Synthesis of immunomodulatory lyso-phosphatidylinositol

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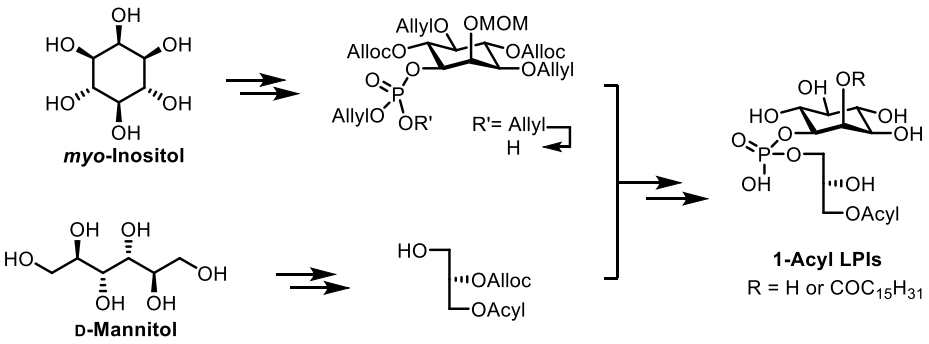
Phosphatidylinositol (PI) is a lipid widely observed in eukaryotic cells and play important roles in lipid signaling. Among the PI, lyso-type structures show characteristic immunomodulatory activities. 2-Acyl lyso-phosphatidylinositols (LPIs) have been known as the ligands of GPR55, but the comprehensive synthetic study and the detailed immunomodulatory activities of 1-acyl LPIs have not been fully investigated. Although it has been known that various organisms including human have the variety of 1-acyl LPIs. We have thus envisioned to build the compound library of 1-acyl LPIs, based on our previous synthesis of 1-acyl LPIs, eg. *Eh*PIs from *Entamoeba histolytica*, which activate NKT cells via lipid antigen presentation of CD1d.[1,2] The 1-acyl LPI have been found in various organisms, and we focused on the 1-acyl LPIs from human serum along with microbial structures.

For the investigation of the structure-immunomodulatory activity relationships of lyso-phosphatidylinositol focusing on the structure of fatty acids, we firstly synthesized various 1-acyl LPIs. As for the synthetic strategy, we used allyl-protecting groups for the protection of hydroxy groups and phosphate for its mild deprotection reaction conditions at the final stage of the synthesis.[2] The regioselective phosphorylation reaction of inositol moiety[1] was also applied for the LPI. We established the synthetic route of 1-acyl LPI, and then used the methods for the synthesis of the lyso-type phospholipids including 1-acyl LPI.



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