

Synthetic approaches for the preparation of new galactoglycerolipids and other lipids esterified with ω 3/6 polyunsaturated fatty acids

Stratégies de synthèse pour la préparation de nouveaux galactoglycérolipides et d'autres lipides estérifiés par des acides gras insaturés de type ω 3/6

Laurent Soullère

Equipe Chimie Organique et Bioorganique ICBMS - UMR 5246 CNRS - Université Lyon 1 INSA Lyon - CPE Lyon-Université Claude Bernard- Bâtiment Lederer, 1 Rue Victor Grignard, F-69622 Villeurbanne cedex

(laurent.soulere@insa-lyon.fr)

Mono/di-galactosyl diacylglycerol (MGDG and DGDG) branched with the same fatty acid or with mixed fatty acids (Figure 1) are of biological interest in particular regarding their nutritional properties [1-3].

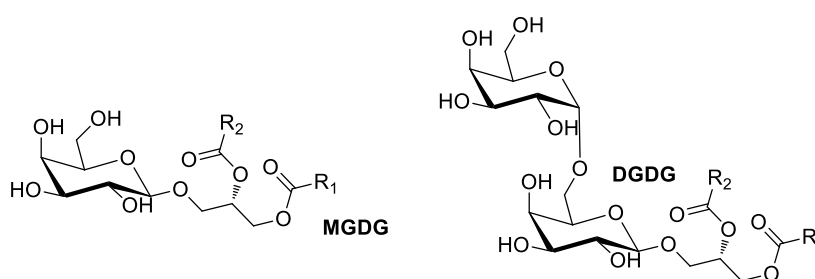


Figure 1: Structure of mono/di-galactosyl diacylglycerol (MGDG and DGDG with $R_1 = R_2$ and $R_1 \neq R_2$).

The PhD proposal will be focused on synthetic challenges toward the development of synthetic method for the preparation of these compounds [4]. In particular, the synthesis of galactoglycerolipids branched with natural or unnatural ω 3/6 polyunsaturated fatty acids will be investigated.

The total synthesis of ω 3/6 polyunsaturated fatty acids still remains a challenge in organic chemistry. The present project aims also to develop a flexible synthesis of these fatty acids using a method allowing chain elongation of alkyne derivatives followed by a coupling reaction and subsequent reduction to provide the corresponding unsaturated fatty acid esters (Figure 2). The preparation of new triglycerides as well as phospholipids esterified with ω 3/6 polyunsaturated fatty acids will be also undertaken [5, 6].

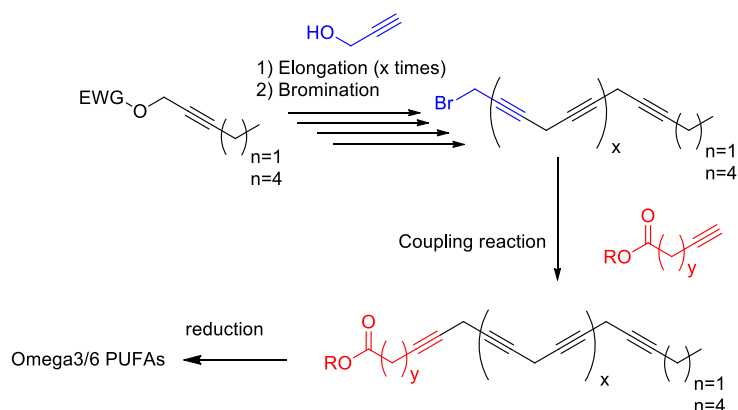


Figure 2: Synthetic approach to natural or unnatural ω 3/6 polyunsaturated fatty acids (PUFAs).

The synthetic lipids in particular mono/di-galactosyl diacylglycerol (MGDG and DGDG) will be studied for their nutritional properties, in collaboration with the CARMEN laboratory (Dr Cécile VORS and Marie-Caroline MICHALSKI) expert in nutrition [1-3]. These lipids are indeed mainly found in the membranes of plants, algae and photosynthetic microorganisms. These compounds will be also tested as substrates of different type of lipase in collaboration with the GEMBAS team (ICBMS, Pr Abdelkarim ABOUSALHAM).

Collaboration

CARMEN laboratory (UCBL, Dr Cécile VORS and Dr Marie-Caroline MICHALSKI)

GEMBAS team (ICBMS, Pr Abdelkarim ABOUSALHAM)

Candidates

The COB team, ICBMS, has a strong expertise in the field of organic synthesis [7] and we are looking for PhD candidates highly motivated with an experience in organic chemistry.

References

- [1] J.C. Bakala-N'Goma, L. Couédelo, C. Vaysse, M. Letisse, V. Pierre, A. Géloen, M.C. Michalski, M. Lagarde, J.D. Leao, F. Carrière, The digestion of diacylglycerol isomers by gastric and pancreatic lipases and its impact on the metabolic pathways for TAG re-synthesis in enterocytes, *Biochimie* 203 (2022) 106-117.
- [2] C. Robert, L. Couédelo, C. Knibbe, L. Fonseca, C. Buisson, E. Errazuriz-Cerda, E. Meugnier, E. Loizon, C. Vaysse, M.C. Michalski, Rapeseed Lecithin Increases Lymphatic Lipid Output and α -Linolenic Acid Bioavailability in Rats, *J Nutr* 150(11) (2020) 2900-2911.
- [3] C. Vors, M. Le Barz, C. Bourlieu, M.C. Michalski, Dietary lipids and cardiometabolic health: a new vision of structure-activity relationship, *Curr Opin Clin Nutr Metab Care* 23(6) (2020) 451-459.
- [4] I. Belhaj, S. Amara, G. Parsiegla, P. Sutto-Ortiz, M. Sahaka, H. Belghith, A. Rousset, D. Lafont, F. Carrière, Galactolipase activity of *Talaromyces thermophilus* lipase on galactolipid micelles, monomolecular films and UV-absorbing surface-coated substrate, *Biochim. Biophys. Acta Mol. Cell Biol. Lipids* 1863(9) (2018) 1006-1015.
- [5] M. El Alaoui, A. Noiriél, L. Soulère, L. Grand, Y. Queneau, A. Abousalham, Development of a high-throughput assay for measuring phospholipase A activity using synthetic 1,2- α -eleostearoyl-sn-glycero-3-phosphocholine coated on microtiter plates, *Anal Chem* 86(21) (2014) 10576-83.
- [6] M. El Alaoui, L. Soulère, A. Noiriél, Y. Queneau, A. Abousalham, α -Eleostearic acid-containing triglycerides for a continuous assay to determine lipase sn-1 and sn-3 regio-preference, *Chem Phys Lipids* 206 (2017) 43-52.
- [7] T. Barbier, C. Badiou, F. Davy, Y. Queneau, O. Dumitrescu, G. Lina, L. Soulère, Structural Variations in the Central Heterocyclic Scaffold of Tripartite 2,6-Difluorobenzamides: Influence on Their Antibacterial Activity against MDR *Staphylococcus aureus*, *Molecules* 27(19) (2022).