S. Mandal, V. K. Rajput, H. Leffler, B. Mukhopadhyay, U. J. Nilsson (2016). Synthesis of *O*-galactosyl amidines as selective antagonists of galectin-1 and N-terminal of galectin-9. *Can. J. Chem*., in press: DOI:10.1139/cjc-2015-0598.

The family of galectin proteins involved in adhesion, growth regulation, immunity, and inflammatory events are important targets for development of small molecule antagonists. Here, *N*-sulfonyl amidine galactopyranoside derivatives obtained via a multicomponent reaction between galactose alkyne derivatives, sulfonyl azides, and amines were evaluated as antagonists of galectin-1, 2, 3, 4N (Nterminal domain), 4C (C-terminal domain), 8N, 9N, and 9C in a competitive fluorescence polarization assay. Highly selective compounds against galectin-9N with up to 30-fold improved affinity compared to the reference methyl β-Dgalactopyranoside were identified. Molecular dynamics simulation suggested that the selectivity and affinity for galectin-9N originates from the *N*-sulfonylamidine moieties forming tridentate hydrogen bonds to two asparagine side chains and one phenyl stacking edge-to-face to an arginine side chain. These selective galectin-9N antagonists are of significant value as chemical tools for studying galectin-9 biology and chemistry, as well as possible starting structures for the discovery of galectin-9- targeting drugs influencing *e.g.* immune regulation.