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Synthesis of a rosamine-based lipid probe for the study of lipid phenomena in membrane biomimetic models

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Abstract

Background: Rosamines are a class of fluorescent dyes, structurally related to rhodamines, that are commonly used as fluorophores in biological research since they have high quantum yields, photostability, and sensitivity to changes in their environment [1,2]. Rhodamines can also be derivatized to be coupled with lipids to create fluorescent lipid probes. These probes are useful for visualizing and studying various lipid-related processes, such as lipid metabolism, lipid transport, lipid signaling, and lipid dynamics in real-time [3]. **Objective:** The aim of the present work was to synthesize and characterize the spectroscopic fluorescence properties of lipids tagged with a rhodamine derivative for assessment of lipid phenomena using liposomes as biomimetic models. **Methods:** The synthetic strategy envisioned considers the preparation of a rosamine containing a (2-iodoacetyl)piperazin-1-yl moiety (RosPi) that would allow the bioconjugation with the amino group of 2-oleoyl-1-palmitoyl-*sn*-glycero-3-phosphoethanolamine (POPE). **Results:** The synthesis of RosPi, based on previously described procedures, was achieved in seven steps in 12% overall yield [4,5]. Firstly, a microwave assisted cyclization of a tetrahydroxybenzophenone in water led to the synthesis of the xanthone intermediate (90% yield). Then, triflic anhydride was used to form the corresponding ditrifilxanthone (94% yield) which in turn reacted with the Boc-piperazine to deliver the aminated xanthene (65%). Nucleophilic addition of 1,3-dimethoxybenzene to the xanthone carbonyl (66%) followed by Boc-deprotection provided the unmasked bisammonium salt (74%). Finally, the salt was reacted with the 2-chloroacetyl chloride to give the diamide (67%) which was transformed into the final iodoacetamide derivative by reaction with sodium iodide (69%). Several attempts for the bioconjugation of RosPi with POPE were performed and purification and structural characterization of the product are in progress. **Conclusions:** The preparation of RosPi was successfully achieved. The structural characterization and spectroscopy studies of the bioconjugate POPE-RosPi are ongoing.

Keywords: xanthene; fluorescence; bioconjugation; sensor

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