NMR INVESTIGATION OF RUTHENIUM-BASED SELECTIVE GALECTIN-1 INHIBITOR

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Human galectin-1 is a carbohydrate-binding protein that has emerged as a promising target for therapeutic intervention in cancer [1]. However, the development of bioactive compounds with high selectivity and inhibitory potency towards human galectin-1 is quite challenging due to its structural similarity with other human galectins. This study focuses on the NMR investigation of novel hybrid *N*-acetyllactosamine-based ruthenium-containing compound **1** (Figure 1A), developed in our laboratory at the Institute of Chemical Process Fundamentals. Inhibitor **1** showed surprisingly high selectivity to human galectin-1 over galectin-3. To understand the origin of this selectivity, we investigated the molecular recognition process using established NMR methods such as ^{1}H-^{1}H saturation transfer difference spectroscopy (STD), ^{1}H-^{1}H transferred NOESY, or ^{1}H-^{15}N chemical shift perturbation analysis [2]. This investigation uncovered that selectivity to galectin-1 is most likely attributable to the unique “piano-stool” geometry of the ruthenium complex, which fits well into the binding site of galectin-1 but discriminates binding to galectin-3 (Figure 1B).

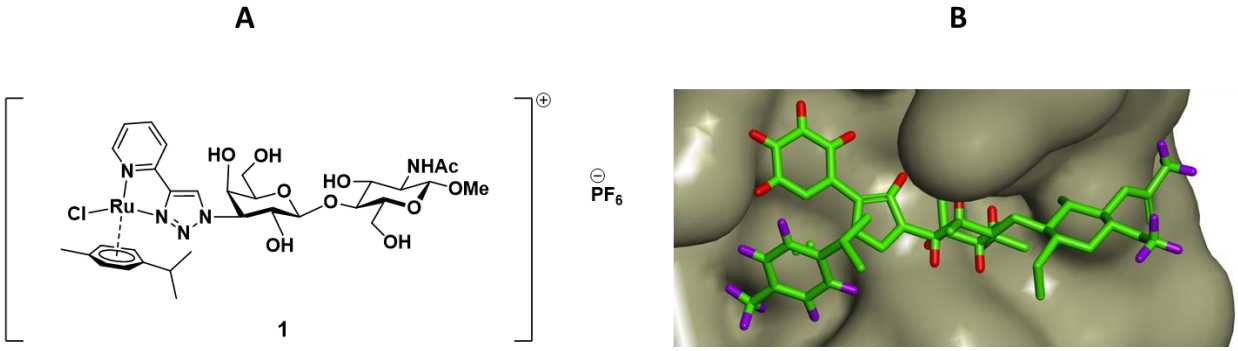

Figure 1. A) Structure of ruthenium-containing galectin inhibitor **1**. B) Conformation of compound **1** in the binding site of human galectin-1, refined on the basis of ^{1}H-^{1}H STD measurement (red protons = high STD saturations, purple protons = low STD saturations).

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References:

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