Women in Science – 2nd Erlangen Symposium

Enzyme-mediated dynamic combinatorial chemistry with cyclodextrins

Sophie R. Beeren[1]

[1]Department of Chemistry, Technical University of Denmark, Kemitorvet Building 207 Kongens Lyngby 2800 Denmark
sopbee@kemi.dtu.dk

Biomolecular templates define the outcomes of enzymatic reactions in some of the most fundamental of biological processes, such as DNA replication, transcription and translation. In synthetic chemistry, molecular templates have enabled the synthesis of highly complex molecular architectures and interlocked structures. With *Enzyme-Mediated Dynamic Combinatorial Chemistry*[1] we explore the possibility to use synthetic templates to direct enzymatic reactions and obtain alternative products to those generated in Nature.

Cyclodextrins (CDs) are macrocycles formed from α-1,4-linked glucopyranose units, and the cyclodextrins with 6, 7, and 8 glucose units (α- β- and γ-CD) are industrially important hosts for the encapsulation of hydrophobic molecules, such as pharmaceuticals, flavours and aromas. While these cyclic oligosaccharides are usually considered as stable, static molecules, we can generate dynamic mixtures of interconverting cyclodextrins by the action of *cyclodextrin glucanotransferase* (CGTase), which catalyses reversible transglycosylation.[2] When the system is dynamic, it can be manipulated via supramolecular interactions with artificial template molecules to alter the product distribution. We use templates to direct the selective synthesis of specific cyclodextrins, including modified cyclodextrins[2] and unusual large-ring cyclodextrins with more than 8 glucose units.[3] By using stimuli-responsive templates, we can also control the outcome of this enzymatic reaction by means of external stimuli, such as light.[4]

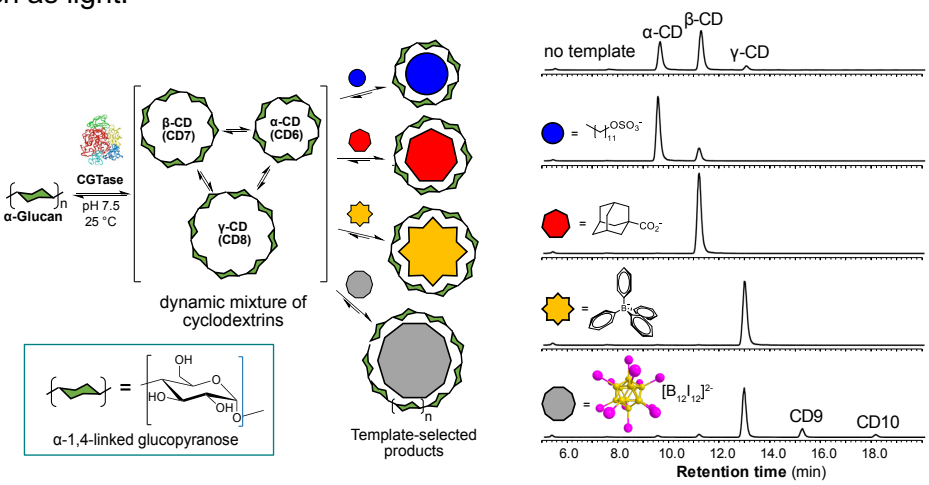

Figure 1. Cyclodextrin glucanotransferase (CGTase) converts cyclodextrins from static molecules into a dynamic mixture of interconverting cyclic and linear oligosaccharides. Templates (guest molecules) can be added to control which cyclodextrin products are formed.

References

[1] Larsen, D.; Beeren, S. R., *Chem. Sci.*, **2019**, *10*, 9981–9987.
[2] Larsen, D.; Ferreira, M.; Tilloy, S.; Monflier, E.; Beeren, S. R., *Chem. Commun.*, **2022**, *58*, 2287–2290.
[3] Erichsen, A.; Peters, G. H. J; Beeren, S. R., *J. Am. Chem. Soc.*, **2023**, *145*, 4882–4891.
[4] Yang, S.; Larsen, D.; Pellegrini, M.; Meier, S.; Mierke, D. F.; Beeren, S. R.; Aprahamian, I., *Chem.*, **2021**, *7*, 2190–2200.