AL05 **Development of New Synthetic Reactions Using Hetero-heavy Atoms and Their Application to Synthesis of Biofunctional Molecules**

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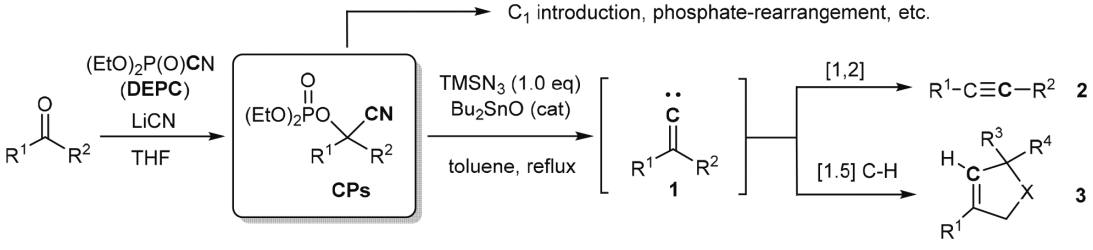
Novel reactions using hetero-heavy atoms (P, S, Se, and Sn) were developed and applied to the synthesis of biofunctional molecules and some medicine-candidates, as shown below.

1) Development of introduction of C_1-unit and carbene-generation using cyanophosphates (CPs)

DEPC [$(EtO)_2P(O)CN$][1)] is a liquid safe and easy to use. Reaction of carbonyl compounds with DEPC easily affords cyanophosphates (CPs),[1)] which have been used for introduction of C_1-unit. Meanwhile, a novel generation of alkylidene-carbene under neutral condition from CPs led to new synthetic methods for alkynes **2** and cyclopentenes **3**.

1) A recent review on DEPC: S. Harusawa and T. Shioiri, *Tetrahedron*, **72**, 8125-8200 (2016).

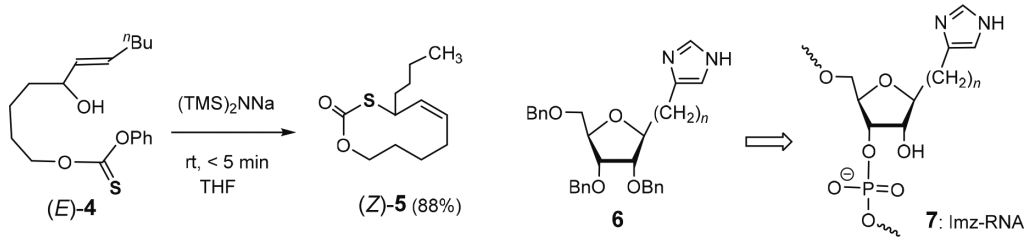


2) [3,3]Sigmatropic rearrangement-ring expansion reactions of medium-sized cyclic thionocarbonates

Treatment of *E*-allyl alcohol **4** with base causes formation of an 8-membered cyclic intermediate followed by spontaneous ring expansion to give a ten-membered cyclic thiolcarbonate **5** bearing (*Z*)-alkene. Furthermore, a unique stereoselective synthesis of (-)-yellow scale pheromone was achieved utilizing this reaction.

3) Synthesis of imidazole C-nucleosides and study of ribozyme reaction mechanism

Stereoselective synthesis of β -imidazole C-nucleosides **6** was carried out. Furthermore, novel chemo-genetic strategy for the reaction mechanism of ribozymes was developed using imidazole-containing RNA probe **7** derived from **6**.



4) Developments of histamine H_3 (H_3R) and H_4 (H_4R) receptor ligands

H_3R ligands are expecting as therapeutic agents on central nerves systems. We found a H_3R agonist (imifuramine) using chemistry of Se efficiently and then discovered the first H_4R agonist (OUP-16). Furthermore, a potent and non-imidazole H_3R antagonist, OUP-186, was found.