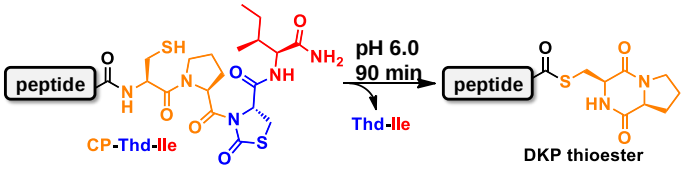
Fmoc 固相合成に適したチオエステル前駆体システイニルプロリルイミドによるタンパク質化学合成

（東大院工 [1]・名大院工 [2]・東大先端研 [3]）○中津 幸輝 [1]・梁瀬 将史 [1]・林 剛介 [2]・岡本 晃充 [1,3] Design of cysteinylprolyl imide (CPI) peptide and application to chemical protein synthesis ([1]*Graduate School of Engineering, The University of Tokyo,* [2]*Graduate School of Engineering, Nagoya University,* [3]*Research Center for Advanced Science and Technology, The University of Tokyo*) ○Koki Nakatsu,[1] Masafumi Yanase,[1] Gosuke Hayashi,[2] Akimitsu Okamoto[1],

Native chemical ligation[1)] is a promising strategy to ligate two unprotected peptide segments between an N-terminal cysteine peptide and a C-terminal peptide thioester. To prepare peptide thioester through Fmoc solid-phase peptide synthesis, many thioester surrogates were designed and reported. Recently, we developed an N−S acyl-shift type thioester surrogate, cysteinylprolyl imide (CPI),[3)] in which the equilibrium of the N−S acyl shift can be trapped by intramolecular diketopiperazine formation[2)]. Here, we will present a new CPI peptide tethering thiazolidinone as the imide moiety and compared it to the previously developed CPIs. The conversion of CP-Thd to alkyl thioester proceeded almost quantitatively in a neighboring-sequence independent manner via intramolecular DKP formation under relatively mild conditions (pH 6.0, 37 °C). This thioester preparation method was applied to the chemical synthesis of histone H3 bearing K56 acetylation.[4)]
Keywords：Chemical Protein Synthesis, Native Chemical Ligation, Fmoc Solid-Phase Peptide Synthesis, Peptide Thioester, Diketopiperazine

Native Chemical Ligation[1)]は信頼性の高いペプチド連結法であり、N 末端システインと C 末端チオエステルが連結してアミド結合を形成する。この C 末ペプチドチオエステルを、Fmoc 固相合成法で合成するため種々のチオエステル前駆体が開発されてきた。近年我々は N-S アシル転移平衡とジケトピペラジン（DKP）形成機構を用いる[2)]システイニルプロリルイミド（CPI）を開発した[3)]。本発表ではチアゾリジノン（Thd）構造を持つ CPI を報告し、C 末端 CP-Thz ペプチドが pH 6 の変性剤を含む緩衝液中、37 °C という温和な条件で、隣接配列非依存的にほぼ定量的かつ短時間でチオエステルペプチドへと変換されること示した。この分子内反応によるチオエステル化法を用い、3 つのペプチド断片を NCL で連結して histone H3.2-K56Ac の全合成を行った。[4)]



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