

Good Memories of Prof. Yingyan Jiang and International Conference on Fine Chemistry and Functional Polymers: Fruitful Discussions Resulted in Excellent Findings

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About 15 years have passed since I first attended the International Conference on Fine Chemistry and Functional Polymers (FCFP). One day, I was asked by Prof. Inomata of Kanazawa University to attend the conference, and after a while Prof. Jiang sent me a kind invitation letter. This is the beginning of my first trip to China. Prof. Takemoto of Osaka University was also very active to organize the FCFP conference together with Prof. Jiang, and we experienced very warm and friendly atmosphere throughout the conference. (Picture from left: Mr. Tanaka, Prof. Takemoto, Prof. Huang, myself, and Prof. Jiang)



During the conference, Prof. Jiang always made the most of the conference not only in the invited lectures and the presentations of the contributed papers but also in various personal contacts and discussions among the participants. I always remember his great contribution to this wonderful and ever expanding conference.

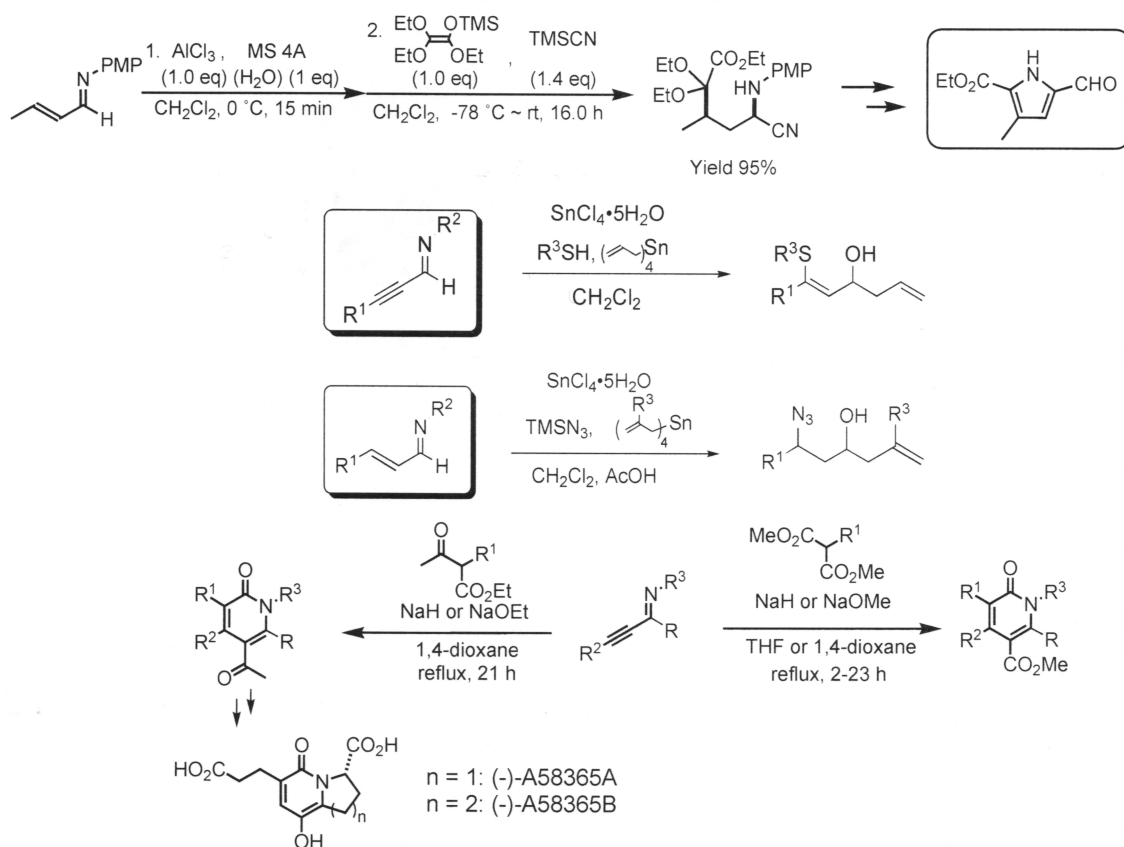
He visited our University on January 19, 2004 as a visiting Professor to deliver a lecture, in which he talked about asymmetric reactions using naturally occurring materials as chiral sources. After the lecture, we discussed a lot about new synthetic reactions based on unsaturated imino compounds. Several new ideas came from discussions, and we discovered a variety of interesting synthetic reactions using unsaturated imino compounds. I will disclose here some of interesting results:

Widespread existence of nitrogen-containing compounds such as amino acids, alkaloids, and functional materials coupled with their use as useful synthons always prompted us to explore new activation methods for imino compounds and subsequent intriguing reactions. For the synthesis of nitrogen-containing compounds, addition reactions to α,β -unsaturated imines constitute one of the most straightforward approaches. However, difficulties are always encountered regarding the regioselectivity. On the

other hand, imino compounds do not always have enough electrophilicity as compared with their parent carbonyl counterparts. For the activation of imino carbons, use as iminium salts offers one of the solutions. The following new reactions were discovered after the discussion with Prof. Jiang:

1 Regioselective Addition Reactions to α,β -Unsaturated Imines

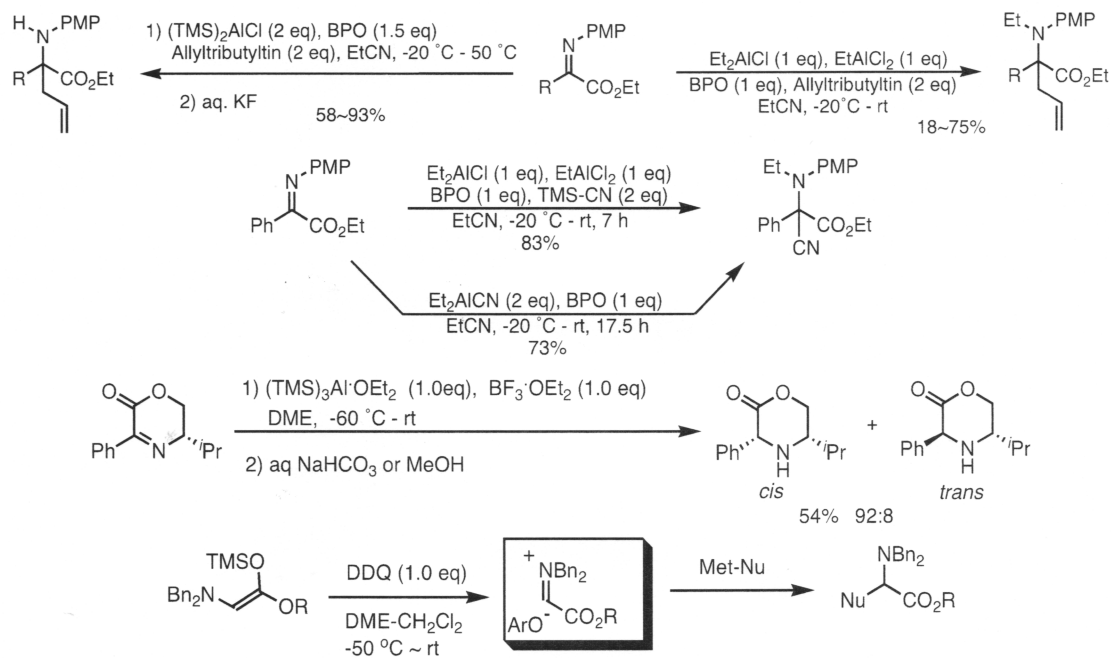
2, 3, 5-Trisubstituted pyrroles were prepared in a regioselective manner using the double nucleophilic addition of α,α -dialkoxy ketene silyl acetals and ketene silyl thioacetals or trimethylsilyl cyanide to α,β -unsaturated imines followed by acid-promoted cyclization and oxidation with DDQ. Using this methodology an imidazole glycerol phosphate dehydratase inhibitor possessing a monopyrrole aldehyde moiety was synthesized. In the presence of $\text{SnCl}_4 \cdot 5\text{H}_2\text{O}$, a mixture of thiols and tetraallyltin underwent 1,4- and 1,2-addition, respectively, with the imines derived from 3-alkynals, where the hydrolysis of the intermediary imino species proceeded to behave them as latent carbonyls. An intriguing 2-pyridone synthesis was found from the nucleophilic addition of malonic esters to alkynyl imines. Addition reaction of ketene silyl acetal to alkynyl ketimines gave α -iminocyclobutenones which in turn were chemoselectively reduced at the imine moieties followed by thermal rearrangement to give β -lactams.



2 New Generation Method of Iminium Salts

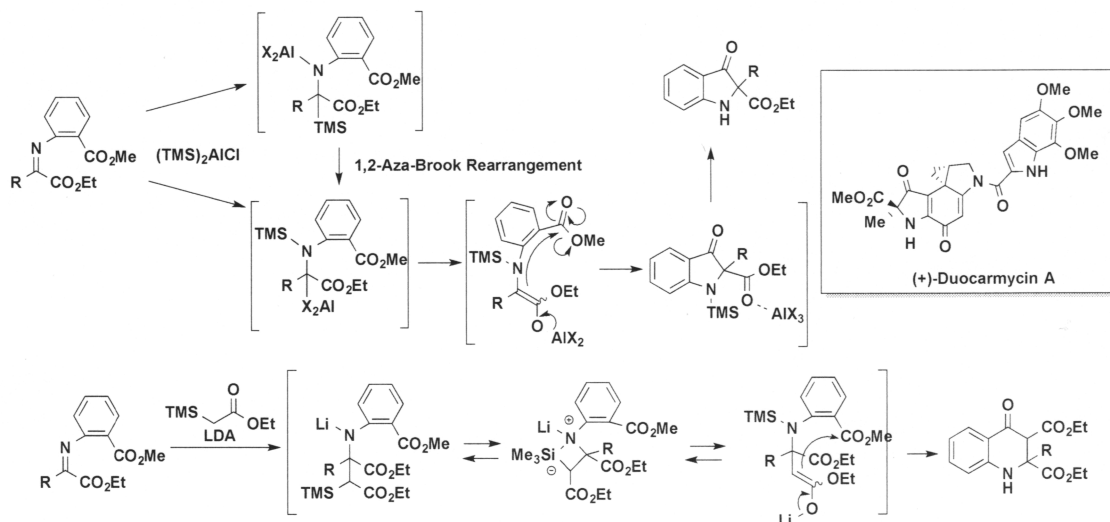
N-Alkylation of the imines derived from glyoxylate esters was conducted with dialkylaluminum chloride in acetonitrile to give an *N*-monoalkylated intermediate, which in turn was oxidized with benzoyl peroxide in the presence of allyltributyltin to give *N*-alkylation-*C*-allylation products. An easy convenient method was also found for the generation of iminium species using the oxidation of amino

ketene silyl acetals with certain oxidants such as DDQ. The iminium salts thus generated showed excellent reactivity as electrophiles.



3 New Synthetic Method of Indolin-3-one and Tetrahydro-4-quinolone

Heterocyclic compounds possessing indolin-3-one and tetrahydro-4-quinolone skeletons have received a considerable amount of attention because of the widespread existence of naturally occurring bioactive materials containing these heterocycles. We are interested in the reactivity of α -imino esters in the recently developed umpolung reactions. In these reactions, the initial *N*-alkylation generates an enolate species, which allows the subsequent formation of important C-C bonds. In an effort to find alternative methods for the generation of enolate species, we focused our attention on reductive cyclization and 1,3-aza-Brook rearrangement, as shown below.



α -Imino esters possessing alkoxycarbonyl electron-withdrawing groups at the α -position of the imines are transformed into indolin-3-ones via a reductive cyclization using bis(trimethylsilyl) aluminum chloride. The synthesis of trisubstituted tetrahydro-4-quinolone is also developed via a 1,3-aza-Brook

rearrangement/Dieckmann condensation of the α -imino ester with the lithium enolate of trimethylsilylacetate. The present *N*-versus the normal *C*-addition reaction of α -imino esters is of interest, and is dependent on the nucleophiles used. This facile process will allow the use of α -imino esters as useful precursors to the aza-Brook rearrangement. Application to the synthesis of (+)-Duocarmycin A, which is a novel antitumor antibiotics produced by *Streptomyces* sp. and effective against murine lymphocytic leukemia p388 and murine Sarcoma 180 in mice is actively under investigation.

In summary, I always remember Prof. Jiang with his great achievements. Everyone knows his very warm and thoughtful personality as well as excellent ability to organize and run research groups. He also organized several international symposiums and conferences, one of which is FCFP conference. Now, Prof. Yuping Wu of Fudan University successfully organizes the FCFP jointly with the international conference on novel materials and synthesis (NMS). The NMS has become one of the most prominent IUPAC conferences and is ever expanding steadily with Prof. Jiang's memory. I am very thankful to Prof. Jiang for leading us to share warm friendship, joy and happiness of the discovery of reactions, and the accomplishment of the synthesis. His way of carrying out research will be passed down though generations, and we will never forget this great scientist forever.