Dynamic combinatorial libraries of glycoclusters: When glycoclusters go dynamic

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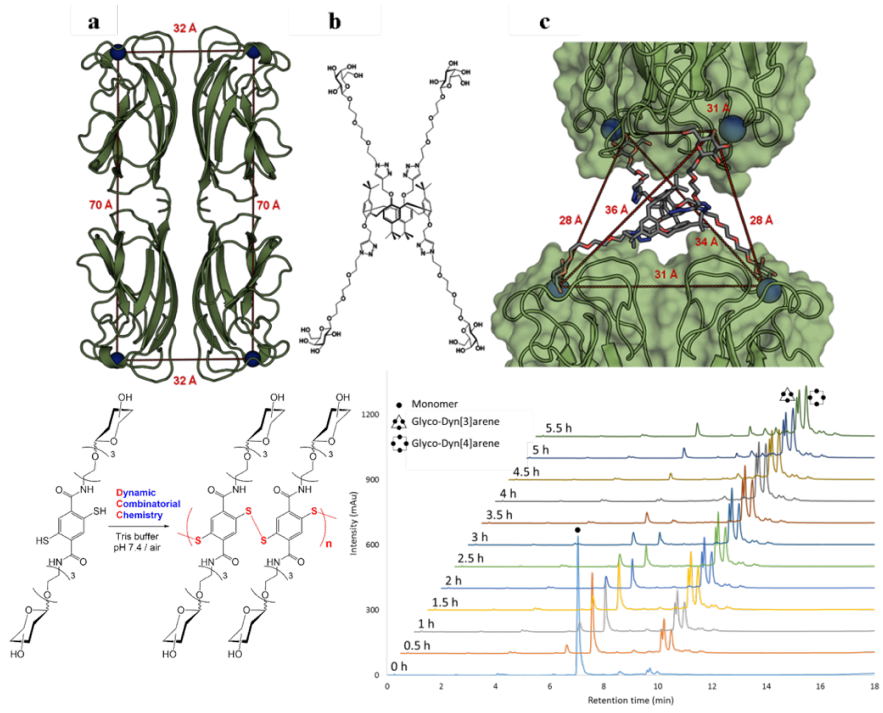
Pseudomonas aeruginosa is a well-known pathogen responsible for pulmonary infections among others. It is most notably found in hospitals as a cause for nosocomial infection. Anti-adhesive strategies are inhibiting the adhesion of bacteria to the host cells. Two soluble tetrameric lectins (LecA and LecB) have been identified in this process. LecA is known for its affinity for b-galactosides while LecB exhibit an affinity for a-fucosides. We have designed multivalent glycoclusters to inhibit these lectins with applications *in vivo* as potential therapeutic anti-infectious agents.[1] The calix[4]arene-based glycocluster (Figure top) displayed nanomolar affinity for LecA and provided protection against pulmonary infection in animal.[2] We have now developed self-assembling glycoclusters based on the concept of dynamic combinatorial chemistry (Figure bottom).[3] The building block is composed of an aromatic core, a spacer and a carbohydrate and will self-assemble in solution through disulfide bonds to generate a dynamic combinatorial library of glycoclusters. In this communication, we will detail the synthesis of the building-blocks and the results obtained during the dynamic combinatorial libraries. We can now evaluate simultenaously in a single experimental process, the binding affinities of the dynamic glycoclusters to several lectins of interest (LecA, LecB, ConA and AFL) from simple 1,4-dithiophenol building blocks.



Top: (a) LecA (b) glycocluster (c) complex / Bottom: (left) library of glycoclusters (right) equilibration.

Bibliographic references:

[1] Cecioni, S.; Imberty, A.; Vidal, S. Chem. Rev. 2015, 115, 525-561.
[2] Boukerb, A. M. et al. J. Med. Chem. 2014, 57, 10275-10289.
[3] (a) Corbett, P.T. et al. Chem. Rev. 2006, 106, 3652-3711. (b) Skowron, P.-T. et al. J. Org. Chem. 2016, 81, 654-661.