

HETEROCYCLES, Vol. 93, No. 1, 2016, pp. 1 - 6. © 2016 The Japan Institute of Heterocyclic Chemistry  
DOI: 10.3987/COM-15-S(T)Foreword

## PREFACE TO HETEROCYCLES ISSUE

### HONORING THE 75TH BIRTHDAY OF Prof. Dr. *h.c.* LUTZ F. TIETZE

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When I met Professor Lutz F. Tietze for the first time about ten years ago I applied for the position of a habilitand in his esteemed research group. We had never met each other before in person and had had only electronic contact. At that day, I approached Göttingen by train from the south; in an email he had promised to pick me up at the train station. Questions whether he, one of the most prominent professors of organic chemistry in Germany, would accept me as habilitand, whether we might come along with each other - or in other words - whether the chemistry between him and me would be right came into my mind and led to some discomfort in the minutes immediately before the train in Göttingen stopped. I got off the train, he saw me and welcomed me and immediately an intense conversation (not about chemistry) started and all my initial concerns and fears were quickly forgotten. Several months later, I became his last habilitand. Therefore, it is a special pleasure for me to write this preface on honor of his 75<sup>th</sup> birthday.

Lutz F. Tietze was born in the mid of the Second World War, on March 14, 1942 in the city of Berlin. Soon after its end he moved as a child to the most northern part of Germany where he was raised up. In 1961 he started to study chemistry at the University of Kiel located at the Baltic Sea. An intermezzo at the University of Freiburg in the very southern part of Germany did lead to a dramatic change in his private life since he met his future wife Karin there to whom he has been married since 1966. Together they have become parents of four children. Karin was also responsible for the decision to become a university professor since it is told that Lutz asked her what kind of job he should look for and she gave him two professions to choose: one of them was professor. In his further studies Lutz was highly efficient and obtained after diploma (1966) in only a bit more than two years his Ph.D. degree in the group of Burchhard Franck in Kiel. This thesis dealing with the selective oxidation of laudanosolin derivatives<sup>1</sup> paved the way for his future research interests in the field of natural products. From 1969 he performed postdoctoral studies at the MIT in Boston working with Prof. George Büchi.<sup>2</sup> This research stay in the field of total synthesis was supported by a Fulbright Fellowship. In the meantime the group of his Ph.D. advisor Burchhard Franck had moved to the University of Münster. As it was very common in those days, Lutz returned as habilitand to his former group, but was working independently on the natural product secologanin which is a key intermediate for a variety of indole, ipecacuanha and chinchona alkaloids.<sup>3,4</sup> Interrupted by a another research stay in Prof. Alan Battersby's lab he obtained his habilitation in 1975. For only several months he became an Associate Professor at the University of Dortmund in 1977, but quickly moved on to Georg-August University Göttingen in 1978 to become full professor where he served as a director until 2012.

In Göttingen the research of the Tietze lab has developed in various branches. *Cantus firmus* has been natural product chemistry. But not only routes leading to total syntheses were conducted in his lab, also respective methodology was developed. Novel domino reactions were designed and exploited for target-oriented synthesis. This success story started with the design of the domino-Knoevenagel hetero Diels-Alder reaction in which a heterodiene is obtained through Knoevenagel condensation of a 1,3-dicarbonyl compound and an aldehyde. A variety of dihydropyran moieties proved to be easily accessible by this methodology.<sup>5</sup> Other domino transformations consisting of a Knoevenagel ene<sup>6</sup> and a Sakurai carbonyl-ene reaction<sup>7</sup> followed. Natural products such as hexahydrocannabinol,<sup>8</sup> emetine<sup>9</sup> and tubulosine<sup>10</sup> were easily accessed by using these key reactions.

In a famous review article in *Chemical Reviews* in 1996 with the title "*Domino Reactions in Organic Synthesis*" which has been cited more than 3000 times so far he defined the term *domino reaction* and classified different types of these transformations.<sup>11</sup> The group also commenced to use transition-metal catalyzed processes to selectively access complex targets in a highly efficient manner under mild

conditions in an ecologically and economically friendly way. Especially the Heck reaction was extensively exploited in domino processes resulting in the fact that Lutz F. Tietze is the scientist with the most papers dealing with the Heck reaction. Early work in this field concentrated on the assembly of (-)-cephalotaxine based on the Pd-catalyzed allylic alkylation and a subsequent Heck reaction.<sup>12</sup> Stereoselective syntheses of steroids were designed by using using a domino Heck-Heck approach.<sup>13</sup> A twofold Heck reaction proved also to be the key step in the synthesis of analogues of the highly potent insecticide spinosyn A.<sup>14</sup> In combination with Wacker-type reactions he elegantly made use of a domino Wacker-Heck reaction to access vitamin E.<sup>15</sup> (-)-Diversonol<sup>16</sup> as well as related xanthenone (-)-blennolide<sup>17</sup> and chromenone (-)-gonytolide<sup>18</sup> were created by a domino Wacker/ carbonylation/ methoxylation sequence. The carbopalladation of alkynes as the first step of such a metal-catalyzed domino reaction afforded tetrasubstituted double bonds; the respective Pd-vinyl species could be further reacted either in Heck reactions, typical cross coupling reactions or C-H activations. This approach paved the way to access molecular switches in a highly efficient manner,<sup>19,20</sup> but was also employed in the enantioselective total synthesis of the lignan (+)-linoxepin.<sup>21,22</sup>

He was also interested in the development of enantioselective methods. His group designed, developed and exploited a highly diastereoselective allylation of aldehydes and ketones based on a domino reaction.<sup>23</sup> Highly enantioenriched homoallylic alcohols were formed; norpseudoephedrine was utilized as chiral auxiliary. To date, this method also known as Tietze allylation is the best approach to access homoallylic alcohols in an enantioselective fashion. Later, the method was not only employed for the total synthesis of cembrenes,<sup>24</sup> but also deeply investigated on a highly sophisticated theoretical level by quantum chemical computations.<sup>25</sup>

Besides numerous total syntheses which his co-workers have finished Lutz was especially fascinated by concept of antibody-directed enzyme prodrug therapy (so called ADEPT concept) to selectively recognize and kill malignant tumor cells. With the eye of an experienced organic chemist he knew what to do. A glycoconjugate of a duocarmycin derivative (the so-called prodrug) which is much less toxic than duocarmycin itself (the drug) has been used in combination with a glycosidase attached to the monoclonal antibody which binds to the targeted malignant cell. At the surface of the malignant cell the enzyme triggers the transformation from the prodrug to the drug and the drug kills the cell.<sup>26</sup> Recently, the Tietze group has developed novel duocarmycin-based prodrugs which are about 1 000 000 less toxic than the corresponding drugs. The drugs even reached IC<sub>50</sub> values of about 100 fM.<sup>27</sup> In collaboration with a more biochemical-oriented group, he was even able to elucidate the mode of action of these drugs.<sup>28,29</sup>

Not only his scientific output in form of nowadays 474 scientific publications, 34 patents, numerous book chapters and six books, either edited or written (two of them are standard references on domino

reactions),<sup>30,31</sup> is incredibly impressive, but also the number of people who received their Ph.D. degrees under his mentorship is outstanding. He has been serving for 175 students as Ph.D. supervisor and for more than 20 postdocs as postdoctoral mentor. Eight of his former co-workers or habilitands are now professors in Germany, nine of them have become professors in countries such as India, China, Australia, Uruguay, Hungary, Italy and Mexico. Although successful former co-workers working either in industry or in academia might be considered as the greatest award a mentor is able to get, Lutz has also received numerous “real” awards in recognition of his outstanding work. I only would like to mention a few of them: Member of the Academy of Science in Göttingen (1990), JSPS Fellow in Japan (1991), Fellow of the Royal Society of Chemistry (1991), Honorary Doctorate of the University of Szeged in Hungary (1994), Novartis Chemistry Lectureships for Switzerland and the US (1999 and 2000), Merck Lectureship (2000), Grignard-Wittig Prize of the French Chemical Society (2002), Silver Medal of the University of Szeged (2002), Emil Fischer Award of the German Chemical Society (2004), Hevesy Lectureship Award (2008), UR Ghatak Gold Medal of the Indian Association for Cultivation of Science (2011) and Honorable Fellow of the Indian Chemical Society (2014).

Of course, such a preface can only provide a glimpse on Lutz’ tremendous achievements in organic chemistry. However, it would not be complete without mentioning that he has been serving the University of Göttingen, but also the German chemical community in various functions broadly shaping organic chemistry in our country. He had been the director of the Institute of Organic and Biomolecular Chemistry in Göttingen from 1978-2012 before he received in 2012 as Professor *emeritus* a Lower Saxony Research Professorship which has allowed him to continue his research projects. He was Dean of the Faculty of Chemistry and spokesperson of a collaborative research center (SFB 416) funded by the DFG focusing on natural product chemistry and biology. He had been serving as an elected member of the German Science Foundation (DFG) and has been asked at numerous occasions to be a competent reviewer. For the last 20 years he has been president for the German Central Association of Chemistry.

Whoever has met Lutz F. Tietze in person is impressed by this character showing so much activity and radiating energy. He still enjoys sports such as sailing, skiing and difficult (!) hiking tours. He really loves to face and to overcome challenges, not only in chemistry, not only in chess, but also in sports and in his daily life. Coming back to my introduction, during my years in Göttingen I have become acquainted with him as an excellent scientist, a highly efficient group leader and wise mentor. I greatly appreciate these times that I would not like to miss.

Happy birthday, Lutz! Please enjoy this special issue of *Heterocycles* dedicated to your multifaceted contributions to organic chemistry! I wish you and Karin a happy and healthy, but still challenging life.



**Daniel B. Werz** received a BS in chemistry at Heidelberg University, Germany, in 1997 and a Ph.D. in organic chemistry from Heidelberg University in 2003 with Rolf Gleiter working on alkyne chemistry. Following his doctoral studies, he was a Postdoctoral Fellow with Peter H. Seeberger at ETH Zurich, Switzerland. In December 2006 he joined the Chemistry Faculty of Göttingen University as habilitand under the mentorship of Lutz F. Tietze. In 2013 he took the position of an Associate Professor at the Technical University of Braunschweig, Germany. His main research interests include the development of novel efficient methods for the synthesis of hetero- and carbocyclic compounds (e.g. by cyclopropane chemistry, domino reactions and Pd catalysis). In addition, he is interested in carbohydrates and their mimics.

His awards include an Emmy Noether Fellowship of the German Research Foundation, the ORCHEM Award of the German Chemical Society, a JSPS Visiting Professorship in Japan, and most recently, an ERC Consolidator Grant of the European Union.

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- <sup>1</sup> B. Franck, L. F. Tietze, *Angew. Chem. Int. Ed. Engl.* **1967**, *6*, 799.
- <sup>2</sup> G. Büchi, J. A. Carlson, J. E. Powell, Jr., L. F. Tietze, *J. Am. Chem. Soc.* **1970**, *92*, 2165.
- <sup>3</sup> L. F. Tietze, *J. Am. Chem. Soc.* **1974**, *96*, 946.
- <sup>4</sup> G. Kinast, L. F. Tietze, *Chem. Ber.* **1976**, *109*, 3640.
- <sup>5</sup> L. F. Tietze, G. v. Kiedrowski, K. Harms, W. Clegg, G. M. Sheldrick, *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 134.
- <sup>6</sup> L. F. Tietze, A. Steinmetz, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 651.
- <sup>7</sup> L. F. Tietze, M. Rischer, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1221
- <sup>8</sup> L. F. Tietze, G. v. Kiedrowski, B. Berger, *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 221.
- <sup>9</sup> L. F. Tietze, N. Rackelmann, G. Sekar, *Angew. Chem. Int. Ed. Engl.* **2003**, *42*, 4254.
- <sup>10</sup> L. F. Tietze, N. Rackelmann, L. Müller, *Chem. Eur. J.* **2004**, *10*, 2722.
- <sup>11</sup> L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115.
- <sup>12</sup> L. F. Tietze, H. Schirok, *J. Am. Chem. Soc.* **1999**, *121*, 10264.
- <sup>13</sup> L. F. Tietze, T. Nöbel, M. Spescha, *J. Am. Chem. Soc.* **1998**, *35*, 8971.
- <sup>14</sup> L. F. Tietze, G. Brasche, C. Stadler, A. Grube, N. Böhnke, *Angew. Chem. Int. Ed.* **2006**, *45*, 5015.
- <sup>15</sup> L. F. Tietze, K. M. Sommer, J. Zinngrebe, F. Stecker, *Angew. Chem. Int. Ed.* **2005**, *44*, 257.
- <sup>16</sup> L. F. Tietze, S. Jackenkroll, C. Raith, D. A. Spiegl, J. R. Reiner, M. C. Ochoa Campos, *Chem. Eur. J.* **2013**, *19*, 4876.
- <sup>17</sup> L. F. Tietze, L. Ma, J. R. Reiner, S. Jackenkroll, S. Heidemann, *Chem. Eur. J.* **2013**, *19*, 8610.
- <sup>18</sup> L. F. Tietze, S. Jackenkroll, J. Hierold, L. Ma, B. Waldecker, *Chem. Eur. J.* **2014**, *20*, 8628.
- <sup>19</sup> L. F. Tietze, A. Düfert, F. Lotz, L. Sölter, K. Oum, T. Lenzer, T. Beck, R. Herbst-Irmer, *J. Am. Chem. Soc.* **2009**, *131*, 17879.
- <sup>20</sup> L. F. Tietze, B. Waldecker, D. Ganapathy, C. Eichhorst, T. Lenzer, K. Oum, S. O. Reichmann, D. Stalke, *Angew. Chem. Int. Ed.* **2015**, *54*, 10317.
- <sup>21</sup> L. F. Tietze, S.-C. Düfert, J. Clerc, M. Bischoff, C. Maaß, D. Stalke, *Angew. Chem. Int. Ed.* **2013**, *52*, 3191.
- <sup>22</sup> L. F. Tietze, J. Clerc, S. Biller, S.-C. Düfert, M. Bischoff, *Chem. Eur. J.* **2014**, *20*, 17119.
- <sup>23</sup> L. F. Tietze, C. Wulff, C. Wegner, A. Schuffenhauer, K. Schiemann, *J. Am. Chem. Soc.* **1998**, *120*, 4276.

- <sup>24</sup> L. F. Tietze, C. C. Brazel, S. Hölsken, J. Magull, A. Ringe, *Angew. Chem. Int. Ed.* **2008**, *47*, 5246.
- <sup>25</sup> L. F. Tietze, T. Kinzel, S. Schmatz, *J. Am. Chem. Soc.* **2008**, *130*, 4386.
- <sup>26</sup> L. F. Tietze, B. Krewer, H. Frauendorf, F. Major, I. Schuberth, *Angew. Chem. Int. Ed.* **2006**, *45*, 6570.
- <sup>27</sup> L. F. Tietze, J. M. von Hof, M. Müller, B. Krewer, I. Schuberth, *Angew. Chem. Int. Ed.* **2010**, *49*, 7336.
- <sup>28</sup> T. Wirth, K. Schmuck, L. F. Tietze, S. A. Sieber, *Angew. Chem., Int. Ed.* **2012**, *51*, 2874.
- <sup>29</sup> M. F. Koch, S. Harteis, I. D. Blank, G. Pestel, L. F. Tietze, C. Ochsenfeld, S. Schneider, S. A. Sieber, *Angew. Chem. Int. Ed.* **2015**, *54*, 13550.
- <sup>30</sup> L. F. Tietze, G. Brasche, K. Gericke, *Domino Reactions in Organic Synthesis*, Wiley-VCH, Weinheim, **2006**.
- <sup>31</sup> L. F. Tietze (Ed.), *Domino Reactions: Concepts for Efficient Organic Synthesis*, Wiley-VCH, Weinheim, **2014**.