Development of Catalytic Chemoselective Conjugate Addition

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論　文　名	Development of Catalytic Chemoselective Conjugate Addition （化学選択的触媒的共役付加反応の開発）
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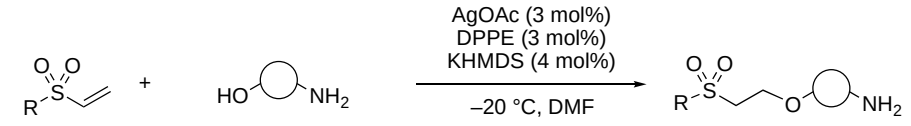
論文審査の結果の要旨

下記に示すように、論文提出者は Ag 触媒による化学選択的共役付加反応の開発に成功し、適用基質を不飽和ニトリルから不飽和スルホニル化合物、更には不飽和エステルへと拡張し、さらに、位置及び化学選択性を同時に制御可能な触媒系の創出にも成功している。これらの反応は、基礎反応として重要であるだけではなく、医薬品や生体内高分子の機能化にも応用可能であることから、本学位請求論文は博士（創薬科学）の学位に値すると判断した。

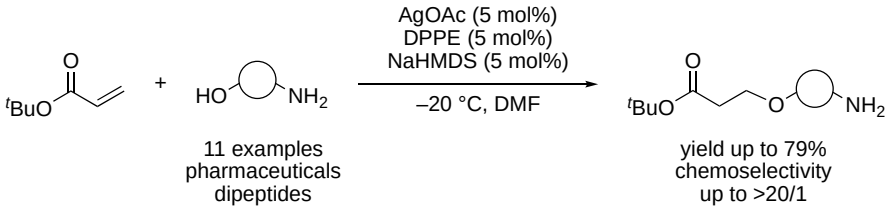
Amino groups and hydroxy groups were widely found in natural and artificial molecules. Because the innately high nucleophilicity of amino groups than hydroxy groups, chemoselective reactions of hydroxy groups over amino groups still depended on the use of protecting groups, causing more unwanted steps and waste. Therefore, much attention was focused on catalytic chemoselective reactions of hydroxy groups over amino groups, which would offer new opportunities for the minimal reliance on protecting groups, contributing to both the atom economy and the step economy.

In order to install lots of functional groups to hydroxy groups in the presence of amino groups directly and selectively, α,β-unsaturated sulfonyl derivatives were selected, where functional groups were installed readily. Basing on former research using nitriles as electrophiles, a catalytic chemoselective functional group installation method was developed. This catalytic method had a broader scope of both α,β-unsaturated sulfonyl compounds and unprotected amino alcohols.

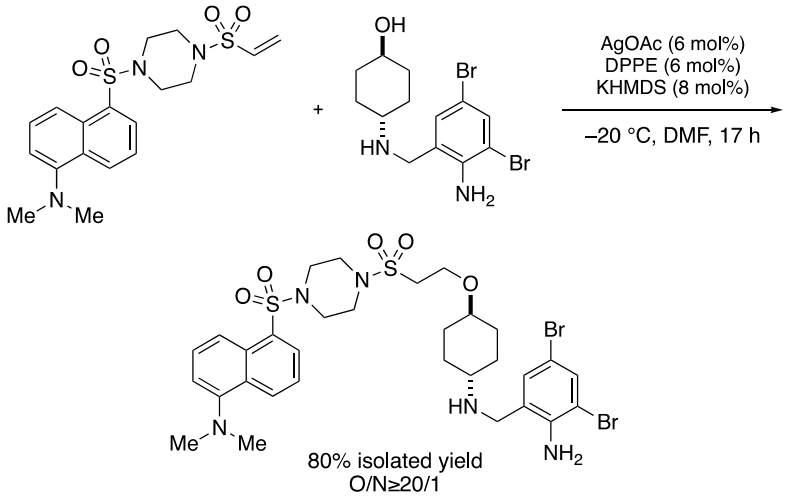


Although the use of α,β-unsaturated ester as an electrophile for catalytic conjugate addition reactions of alcohols was more advantageous for their further transformation, research was hammered by the difficulty in controlling chemoselectivity between conjugate addition and transesterification. Therefore, a catalytic

chemoselective conjugate addition using acrylates was also developed. Various amino alcohols, including unprecedented cyclic β-amino alcohol, were applicable to this catalysis.



Next, research interest moved to the development of catalytic chemo-, regioselective conjugate addition of amino diol. This kind reaction faced a new problem that was the regioselectivity between two hydroxy groups. To date, only one non-enzymatic catalytic regioselective acylation of primary hydroxy groups of protected amino diol was reported. A chemo-, and regioselective conjugate addition was successfully developed by using rac-BINAP as the ligand. The utility of this reaction was highlighted by the reaction below, where dansyl group was chemo-, and regioselectively installed to the β-hydroxy group with good yield.



Besides these successful development of the catalytic conjugate addition of hydroxy groups in the presence of amino groups mentioned above, attempts were made to develop the catalytic strain-release reaction of hydroxy groups in the presence of amino groups, which would present a catalytic chemoselective cyclobutane motif installation method to hydroxy groups, which has not been developed.