OPEN ACCESS

Scientific Letters

II TOXRUN
International Congress 2023
27-28 April, 2023 | Porto, Portugal

Poster 18

Aminoxanthones as building blocks for the development of BINOL-based chemosensors

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Abstract

Background: The existence of D-amino acids (D-aa) in human brain is known for a long time, but only recent findings revealed they are neuro-active and can be therapeutically useful if detected in initial stages of Alzheimer Disease (AD) cognitive decline [1]. D-serine and D/L serine ratio in serum have been proposed as biomarkers for AD progression. Knowledge related to the role of D-aa in AD pathogenesis will facilitate novel therapeutic treatments and hence, improve patient's quality of life. An accurate, timely diagnosis and simple method is crucial to access early treatments and the xanthone scaffold has the desirable photophysical properties to be explore as fluorophores. **Objective:** Develop chiral xanthone derivative-based fluorophores as enantioselective probes for detection and quantification of D-aa and D/L aa ratios for AD diagnoses. **Methods:** To develop the new xanthone-based chiral derivatives, a strategy based in the synthesis of a xanthone containing a maleimide moiety (MX) obtained from an aminoxanthone (XNH2) was envisioned. The MX could then act as Michael acceptor for the reaction with 1,1'-bi-2-naphthol (BINOL), the chiral moiety that will allow the enantioselective interactions with aa. **Results:** The synthesis of XNH2 was achieved in two steps: nitration reaction of the xanthone with KNO_3 in H_2SO_4 followed by reduction with $SnCl_2$ in concentrated HCl [2,3]. The product was recrystallized in ethanol and allowed to react with maleic anhydride followed by reaction with sodium acetate in acetic anhydride to produce the MX derivative. Finally, the 1,4-addition of BINOL to MX was performed [2,3]. Structure elucidation and spectroscopic characterization of the xanthone-BINOL derivative are ongoing. **Conclusions:** The aminoxanthone was successfully employed for the synthesis of the maleimide intermediate that allowed the conjugation with the BINOL chiral moiety. The spectroscopy studies are in progress, but preliminary results revealed the potential use of the new molecule as a fluorescence probe.

Keywords: chirality; enantioselectivity; fluorescence; amino acids; neurodegenerative diseases

Acknowledgments

This research was funded by GI2-CESPU, grant number XANTAAL_GI2-CESPU_2022.

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