NMR structural studies of oligosaccharides and other natural products - DTU Orbit
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NMR spectroscopy is an important tool in chemical analysis and for structural studies in various research areas. The subject of this thesis is liquid state NMR spectroscopy for structural analysis of small molecules, both regarding method development and structure elucidation by NMR spectroscopy.

HMBC+ is a new pseudo-3D NMR experiment for measurement of long-range homonuclear JHH coupling constants in small molecules. Based on two existing experiments, multiplicity edited HMBC and HAT HMBC by Benie, Nyberg, and Sørensen, the new HMBC+ experiment takes advantage of a π phase difference with respect to n+1JHH between these two experiments, observed in the nJCH HMBC cross peak. Through a double editing procedure this enables straightforward determination of both sign and magnitude of n+1JHH, including for very small coupling constants. Excellent results were obtained for the natural product strychnine, and 28 n+1JHH coupling constants were determined, of which 10 had not previously been measured due to their small sizes. By comparing to calculated coupling constants, an RMSD of 0.28 Hz was obtained, all coupling constant signs fit with the calculations, and all errors were below 1 Hz, also when comparing the absolute values to experimental coupling constants measured by Carter et al. using 1D 1H NMR on deuterated strychnine analogues. Providing an excellent tool for measurement of long-range JHH with the extra convenience of labeling the coupling constant information to the 13C chemical shift through the nJCH correlation, this experiment has exciting applications for configurational assignment of e.g. carbohydrates and for residual dipolar couplings.

Identification of known molecules and discovery of novel molecules are other important applications of NMR spectroscopy. Bacteria and fungi produce secondary metabolites for signaling and competing against other organisms, and these molecules are important in drug discovery due to their inherent biological activities. From a marine Photobacterium (P. halotolerans) we isolated the solonamides and the ngercheumicins, two families of cyclic depsipeptides capable of attenuating virulence in S. aureus by quorum sensing inhibition through the accessory gene regulator agr. This is likely due to their structural similarities with the auto-inducing peptides of S. aureus, controlling quorum sensing in bacterial populations. A filamentous fungus, A. fijiensis, was also investigated for production of novel secondary metabolites, and a new pyranonigrin (E) was isolated and structure elucidated by NMR spectroscopy along with JBIR-74 and decumbenone A, two known metabolites previously isolated from Aspergillus and Penicillium species.

Oligosaccharides found in human milk are important for infant nutrition, and a collaborative effort of university and industry partners was aimed at establishing methods for production of human milk oligosaccharides. Two different bioenzymatic methods for production of 3'-sialyllactose were investigated, and a screening of trans-fucosidases enabled the NMR spectroscopic identification of three pNP-fucosylfucopyranosides as major reaction products.

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