量子化学計算に基づく*N*-スルファニルエチルアニリド（SEAlide）の N-S アシル基転移反応におけるリン酸塩の役割の解明

重永　章

Org. Biomol. Chem., **18**, 9706-9711 (2020).

Theoretical study on reaction mechanism of phosphate-catalyzed N-S acyl transfer of N-sulfanylethylanilide (SEAlide)

Akira Shigenaga

ABSTRACT　C-Terminally thioesterificated peptides are essential building blocks for chemical protein synthesis. To date, many acyl transfer auxiliaries have been developed to enable facile preparation of peptide thioesters. We previously developed an *N*-sulfanylethylanilide (SEAlide) auxiliary, which causes an N–S acyl transfer reaction upon addition of phosphate salt to convert a C-terminal amide to a thioester. The mechanism of how phosphate triggers the reaction is speculative, and the details are unknown. In this study, the mechanism by which phosphate promotes acyl transfer is discussed based on density functional theory (DFT) calculations and non-covalent interaction (NCI) analysis. As a result, although the notion that phosphate acts as an acid–base catalyst, as speculated in our previous study, was correct, it became clear that two competing reaction pathways exist: a previously proposed stepwise pathway and a concerted one. Furthermore, calculation was performed in the presence of various additives other than phosphate to uncover the effect of the additives on the stability of transition states.

抄録　タンパク質の化学合成において、C 末端をチオエステル化したペプチドの合成は必須である。以前著者らは、簡便なペプチドチオエステルの合成を可能とする補助基として *N*-スルファニルエチルアニリド（SEAlide）を報告した。さらに、本補助基の鍵反応が温和な条件下、リン酸塩を加えることで進行することを発見した。しかし、その反応機構は不明であった。そこで本論文では、リン酸塩が鍵反応を促進する詳細な機構について、量子化学計算を用いて明らかにした。