

Title: **Building blocks for the synthesis of self-assemblable protacs**

Student: Maria Ruiz García

Date: January 2020

Supervisor/s: Dr. Enrique Pedroso Muller
Departamento de Química Inorgánica y Orgánica

Dr. Antonio Delgado

Dr. José Luis Abad Sáiz

IQAC-CSIC

In cells, the breakdown of proteins (proteolysis) plays a very important role in various key biological processes, this process is carried out through the ubiquitin-protein system (UPS).

PROTAC's ("proteolysis targeting chimeras") are gaining interest in biological and medicinal chemistry for their ability to recruit a protein of interest (POI) for presentation to E3-ligase for its subsequent ubiquitination and degradation by the UPS system.

The PROTAC's are chemical entities composed of a POI ligand, a spacer and an E3 ligase ligand, which despite their high molecular weight and low solubility, are gaining interest from a biological standpoint.

This project focuses on the synthesis and characterization of spacers 11-azido-3,6,9-trioxaundecan-1-ol (4), 23-azido-3,6,9,12,15,18,21-heptaoxatricosan-1-ol and 35-azido-3,6,9,12,15,18,21,24,27,30,33-undecaioxapentatriacontan-1-ol, which share the same structure, but with different lengths (see figure 4), for further study in the operation of the PROTACS, seeing how its activity varies depending on the length of the spacer.

Finally, spacers will be characterized through different analytical methods including ¹H-RMN mono and bidimensional spectroscopy, ¹H NMR, DQCOSY, HRMS and TLC.

Keywords: ubiquitin proteasome, PROTAC's, spacer.