Prof. Dr. Dr. h.c. Lutz F. Tietze

A Tribute

Lutz F. Tietze was born on March 14, 1942 in the city of Berlin. In the aftermath of World War II his family moved to the northern German state Schleswig-Holstein where he was raised and educated. In 1961 he obtained the "Abitur" and decided to study chemistry at the near-by University of Kiel from which he graduated with the diploma degree in 1966. During his studies he also spent some time at the University of Freiburg which turned out to be a life-changing decision because there he met his wife Karin to whom he has now been married for more than 40 years. From 1966 until 1968 he made experimental studies towards his Ph.D. degree in the group of the natural product chemist Prof. Burchard Frank in Kiel, investigating the selective oxidation of laudanosolin derivatives.

Supported through a Fulbright fellowship he crossed the Atlantic ocean to take up a research associate position at the Massachusetts Institute of Technology (Cambridge) in the renowned group of Prof. George Büchi, completing a total synthesis of the natural product loganin. While working hard on his synthesis project he still had some spare time and enjoyed sailing on the Charles river and off the Massachusetts coast at Marble Head. In 1971 he returned to Germany and started his independent career at the University of Münster. Having broad experience both in natural product and synthetic chemistry he picked as the initial project for his habilitation work the natural product secologanin, a key biogenetic precursor to the monoterpenoid indole-, ipecacuanha-, and cinchona- alkaloids. He probably did not anticipate that this compound would consume most of his attention for the next decade or so, as it turned out to be an extremely challenging target. Eventually, he accomplished a total synthesis of the aglucon of secologanin, developed a general glycosidation method of the iridoids and secoiridoids, and made important contributions towards the biogenetic origin and the use of secologanin for the synthesis of other

natural products which earned him the first publications and attention within the scientific community. After a further research period with Prof. Alan Battersby in Cambridge in 1974 he obtained his habilitation in 1975 and was shortly thereafter awarded the Karl-Winnacker fellowship of the Hoechst A.G. In 1977 he was appointed Associate Professor at the University of Dortmund and eventually in 1978 became Full Professor and director at the University of Göttingen where he has remained ever since.

In Göttingen he developed a broad research program over the years, which was fueled in part by the secologanin project. Thus, he and his coworkers developed a broadly used method for the stereoselective synthesis of so-called acetal glycosides. Being very acid-labile these compounds were later used as prodrugs for a selective cancer chemotherapy when containing cytotoxic residues as acetal components which liberated the toxic principle in the slightly acidic medium of cancer cells. More recently, his group has applied the antibody-directed enzyme prodrug therapy (ADEPT) for the selective recognition and fighting of tumor cells. For that purpose as a non-toxic prodrug a β-D-galactoside of a CC-1065 analogue was used in combination with an immunoconjugate of a β-D-galactosidase and a monoclonal antibody which selectively binds to the malignant cells, and cleaves the glycosidic bond in the prodrug with the liberation of the toxic principle only in the tumor tissue. Extremely high selectivity factors of >4000 between malignant and normal cells have been observed, suggesting that this strategy might be applied in clinical trials one day. In fact, a pharmaceutical company has meanwhile taken on this goal and is further developing these compounds.

For the construction of the secologanin aglucon he and his coworkers utilized hetero- Diels-Alder reactions with inverse electron demand of 1-oxa- butadienes and enol ethers. It turned out that this strategy was applicable not only to the secologanin problem but also proved well suited for the stereoselective synthesis of dihydropyrans in general, and a number of related natural products in particular, such as (-)-talaromycin B. Even more important was the observation that this hetero Diels-Alder reaction may be coupled to the synthesis of the heterodiene itself through a Knoevenagel condensation of a β-dicarbonyl compound and an aldehyde. Thus, the first domino- Knoevenagel hetero Diels-Alder reaction was born, which was followed shortly thereafter by the domino Knoevenagel ene reaction and the domino Sakurai ene reaction. These three transformations were successfully employed as key steps in the syntheses of hexahydrocannabinol, veticadinol, deoxyloganin, hirsutine, emetine, and tubulosine.

Tietze and his coworkers extended the concept of domino reactions to transition-metal-catalyzed processes and asymmetric synthesis. In a very elegant synthesis of (-)-cephalotaxin two sequential Pd-catalyzed reactions, an allylic alkylation, and a Heck reaction, were employed to assemble the complete carbon skeleton of the natural product in one pot. In a similar manner, enantiomerically pure estrone and further derivatives were synthesized by way of two consecutive Heck reactions. The latest success in this field was the enantioselective synthesis of vitamin E through a domino-Wacker–Heck reaction. Thus, the new strategy of domino reactions developed by the Tietze group allows chemists to improve the efficiency in synthesis in an environmentally beneficial way, with the preservation of natural resources.

His group has also developed a highly stereoselective method for the allylation of aldehydes and ketones based upon the chiral auxiliary pseudoephedrine which has been applied to the total synthesis of macrolide antibiotics as well as cembranoid natural products.

Altogether Prof. Tietze's work has been published in more than 360 original papers, 31 patents, and three books — the latest one being, "Domino Reactions" which has just been published by Wiley-VCH. His work has received a great deal of international attention documented by numerous plenary lectures at conferences all over the world which he has given. In 1994 he was awarded the honorary doctorate of the University of Szeged (Hungary), in 1999 the Novartis lectureship in Switzerland, in 2000 the Novartis lectureship in USA and the Merck lectureship in the UK, in 2002 the Grignard-Wittig prize of the French Chemical Society and a silver medal of the Hungarian Chemical Society, and in 2004 the highly prestigious Emil-Fischer medal of the German Chemical Society (GDCh). He is a Fellow of the Royal Society of Chemistry (UK), the Japanese Society for the Promotion of Science and Member of the Academy of Science in Göttingen and an Honorary Member of the Argentine Chemical Society. In 1992 he received a call for a Chair at the University of Münster as successor to his mentor Prof. B. Franck, which he declined.

He has served his home university and the scientific community in many different functions. He is Director of the Institute of Organic and Biomolecular Chemistry in Göttingen, was Dean of the Faculty of Chemistry and speaker of the Sonderforschungsbereich 416, "Chemical and Biological Synthesis and Transformation of Natural Products and Natural Product Analogues" funded by the DFG. Since 1997 he has been president of the German Central Association of Chemistry and since 2004 member of the committee of the German Research Council (DFG).

In his spare time, Lutz Tietze enjoys playing hockey, sailing and skiing.

With his group he goes on a trip every year either to the sea for sailing, or to the mountains on a hiking tour. As a former member of his research group I look back on those times with deep appreciation and gratitude.

Christoph Schneider
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Selected Publications

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