Book review

Sustainable synthesis of pharmaceuticals: using transition-metal complexes as catalysts

https://doi.org/10.1515/gps-2018-0159

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Royal Society of Chemistry, 2018
Hardcover, 286 pp.
ISBN: 978-78262-934-4

Catalysis is considered one of the most powerful tools in organic chemistry. Not surprisingly, it has been studied and applied intensively throughout the last century. It never lost its attraction to chemists, and especially (transition-)metal catalysis has received much attention with different complexes, showing great diversity and overall performance in organic synthesis. Whereas metal catalysis was adapted early for bulk chemistry applications, its importance for fine chemicals and pharmaceutical compounds was discovered more recently. While the pharmaceutical industry focused for a long time solely on the desired end product with no respect to the amount of waste generated or the influence on the environment, recently a change of paradigm has occurred. With the emerging newly developed asymmetric catalysis, defining sustainability as a key factor in every process and cost optimisation, catalysis has become a key technology for the synthesis of new pharmaceutical compounds.

The book entitled *Sustainable synthesis of pharmaceuticals: using transition metal complexes as catalysts* gives a comprehensive overview of some of the most used catalysts for the synthesis of pharmaceuticals, especially focusing on recently developed synthetic routes, which include transition metals, and sometimes have been analysed with green chemistry tools.

This first part of the book introduces the topic and defines a number of abbreviations and phrases used throughout the book. In Chapter 3, the metrics and basic principles behind green chemistry analysis are summarised before a short insight into alternative techniques, such as microwave, sonochemistry and mechanochemistry, is given. The rest of the book is structured clearly with one chapter for every catalysis type.

In Chapter 4, the use of carbon monoxide-based carbonylation reactions for the synthesis of pharmaceutical compounds is discussed. It explains how carbon dioxide (CO), a toxic molecule, can be used for the selective introduction of a carbonyl moiety into a molecule with several different metal catalysts. Furthermore, it presents how this process can be made "greener" by switching to more efficient catalysts, using CO equivalents or replacing the starting materials, typically iodides, by bromides and chlorides.

Chapter 5 is dedicated to the already-mentioned important hydroformylation technology. Coming from a bulk chemistry process, it states how hydroformylation is currently used in an enantio- and diastereo-selective way in the synthesis of biologically active compounds. Whereas rhodium is still considered the metal of choice, scientists have developed new phosphorus ligands and utilised less toxic solvents for a number of syntheses.

Transfer hydrogenation technology and its importance for drug synthesis are reviewed in Chapter 6. This part focuses on non-toxic and cheap metals as well as the borrowing hydrogen methodology. Recent examples and industrial applications are also included in this chapter.

Chapter 7 gives special attention to oxidative reactions, such as epoxidations and sulfoxidations. Both share a single oxygen transfer and can be realised with similar metal complexes. Owing to the fact that epoxides and sulfoxides are frequently used motives in and precursors for pharmaceuticals, the synthesis of enantiomerically pure products with "green" metal catalysis is of utmost importance.

Often, the C-C bond formation is required in pharmaceutical synthesis. Therefore, Chapter 8 explores the possibilities of using transition-metal-catalysed C-C bond formations in terms of sustainability. Several aspects, such as the choice of metals, ligands, solvents and additives, are analysed. After a brief introduction, the several different types of reactions are sorted and presented, and recent examples of applications are given.

However, it may not occur to many at first sight that the metathesis reaction can be a valuable synthetic tool for pharmaceuticals as well. Chapter 9 compares different approaches towards sustainable metathesis reactions.

Initially, metathesis reaction in general and the different parameters are discussed; later, the often-used ring-closure metathesis (RCM) and other metathesis types that are of importance for pharmaceutical synthesis are presented based on recent examples.

The last chapter of the book explores the usage of tetravalent boron-based therapeutics, undoubtedly an important and interesting class of pharmaceuticals. However, the last chapter does not fit perfectly into this book. Since boron is not considered a transition metal, nor is it presented as a catalyst in this chapter, the idea behind this chapter remains a little unclear.

When talking about catalysis, it is clear that one will never be able to give a complete overview. Therefore, it is not surprising that hydrogenation via molecular hydrogen activation is completely absent in this book. The authors rightly point at several reviews and books published in this field. Arguably, the part of Chapter 3 focusing on microwave, sonochemistry and mechanochemistry could have been shifted to the end of the book, since only a few examples of each transition-metal catalysis are provided with the technologies and it is not mandatory to read about this beforehand. Apart from this, the book is well structured and gives an excellent overview on transition-metal catalysis in the synthesis of pharmaceuticals. Each chapter gives a short and understandable introduction to the readers who have not been working in this field earlier. Recent and interesting examples have been chosen to underline the importance of each technology. The clear and understandable schemes, figure and tables point out the major accomplishments described in the text, making it easy to follow the discussion of the authors.

Since this book is dedicated to scientists interested in pharmaceutical chemicals synthesis via transition-metal catalysis, basic knowledge of organic chemistry is an advantage, but no special knowledge in transition-metal catalysis is required. It can give a good first insight into pharmaceutical synthesis with transition-metal complexes for anyone who is interested in this field.

Acknowledgement: FET-OPEN EU project ONE-FLOW, grant no. 737266.

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