. Galano, submitted.