THE HYDROGEN BOND DONATING CAPACITY OF INDIVIDUAL ALCOHOL GROUPS IN CARBOHYDRATES

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Alcohol groups play a crucial role in determining the chemical and physical properties of carbohydrates. The extensive hydrogen bonding with water results in their excellent aqueous solubility and low lipophilicity, and the hydrogen bonding with protein receptors is one of the main determinants for binding selectivity and affinity. Intramolecular hydrogen bonding, and – in glycans – interresidue hydrogen bonding contributes to sugar/glycan conformation. Hence, sugar hydrogen bonding and hydration has been extensively investigated.
Knowledge of innate sugar alcohol hydrogen bond donating capacities and how these are influenced by modification elsewhere will aid glycomimetic development as well as the interpretation of binding data of carbohydrate probes in chemical biology.
Here we report the first efforts to map the hydrogen bond donating capacity of individual alcohol groups in carbohydrates onto a scale relevant to medicinal chemistry (pK_{AHY} scale). For this purpose, model compounds were designed that not only allow measurement (by IR), but also exclude any cooperative effects. The results show that the hydrogen bond donating capacities of alcohol groups in carbohydrates strongly depends on the position in the ring, and on the relative stereochemistry even of remote substituents, and a rationalisation of the data is proposed. We also show the considerable effect of alcohol deoxygenation and deoxyfluorination.