RATIONAL DESIGN OF COOPERATIVITY IN A SYNTHETIC RECEPTOR

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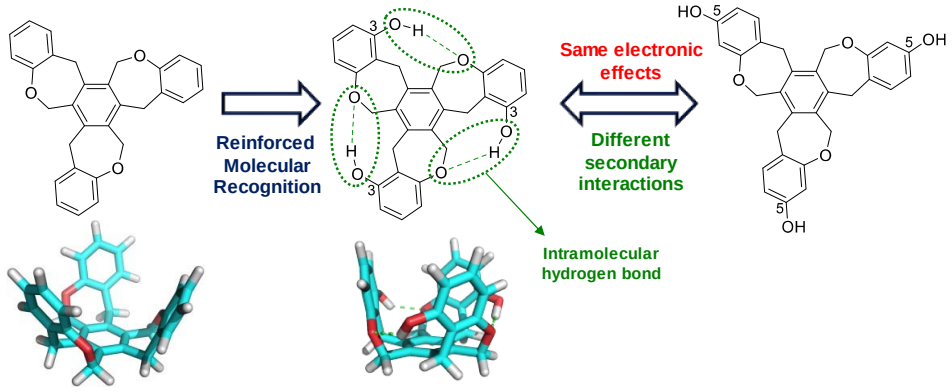
Benzocyclotrimers (BCTs) are C_3-symmetrical molecules consisting of a central benzene ring fused to three bicycles that are capable of recognizing guest molecules in gas phase and in solution.[1-4] Recently, we developed an alternative synthetic pathway to access diversely-functionalized BCTs in good yields.[5]

A cone conformation is necessary for the recognition events to take place in the benzocyclotrimers analogues. However, this is not the most stable conformation for flexible BCTs. To account for this problem, we envisaged the incorporation of functionalities that are able to stabilize the cone conformation by the formation of intramolecular hydrogen bonds. These intra-receptor interactions are not directly involved in the binding event, nonetheless they do affect the conformational landscape of the receptor and can impose the same restrictions than guest binding. If such is the case, then the adverse entropic cost of the binding is shared between secondary (intra-receptor) and primary (receptor-substrate) interactions and therefore binding is enhanced. Our idea is to place a hydroxyl group in position 3 of each aromatic ring. These could form hydrogen bonds with the three oxygen atoms of the neighboring oxepanes, favoring the optimal concave conformation for the binding.



Acknowledgement: This research was supported by the Spanish MINECO, co-financed by the European Regional Development Fund (ERDF) (CTQ2014-59649- P) and the Government of the Canary Islands (ProID2017010019). Congress participation is financed by staff training grant of the ULL by the Ministry of Economy, Industry, Commerce and Knowledge, co-financed by 85% by the European Social Fund.

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