Application of 3-Nitro-2-Pyridinesulfenyl (Npys) Derivatives to
Chemical Biology, Peptide Chemistry and Medicinal Chemistry

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3-Nitro-2-pyridinesulfenyl group (Npys) is a classical protective group developed in 1980, particularly for protecting a thiol (SH) group with a unique characteristic; “-Cys(Npys)-“ readily reacts with an unprotected SH group to form a disulfide bond. Based on this chemistry, we recently developed SH-selective solid-supported biotinylation and oligoarginylation reagents as tools of Chemical Biology. A compound with an SH group can be selectively labeled and the resulting labeled compound can be released from the resin and easily recovered in a high purity by filtration. Moreover, using a synthesized “Npys chloride resin”, we developed a “solid-phase disulfide ligation” method to prepare a disulfide peptide from two kinds of peptide fragments with cysteine residues. Application of this strategy realizes a “disulfide-led synthetic methodology” for disulfide-containing cyclic peptides. Oxytocin was efficiently synthesized as a fundamental model for more complex cyclic peptides. In the seminar, I would like to discuss further about the application of this method to the synthesis of a noncovalent–type antibody–drug conjugate (NcADC) in Medicinal Chemistry. As more recent data, I also discuss about new a solid- or no-solid-supported Npys reagent that enhances intra-molecular disulfide bond formation between two cysteine residues for the effective synthesis of cyclic-disulfide peptides. In use of this reagent, we successfully synthesized hANP and α-conotoxin without oligomer formation. Finally, if time allows, I would like to discuss another topic regarding our mid-sized peptides research in Medicinal Chemistry that is related to the development of myostatin inhibiting peptides as an attractive therapeutic approach towards muscle atrophic disorders.