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University of Zurich Hosts Symposium in Honor of Professor Heinz Heimgartner

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Abstract: The Institute of Organic Chemistry of the University of Zürich hosted a symposium in honor of Prof. Heinz Heimgartner on June 9, 2006. PD Dr. Simon M. Ametamey, Dr. Kurt Dietliker, Prof. Grzegorg Mloston, Dr. Daniel Obrecht, Prof. José Villalgordo and Prof. Peter Wipf, all former graduate students and collaborators of the Heimgartner group gave insight into their research efforts that are still connected to greater or lesser extent to Prof. Heimgartner's main research interest in heterocyclic chemistry.

Keywords: Azirine · Bicyclobutane · Conformational analysis of dimethoxycarbene · Heimgartner, H. · Heterocycles · High-throughput synthesis of pyrazines · Photo-initiated curing of automotive coating · Positron emission tomography (PET) · Protein epitrope mimetics (PEM) · Pyrrolidines · Strained rings

On June 9th, a very bright and sunny day, the Institute of Organic Chemistry (OCI) hosted a symposium in the honor of Prof. Dr. Heinz Heimgartner of the University of Zürich. Prof. Dr. Heinz Heimgartner received his Diploma in Chemistry from the University of Zürich (1968) and completed his Ph.D. work under the guidance of Prof. Dr. H. Schmid in 1972. Throughout his career, he remained loyal to the OCI at Zürich. He was named Privatdozent in 1980, and in 1987 he was appointed Titularprofessor. He was awarded the Werner Prize and Medal of the Swiss Chemical Society in 1978, and the Kametani Award in 2005. He has distinguished himself by outstanding research in heterocyclic chemistry. Moreover, for decades Prof. Heimgartner was THE chemistry teacher for students in the Medical School. Towards the end of this year, he will be retiring officially from (most of) his duties at the University.

The symposium was initiated by Prof. Peter Wipf, from the Department of Chemistry at the University of Pittsburgh, a prominent former member of the Prof. Heimgartner's research group, and by Prof. Jay Siegel, from the OCI at the University of Zürich. A significant number of former undergraduate, graduate, and postdoctoral students as well as collaborators of the Heimgartner research group contributed to the organization of the meeting and all speakers were former Heimgartner group members – an indicative gesture of saying "thank you". His kind mentorship and his scholarship inspired and motivated his students and coworkers, and his calm and yet exceedingly focused and devoted attention generated a productive and collegial atmosphere. Thus, it was not surprising that numerous former members of the research group and many past and present colleagues of his happily came together and met for the day in honor of Prof. Dr. Heinz Heimgartner.

The day started out with a presentation by ***PD Dr. Simon M. Ametamey*** of the Center for Radiopharmaceutical Science, ETH, PSI & USZ on the subject of *Pet Radiopharmaceuticals: From Development to Human Studies*. Simon Ametamey gave an overview of PET (positron emission tomography) as an imaging modality and explained its application in diagnostic imaging. He also described the stages in PET ligand development and illustrated this with a new PET ligand which was developed very recently for the *in vivo* imaging of the metabotropic glutamate receptor subtype5 (mGluR5). It was rather intriguing to see how short-lived compounds with positron emitting isotopes (*e.g.* the half life of ^{18}F is just about 2 h and the half live of ^{11}C is about 20 min) were developed, scaled up under GMP conditions, and are being applied to provide therapeutically useful PET images.

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The next talk was presented by ***Dr. Kurt Dietliker*** of Ciba Specialty Chemicals Inc. He was the first doctoral student in Prof. Dr. Heinz Heimgartner's research group. In his talk titled *The Light Shines on – From Amino-azirines to Industrial Photopolymerization*, Dr. Dietliker gave a comprehensive overview of protective and decorative coatings using radiation curing technology and showcased the example of clear topcoats for automotive applications. He described how the structural variation of the binders (urethane acrylate oligomers) influences the properties of the final coating with respect to flexibility, toughness, and mechanical and chemical resistance. Furthermore, he eluded how the viscosity of the 'starting' material can be adjusted without using solvents, and how additives guarantee the long-term weathering stability of the final coating in outdoor use. In the end, Kurt Dietliker described a photoinitiator that is stable for an extended amount of time in the dark and that can be set into action by UV-lamps that are available at low cost to machine shops and that look like oversized IR hairdryers. Once the polymerization is started, the viscous liquid is transformed to the desired coating with excellent properties and a quantum yield for C–C bond formation of over 1000, making this process an attractive application of photochemistry in the industrial realm.

The last seminar before lunch was held by ***Prof. Grzegorg Mloston*** of the Department of Organic & Applied Chemistry at the University of Lodz, Poland. He has been a collaborator of Prof. Heimgartner for many years. With his enthusiastic presentation style, it was easy for Prof. Mloston to keep his audience alert ahead of lunch, lecturing on *New Adventures with Small Ring Heterocycles*. Prof. Mloston elaborated on the reactivity of dimethoxycarbene (DMC), a readily available and nucleophilic carbene, towards C=S double bonds, C≡C triple bonds, C=N double bonds of activated imines, and electron deficient C=C double bonds. For example, dimethyl dicyanofumarate (DCFM) demonstrated an intriguing level of stereoselectivity that could be explained by a two step mechanism of addition of the carbene to the electron deficient C=C bond. The final part of the presentation was focused on the conformational analysis of DMC, suggesting the existence of the *trans,trans*-conformer being the most stable form. The calculated energy of the *cis,trans*-conformer was slightly higher and both stereoisomers were found to exist in equilibrium in the gas phase. The experimental results of spectroscopic studies of the pyrolysate of DMC in low temperature matrices were in good agreement with prediction formulated on the basis of advanced computational calculations (*Eur. J. Org. Chem.* **2006**, in press).

During the lunch break, the audience moved to the Irchel Lichthof and enjoyed a buffet of light and hearty sandwiches, juice and coffee. This was a great opportunity to meet old colleagues and group members, former professors and teachers for a chat – and, of course, to catch up with Heinz Heimgartner. Several posters from various groups and companies provided further stimulation.

The day continued with a talk by ***Dr. Daniel Obrecht*** of Polyphor LTD titled *From Amino-azirines to Protein Epitope Mimetics (PEM)*. Daniel Obrecht is also a member of the early Heimgartner research group, and he explained their company's proprietary PEM technology. In PEM, medium-sized, cyclic, peptide-like molecules are mimicking beta-hairpin secondary structures, an important protein–protein recognition element. PEM favorably combines the advantageous properties of large biopharmaceuticals capable of disrupting protein–protein interactions with the advantages of small molecule drugs with regard to oral administration and considerably lower production costs. PEM are designed by varying the three parts that PEM generally consist of: the loop size and sequence, the building block amino acids, and secondary structure stabilizing templates. In order to achieve a large variety of PEM, they are synthesized in a 96-parallel library format using an efficient mixed solution-solid phase process.

The next speaker was ***Prof. José Villalgordo*** of Villapharma Research who talked about *Privileged Heterocyclic Scaffolds and High Throughput Organic Synthesis*. Dr. José Villalgordo is the Director of a young company in Spain that focuses on early-stage collaborative drug discovery services in the two main areas of high-throughput discovery and FTE-based custom and contract research. In his talk, he described a vast and impressive number of diverse pyrazines-derived heterocycles obtained by numerous coupling reactions. Properly selecting the heterocyclic substrates, in combination with cross-coupling reactions of p-deficient heteroaromatic

thioethers has shown to be a fertile means for obtaining large arrays of molecularly diverse heterocyclic scaffolds.

The last talk of the Symposium was held by ***Prof. Peter Wipf*** of the University of Pittsburgh. In his presentation *From Strained Rings to Heterocycles: The Bicyclobutane Route to Pyrrolidines*, Peter Wipf elaborated on a direct synthetic access to (bicyclo[1.1.0]butylmethyl)amines from propargyl phosphinamides through a Simmons-Smith reaction with Et_2Zn/CH_2I_2 or by addition of bicyclo[1.1.0]butyllithium to activate imines. Phase-transfer conditions proved optimal for the introduction of N-allyl or N-propargyl substituents, and the resulting amides underwent highly diastereoselective cascade rearrangements by formal ene or [2+2] pathways to yield novel spirocyclic and tricyclic pyrrolidine heterocycles. (Citation from P. Wipf, M.A.A. Walczak, *Angew. Chem. Int. Ed* **2006**, *45*, 4172–4175.)

After these presentations, the audience and the speakers moved back into the Lichthof where the OCI hosted an Apero. This provided further opportunities to socialize, to ask questions, and enjoy the refreshments. In the late afternoon, the attendees of the Symposium in honor of Prof. Dr. Heinz Heimgartner walked through the beautiful Irchel Park to the tram station to catch a ride to the harbor. Here, the large group of chemists boarded a boat that brought them to the Halbinsel Au where they met for cocktails and enjoyed the breathtaking view over lake of Zürich into the Alps of the Canton of Glarus.

Dinner was organized by Dr. Peter Tromm at the Restaurant Au and after dessert Prof. H.-J. Hansen told stories of the good old days at the OCI. Dr. Christian Jenny, one of the early graduate students of Heinz Heimgartner, and Dr. Andreas Gebert, one of the last graduate students, added reports on interesting or actually rather wild stories of the daily life in Heimgartner's research lab. With this, a day of celebration and gratitude to Prof. Dr. Heinz Heimgartner came to an end. We wish him all the best in his future scholarly and well deserved leisurely endeavors!

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