The Studies on Reaction Control and Development of New Practical Reagents Based on Characteristics of Reaction Field

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Amides and esters are of great importance in pharmaceutical research and industry because these functional groups occur in various kinds of medicines, natural products, and biomolecules such as proteins and lipids. Among various procedure for synthesizing amides and esters, those that have been adopted as most generalizable and useful are dehydrating condensations of carboxylic acids and amines or alcohols.

Our recent research has been focused on developing useful reagents or systems for dehydrating condensation based on characteristics of reaction fields. We succeeded in developing a water-soluble condensing reagent comprised of 1,3,5-triazines, 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMT-MM), which enables us to conduct activation of carboxylic acids in water or alcohols as well as in common aprotic solvents. The resulting activated triazino esters selectively undergo aminolysis to form amides even in water. On the basis of this finding, artificial acyltransferases were developed by a combination of the triazino reagents and host compounds (cyclodextrins and 18-crown-6); in which the substrate specificity could be controlled in the activation step of the carboxylic acids. We also demonstrated that an interface of micelles acts as a superior reaction field for the condensation. Thus, coupling reaction of fatty acid salts and amphiphilic condensing reagents in a micellar system underwent up to 2,000-fold acceleration due to both local concentration effect and preorientational effect of micelles. The condensation at the interface seems useful for elucidation of the molecular mechanism of membrane fusion; chemical generation of ceramide in the membrane of small unilamellar vesicles (SUV) induced fusion of the vesicles.