GCOE Fellowship Report: November 24^{th} – December 25^{th} 2009
Host: Prof. Yoshihisa Inoue
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Abstract: My preliminary investigation focused on the effect of pressure on intrinsic racemization of molecularly chiral chromophores, *viz.,* acrylanilides, α-oxoamides, and pyridones. The importance of such study is doubly relevant for subsequent investigations that include 6π–photocyclization, γ-H abstraction, and [2+2] photocyclization. The outcome of this study will likely shed light on the effect of pressure on the molecules of interest and the plausible transition state intermediate(s). During my stay in Prof. Inoue's lab, I focused on collecting data related to the effect of pressure on racemization of molecularly chiral acrylanilides and pyridones. And, I partially applied my findings to photochemical γ-H abstraction involving α-oxoamides. The preliminary results I obtained from the conducted experiments demonstrated that molecularly chiral acrylanilides are very stable at elevated pressures; however, the photoreaction experiments part for this project were incomplete, and further investigations are needed to prove the overall stabilization of the molecules of interest to the corresponding photoproduct(s) at elevated pressures.

Results/Discussion: I am pleased to report that the Global Education and Research Center for Bio-Environmental Chemistry fellowship has enabled me to discover another facet of empirical (photo)chemical sciences. As I outlined in my original plan of study, my project aims to uncover the effect of pressure on the racemization of molecularly chiral chromophores, its overall effect on the transition state intermediate(s) leading to the expected photoproducts. It is well established in the literature that axially chiral moieties or atropisomeric compounds represent good systems for stereodynamics studies.[1,2] Recently, studies[3,4] have shown that non-biaryl molecularly chiral compounds undergo relative racemization at room or elevated temperatures under atmospheric pressure. The same observations are sensed in photochemical reactions at various temperatures, where the enantioproducts distribution depends on the temperature of the reaction medium *viz.* activation parameters ($\Delta\Delta S^{\neq}$ and $\Delta\Delta H^{\neq}$) of the studied systems. Thus, it is obvious and expected that such systems behave differently at different pressures, since Pressure, Temperature, and Volume are known for their interplay in various chemical processes. In this picture, varying one of the three parameters for example the pressure (of the reaction medium) will undoubtedly impact the temperature (of the reaction medium) or the volume (of the studied system).

During my early days in Osaka I tried to learn about the equipments (operational instructions) and instruments (instructions for software) needed for my experiments, since Japanese is the spoken and written language. For me the language barrier is not an energy barrier I would have to overcome; for the universality of science, I managed to learn swiftly the operational instructions of most instruments in Prof. Inoue's lab. Here, I would like to sincerely thank Dr. Fukuhara and Dr. Mori for their assistance, patience and guidance. It would be virtually impossible for me to achieve major experimental results without the assistance of Prof. Inoue, his research associates and students, and his secretary, who guided me during the early stay.

For the first experiments, I have chosen to monitor the racemization of (-)-**1a** (*cf.* plan of study) by High Performance Liquid Chromatography (HPLC). This first attempt to understand the effect of a 100 MPa pressure on a sample of optically pure α-oxoamide **(-)-1a** at 50 ^{o}C was compromised for the fact that the appropriate chiral stationary phase to monitor the reaction was unavailable. I had to obtain the HPLC profile of the molecule of interest using other chiral stationary phases; this was a time consuming process. I finally abandoned the HPLC analyses for Circular Dichroism experiments (CD). In CD analyses, it is advantageous to measure the degree of chiroptical purity for each isomer of a given compound while the system is constantly under the desired pressure. Thus, it was a more accurate and reliable technique than the previous methodology, where, the reaction medium has to be depressurized in order to measure the degree of purity of the sample of interest every time. The instrumentation setup for each measurement would take approximately 60 – 90 min to stabilize the system. The data collected were immediately processed in order to understand if the studied system has behaved well. Most of the experiments were run at least twice for to convince ourselves for scientific integrity and to interpret the dynamics of the studied system with the assistance and suggestions from Prof. Inoue. The CD experiments are the most achieved and well understood.

At this point, I would estimate that I have completed approximately 10 % of my data collection with the CD experiments. Sometimes, when someone else is using the CD instrument, I would try to conduct some other experiments outlined in my original plan of study. Because of the time-intensive effort required to collect data, I opted to restrict data collection for experiments which results are not well understood in order to maximize the richness and detail of the collected data for successful experiments. However, I can report that a cursory analysis of the preliminary results indicate that there is promising lead to obtain results especially with the photochemical γ-H abstraction experiments involving α-oxoamides, where partial results show that the enantiomeric ratio of the system has changed from 79:21 to almost 50:50 (in the case of **(-)-1a** yielding **2a** and ***ent*-2a**) at elevated pressures. Although this result is incomplete to scheme the effect of elevated pressures on photochemical γ-H abstraction of α-oxoamides, it is promising that further investigations would undeniably confirm the current findings.

I managed to accomplish two more CD experiments in order to obtain two data points for a differential activation volume. Even though it would be tricky to find the appropriate pressures, at which the studied system would behave well, I ended up with accurate results, which allowed me to graph the differential activation volume data. We found that optically pure isomers of **5b** (*cf.* plan of study) have a differential activation volume of **-0.019 $Kcal \bullet mol^{-1}$.** A negative differential volume of activation is synonym of compact species. This finding explains the stability of the studied systems at elevated pressures. Thus, the systems of interest were really cooperative, and are expected to yield optically pure enantiospecific photoproducts at elevated pressures. This assumption has to be verified with future studies and investigations (in collaboration with Prof Inoue) towards this aspect. Based on the preliminary results, we strongly believe that molecularly chiral chromophores would be stable at any given temperature if and only if the system is under the appropriate pressure. Also, the effect of elevated pressures on the transition state intermediates during the aforementioned photochemical transformations have to be comprehensively investigated.

In closing, I wish to express my sincere gratitude to the Global Education and Research Center for Bio-Environmental Chemistry for its generous support. Without such opportunity, I would never have been able to get exciting preliminary results over a period of 30 days; the current results have opened up new opportunities to pursue. I am truly appreciative of this fellowship. Beside the research experience gained during my stay, I visited Kyoto on Dec 13th, 2009 with two students (Mr. Ito and Miss Wakai from Prof. Inoue's lab) to get a taste of Japanese culture, an experience that I will cherish. I also enjoyed various Japanese foods. I was told that in order to have a good taste for Japanese foods, I must eat with chopsticks; I quickly accustomed to these funny sticks for the fact that it was sometime hard for me to pick up all the food out of the plate/bowl.

I would also have to thank Prof. Yoshihisa Inoue for accepting to host me in his laboratory and his generosity and help during my stay. Finally, I want to thank Prof. Sivaguru Jayaraman (Ph.D. advisor) for his nurturing advice and for all kind of support.

Reference:

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