DESIGN, SYNTHESIS AND EVALUATION OF BICYCLIC AND SPIRO COMPOUNDS AS GLYCOMIMETIC INHIBITORS OF GALECTINS

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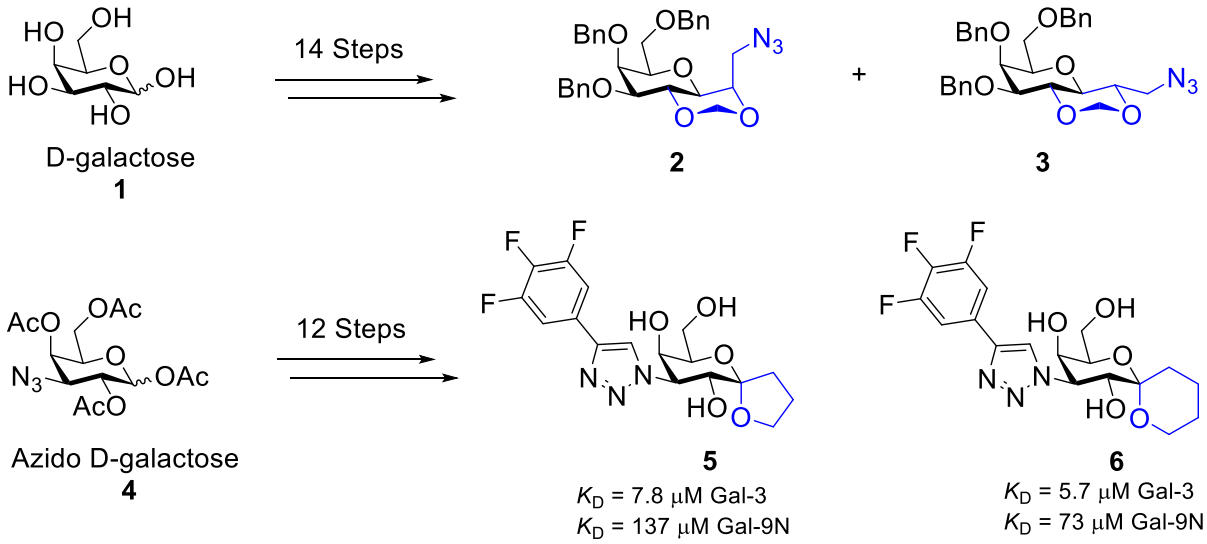
Galectins are soluble β-galactopyranoside binding lectins [1] expressed in numerous cells and play multiple roles in various physiological and cellular processes. Galectin-1 (Gal-1), galectin-3 (Gal-3), galectin-8 (Gal-8), and galectin-9 (Gal-9) were found as the most predominant galectins reported to participate in inflammation, cancer and virus infection.(5) Galectins are classified by the number and structure of CRDs into three major groups: prototype (e.g. galectins-1,7), chimeric (galectin-3) and tandem repeat (e.g. galectin-4,8,9). Tandem repeat galectins have two unique CRDs, referred to as the N and C-terminal domain, separated by a covalently bound peptide linker [2]. Their involvement in disease processes have made galectins interesting targets for inhibitor development.
In this work, both constrained bicyclic compounds and spiro galactopyranosides have been synthesised and evaluated as inhibitors of galectins. The synthetic routes and affinities of various compounds derived from **2** and **3** and spiro compounds **5** and **6** will be presented.



References:
1. Johannes, L.; Jacob, R.; Leffler, H., *Journal of Cell Science* **2018,** *131* (9).
2. Murphy, P. V.; Dhara, A.; Fitzgerald, L. S.; Hever, E.; Konda, S.; Mandal, K., *Chemical Society Reviews* **2024,** *53* (19), 9428-9445.