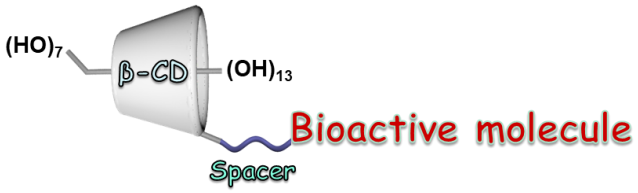
SYNTHESIS AND IMPORTANCE OF CD-TOSYLATES AS INTERMEDIATES IN THE FORMATION OF BIOACTIVE-CD CONJUGATES

Golfo G. Kordopati*, Nikoletta-Melina Konstantinou*, Gerasimos M. Tsivgoulis*

* Department of Chemistry, Univetrsity of Patras, Patras, Greece

Cyclodextrins (CDs) are cyclic oligosaccharides consisted of (*a*-1,4)-linked *a*-D-glucopyranose units and they represent one of the most important categories of molecules in supramolecular chemistry as a result of their peculiar structure (a rigid empty truncated cone composed of glucose units) and their unique properties. They are known for their ability to encapsulate into their hydrophobic cavity via host/guest complexation a variety of bioactive compounds and enhance their pharmacological profile. This property has been extensively exploited in the past in order to change the physicopharmaceutical properties of lipophilic drugs such as water-solubility, bioavailability, stability, and effectiveness. The complexation process can be significantly enhanced if mixtures are replaced with CD-bioactive molecule conjugates[1] (Scheme 1). One difficulty in this "advanced approach" is the necessity for CD derivatization. Unfortunately, chemical modification of CDs is not an easy task since for example to obtain monofunctionalized β-CD only one out of 21 hydroxyls should be reacted, selectively. Furthermore, selective functionalization of the hydroxyls located at the large rim of the cyclodextrin, which usually is more interesting from practical point of view, is even more tricky. Among the various CD derivatives, CD-tosylates[2] are by far the most important as intermediates for the synthesis of systems with either technological or pharmaceutical interest. Additionally, CD tosylates in their permethylated form are valuable intermediates in the case where lipophilic systems are required since it is known that permethylation of the CD hydroxyls can alter dramatically its lipophilicity.



Scheme 1: Bioactive molecule-β-cyclodextrin conjugate cartoon

[1] G. G. Kordopati, N.-M. Konstantinou, G. M. Tsivgoulis*, Comparison of Various Tosylating Reagents for the Synthesis of Mono-2-O-tosyl-β-cyclodextrin, *Synthesis*, **2022**, *54*, 4015-4024. DOI: 10.1055/s-0040-1719927

[2] G. G. Kordopati, T. V. Tselios, T. Kellici, F. Merzel, T. Mavromoustakos, S. Golic Grdadolnik*, G. M. Tsivgoulis*, A novel synthetic luteinizing hormone-releasing hormone (LHRH) analogue coupled with modified β-cyclodextrin: Insight into its intramolecular interactions, *Biochimica et Biophysica Acta- General Subjects*, **2015**, *1850*, 159-168. DOI:10.1016/j.bbagen.2014.10.017