Angewandte International Edition Chemie

Manfred Schlosser (1934–2013)

M. Schlosser

Professor Manfred Schlosser disappeared on June 26, 2013, shortly after his 79th birthday, in the Swiss mountains. Hiking had always been one of his favorite free-time activities.

Born in 1934 in Ludwigshafen am Rhein, he studied chemistry and, to some extent, medicine from October 1952 at the University of Heidelberg. The Diplom exam followed in June 1957 and he then joined the group of Georg Wittig. He completed his doctoral studies in May 1960 and was awarded "Doctor habilitus" (coupled with the conferment of the "venia legendi") from the University of Heidelberg in August 1966.

Manfred Schlosser was appointed as a Research Fellow at the European Research Associates, sponsored by the Union Carbide Co., in Brussels from May 1962 until April 1963. In 1967 he became "Oberarzt" at the Heidelberg Faculty of Medicine, responsible for a group of scientists at the German Cancer Research Centre, and remained connected with the Heidelberg Faculty of Science as a "Privatdozent". In October 1971, he obtained the second Chair of Organic Chemistry at the University of Lausanne (as successor of Prof. Jiři Sicher), where he was professor emeritus since summer 2004.

In his first independently published work, Manfred Schlosser showed how the stereochemistry of the Wittig olefination reaction can be controlled by intercepting the betaine-like intermediates with a second equivalent of the organolithium reagent used. This trick became popular, known as the Schlosser modification of the Wittig reaction (or also as the three-dimensional SCOOPY process).

Manfred Schlosser also showed by means of kinetic studies the critical role of aggregates in organometallic reactions. This allowed him to recognize that only excessive coordination by base-resistant additives will effectively prevent the self-assembly of alkyllithium reagents. This vision led him to conceive the combination of *n*-butyllithium and potassium *tert*-butoxide (Schlosser base) and to similar mixed-metal reagents. The Schlosser superbase soon became a preferred reagent, applied all over the world on laboratory and even on industrial scales. It enables shortcuts by contracting multistep sequences into one-flask protocols. Moreover, allyl and pentadienyl metal species generated from olefins or dienes with *n*-butyllithium in the presence of potassium or cesium *tert*-butoxide exhibit special configurational preferences, which contrast with those of the corresponding pure lithium or magnesium species.

Reactivity and selectivity optimization by metal fine-tuning was always an important goal of the Schlosser group. They showed how organocesium or organopotassium species can be cleanly "metamorphosed" to the sodium or lithium analogues, which in turn can be converted to magnesium derivatives. In this way, allyl-type Grignard reagents have now become much more readily accessible. Directly or indirectly prepared organomagnesium compounds can be condensed with alkyl tosylates and 2-alkenyl acetates under copper(I) catalysis (the Fouquet–Schlosser coupling), the carbon–carbon linking occurring in virtually quantitative yield.

In recent years, Manfred Schlosser focused his work on the regioselectivity of the metalation and, as a corollary, functionalization of aromatic and heterocyclic substrates. A systematic study uncovered *meta*-directed lithiations as a counterpart to Wittig's *ortho*-directed lithiations. Hitherto unknown buttressing effects appear to be at the origin of the phenomenon.

The practical benefits emanating from this buttressing control of regiochemistry is just one piece in a complementary set of methods, which have been elaborated by adapting the classical hydrogen/metal, and halogen/metal permutation processes to specific tasks. Schlosser's "organometallic toolbox" enables the selective introduction of a metal, in particular lithium, at any vacant position of a (hetero)aromatic core compound. The resulting novel criterion of regiochemically exhaustive functionalization will for sure become a benchmark in diversity-oriented synthesis and can provide a route to a wealth of new attractive building blocks for pharmaceutical and agricultural applications.

Schlosser's scientific output comprises about 400 publications and he propagated his concepts and findings as a guest lecturer or visiting professor at countless prestigious academic and corporate institutions both in Europe and further afield. The third edition of *Organometallics in Synthesis: A Manual*, the most widely circulated among his books, has just been published in 2013.

Manfred Schlosser will be remembered for his scientific achievements, which are characterized by a close interplay between synthesis-oriented work and fundamental investigations. His contributions to the scientific community include not only many valuable new methods, but also new insight that provides a mechanistic basis for the rational description of organometallic reactivity. He will remain in our minds as a mentor, a teacher, a colleague, and a friend.

Frédéric Leroux
CNRS/Université de Strasbourg (France)

DOI: 10.1002/anie.201308231