3,3′ – DISUBSTITUTED THIOGALACTOSIDES AS INHIBITORS OF GALECTINS

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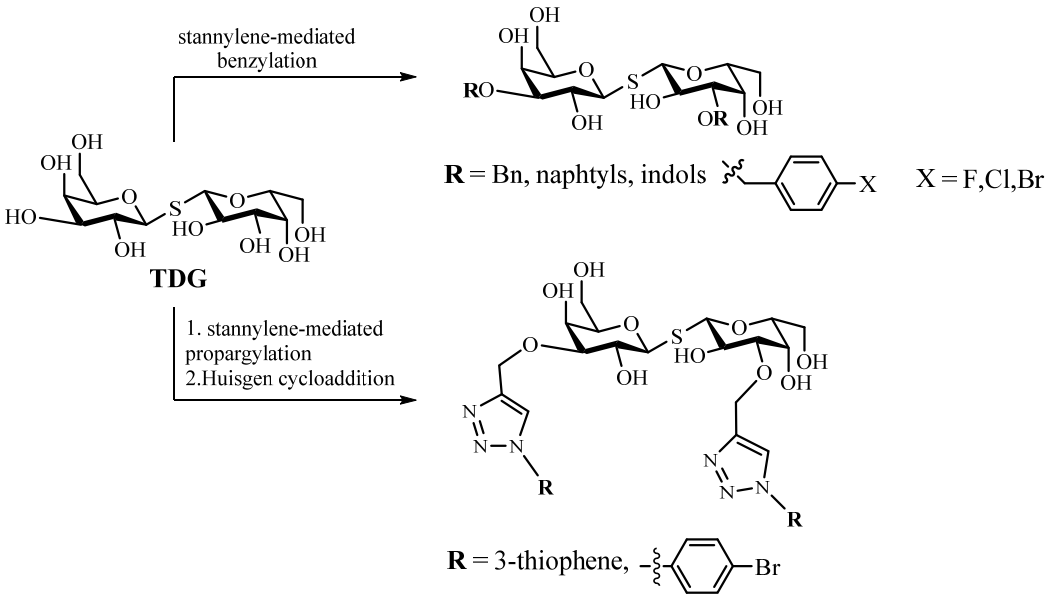
Human galectins are carbohydrate–binding proteins that play central roles in various pathologies including cancerogenesis, heart disorders, inflammation, and fibrosis.[1] Here we present a new straightforward approach towards the synthesis of small molecule inhibitors of galectin-1 and -3 based on 3,3′-disubstituted thiodigalactoside (TDG). The employed methodology is inspired by regioselective stannylene–mediated benzylation or alkylation[2] followed by Huisgen copper-catalyzed azide-alkyne cycloaddition reactions (CuAAC) yielding variously substituted TDGs (*Scheme 1*). Advantageously, the present protocols are based on one- or two-step reactions using an unprotected disaccharide (TDG), which is a great improvement compared to methods leading to similar compounds described so far.[4]



Scheme 1. New synthetic strategies towards 3,3′-disubstituted thiodigalactosides.

The affinity of all compounds was determined in a competitive ELISA assay with recombinant galectins. Molecular modelling of selected compounds revealed structure-affinity relationships between the studied compounds and galectins-1 and -3.

[1] Lin, C.-H., *Int. J. Mol. Sci.* **2018**, *19*(2), 392

[2] Iadonisi, A., *J.Org.Chem*. **2014**, *79*, 213

[3] Zhu, L., *Synthesis* **2013**, *45*(17), 2372

[4] Nillson, U., WO/2013/110704.