Introduction: Zinc Catalysts for Organic Transformations

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The development of methods for sustainable, efficient, and selective synthesis of chemicals with higher values is one of the fundamental research objectives in modern chemistry. Especially, the reduction of waste and the reduction of energy demands are clearly the challenges for the future to use the steadily decreasing resources in a more efficient manner to create a sustainable society [1]. Among all of the chemical methodologies considered thus far, heterogeneous, homogeneous, and biocatalyses offer an efficient approach to achieve this goal, which is underlined by the high impact of catalysis on industrial processes including bulk, fine agrochemicals and pharmaceuticals (~90%) [2]. In particular, metal catalysts are among the most successful examples of practical catalysis. Nevertheless, the use of most of the metals (e.g., Pd, Rh, Ru, Ir) involved difficulties due to their low abundance, high price, or toxicity (Figures 1.1 and 1.2). For example, the current prices are 1460€ per mole of palladium, 2052€ per mole of iridium, 2484€ per mole of rhodium, and 150 € per mole of ruthenium [3]. Moreover, the current trend to establish a "greener" chemistry has initiated the search for more environmentally benign and sustainable alternatives [4]. Hence, current research is focusing, on the one hand, on replacement with cheaper and low toxic metals and, on the other, on the discovery of new protocols with such metals. In this regard, the application of zinc can be of great interest because of its general abundance (twenty-fourth (0.0076%) in the earth crust) and high concentration in ores [5]. For instance, one major mined source for zinc is the mineral Sphalerite, which contains significant amounts of zinc sulfide (~60% zinc concentration) and variable amounts of iron. In contrast to other metals, zinc is easily extracted from the minerals in high purity. Moreover, the zinc-containing minerals Smithsonite (zinc carbonate), Hemimorphite (zinc silicate), and Wurtzite (zinc sulfide) are of importance [6]. Currently, the identified world zinc resources are estimated at 1.8 billion metric tonnes, and several million tons are fixed in man-made materials, from which zinc can be potentially recovered [7]. On the basis of the abundance and accessibility of zinc, the current price for 1 mol is only 0.12€. An additional attractive aspect is the biological relevance of zinc as an essential trace element with a daily dose for humans of 12-15 mg, for instance, to keep several enzymes working [8]. Based on that, a lower toxicity compared to other metals has been found,

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Figure 1.1 Comparison of metal costs [3].



Figure 1.2 Concentration limits for metal catalysts and metal reagents (European Medicines Agency).

which makes it probably attractive for application in pharmaceutical synthesis (Figure 1.2, permitted daily oral exposure: 1300 ppm). Because of these advantages zinc has found numerous applications until now since the first documentation of brass, an alloy made of copper and zinc, dating back to the time of Aristotle (384-322 BC) and Cicero (106-43 BC). However, several centuries passed until the discovery of zinc as an independent metal [9]. The name "zincum" was possibly first written down by Paracelsus (1493-1541) in the sixteenth century, potentially derived from the German word "zinke," which could mean "spike," "jagged," or "tin-like" [10]. Subsequent development during the centuries resulted in its use for today's manifold purposes in galvanizing, alloys, brass, bronze, and others [11]. In contrast, the first attempts of organic chemistry to make use of zinc date back to 1849 when Edward Frankland (1825-1899) synthesized the first organometallic compound diethyl zinc. Since then, numerous stoichiometric applications of zinc have been accounted, for example, the Reformatskii reaction, Fukuyama reaction, and Negishi reaction, which are all breakthrough chemical transformations in organic chemistry. Surprisingly, in comparison to other metals, the application of zinc catalysis in organic chemistry was underdeveloped. Often, this situation is explained by the "transition" position of zinc in the periodic table, between transition metals and main group elements [12]. Based on the [Ar] 3d¹⁰ 4s² electron configuration with filled d-shells the chemistry is different from that of the transition metals and is more related to main group chemistry. Because of this, zinc does not have a distinct redox chemistry compared to other transition metals; mainly Zn(0) and Zn(II) are known, while recently complexes with Zn(I) have been established [13]. Often, the question arose if "zinc is a boring element?" due to the straightforward and "predictable" chemistry [14]. Nevertheless, more recently the situation has changed, and the catalytic potential of zinc has been proved in several applications [15]. This book will therefore focus on a selection of recent achievements applying zinc in organic transformations including major accomplishment in the field of zinc-catalyzed reductions, oxidations, C-C, C-N, C-O bond formations, polymerizations, and applications of zinc in stoichiometric transformations such as cross coupling and the embedment of zinc in total synthesis.

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