

Preface and Overview

Pedagogical Principles. At first, every body of knowledge that is new to us seems to have boundless complexity and creates the initial impression of incomprehensibility and even fear. Organic chemistry provides an excellent example of this phenomenon. The discipline is replete with complex and initially abstract concepts, as a result the information may seem overwhelming, particularly for the young chemist. But as with most new subjects, consistent study and practice reveals patterns, commonalities, rules, and an apparent logic. Eventually, an “architecture” becomes more apparent as we grow to become more experienced chemists. To develop this intuition, it requires close study, repetition, and breadth of exposure. A significant element of that learning is intrinsic and simply requires time and immersion. However, to help with the development of this intuition, an organic chemist would also be wise to focus on mechanisms for organic reactions as a foundation or anchoring point. This, in combination with deep study, can help organize knowledge into skill and expertise. An understanding of reaction mechanisms provides a solid foundation for the field and a scaffold for further study and life-long learning. Mechanisms are highly useful because they can logically explain how a chemical bond in a molecule was formed or broken and help to rationalize the formation of the final synthetic target or an undesired side-product. Moreover, as we parse an increasing number of mechanisms, we begin to see the similarities and an invisible conceptual “thread” then forms in our mind’s eye that was not previously apparent. It helps to organize thinking and brings sense to the otherwise foreign concepts such as reactive intermediates, transition states, charges, radicals, and mechanistic arrows.

The Approach. To help galvanize – and perhaps catalyze – the organic chemist’s inductive ability and to provide a “go-to” reference for closer study, this book strives to present an abridged summary of some of the most important mechanisms. In today’s terms, these are 100 MUST-KNOW Mechanisms. The author draws upon scientific knowledge developed through undergraduate and graduate years, including post-doctoral research and study focused on organic synthesis. With a keen awareness of the incremental learning process, the book curates and presents mechanisms by category, starting with the fundamental and basic mechanisms (e.g., *nucleophilic substitution* or *elimination*), and mechanisms associated with the most well-known named reactions (e.g., the **Diels–Alder** reaction or the **Mitsunobu** reaction). Additionally, the collection is complemented with historically important mechanisms (e.g., the *diazotization* or the *haloform reaction*). Finally, it includes some mechanisms dear to the author’s heart, which he deems elegant or simply “cool” (e.g., the **Paternò–Büchi** cycloaddition or the *alkyne zipper reaction*).

Organization. The mechanisms are organized alphabetically by chapter for ease of reference, and numbered from 1 to 100. The dedicated student will consistently proceed through every single mechanism, giving each one time to study, practice with, memorize, and ponder. At the same time, the book can be used as a quick visual

reference or as a starting point for further research and reading. The 100 mechanisms are selected for being classic and famous, core or fundamental, and useful in practice. Of course, a good degree of personal intuition is involved in the selection and it is definitely not a dogmatic ordering or a comprehensive anthology. The book is intended to be a visual guide as distinguished from a traditional text book. The presentation of each mechanism constitutes a complete InfoGraphic (or “MechanoGraphic”) and provides distilled information focusing on key concepts, rules, acronyms, and terminology. It heavily focuses on the basic core – the starting amount of information, the extract – that a good organic chemist can commit to memory and understanding. Starting initially as a daily micro-blog post with a “hash tag” (#100MustKnowMechanisms) that gained a lot of support from students and chemists around the world, the book is really intended to bring together an array of mechanisms, organize them, provide additional historical context, and enable a conceptual space where the reader can focus on learning them as well as serve as a desk-reference or a “flip-book”.

The book is color-coded: each key reaction is enclosed in a dark blue frame; each key mechanism (the center piece of the book) is presented in a red frame; other reactions and mechanisms related to the core 100 mechanisms covered in this book are usually summarized in grey frames. The book also collects a few useful rules, facts, and concepts that are presented in green frames. The reader may find several star diagrams, representing synthetic diversity, for example, throughout the book as well. Relevant comments and clarifications can be found in footnotes.

Sources. The underlying information stays very close to information usually covered in classic or key organic chemistry text books [1]. More specialized literature may be necessary in some cases (for organometallic or photochemical transformations, for example) [2]. The reader is also encouraged to familiarize themselves with some other supporting bibliography [3]. Where appropriate, it also references texts that the author trusts and cites for further in-depth study if the reader so chooses. Since this book strives to be an abridged visual illustration, students are encouraged to use other, more comprehensive books on the subject, especially those related to the *named reactions* in organic chemistry [4]. Additionally, open on-line sources, when thoughtfully selected, can also be very useful [5]. Such sources may be mentioned here when the information was deemed accurate, thorough, and supported by the references. This is further supplemented by the author’s aggregate knowledge and education gained through college, graduate school, and post-doctoral academic research. The author also found the encyclopedia of organic reagents [6] to be an extremely useful “go-to” starting point in his personal experience and professional career, especially when embracing a new chemistry topic or using a new reagent. Moreover, each *MechanoGraphic* is supported by reference to the likely first original publication where the related reaction or mechanism was first mentioned (see the time-scale after each mechanism). Finally, several key and fundamental reviews; publications on recently elucidated mechanisms; and other research articles are referenced, as needed. The author uses his best judgement in each case. However, even though the

provided information was carefully checked, and presented in agreement with standard and accepted chemistry rules, this does not guarantee that it is free of all errors. A further caveat, the variety of text and scholarly references does not imply a comprehensive and chronological review of the literature and history – it is not a global historic review of mechanisms from 1800–2020. Mechanisms and our understanding of them can also change as this book is being prepared and the corresponding literature revised. Thus, the reader should supplement the use of the book with primary source reading and deeper study through a comprehensive textbook prepared by a cohort of experienced professors and experts. Here, the most common and known pathways, those that do not violate basic standard chemistry rules and that are frequently referenced in the classic and contemporary literature, are summarized visually.

A Few Things to Keep in Mind. It is also important that the reader remain flexible and mindful that mechanisms are represented based on our current understanding, taking into consideration basic chemistry rules, valency, electron pushing rules, charge preservation, Lewis dot structures, etc. They may not be the most “cutting-edge” or up-to-date (e.g., cross-coupling reactions that may not be well-understood). They may also be substrate-dependent and each reaction may undergo a slightly different pathway. Thus, the reader should not treat the book as a dogmatic guide, and should keep an open mind for new data, creativity, and view the book as part of a continuous debate in the subject.

Background Knowledge. To fully benefit from the book, the reader should have basic knowledge of organic chemistry. Figures are presented with an assumption that the reader understands common terms and symbols. Thus, basic concepts are not introduced or explained. Undergraduate students, graduate students, scientists, teachers, and professors in the discipline should be able to utilize the book. The book can also serve as a good condensed “refresher” for the experienced organic chemist who wants to “zero-in” on the most basic and fundamental core mechanisms as judged by the author.

The Inspiration and Further Reading. The author heavily draws upon his personal experience as a student of chemistry and later an academic researcher. Never having taken a formal course on mechanisms in organic chemistry, he approached the material initially through memorization as opposed to derivation. The first impression was fear and a sense of being overwhelmed. However, after many years of experience, more obvious patterns, trends, rules, and dependencies appear to have crystallized providing an inductive ability to navigate and identify the mechanisms behind reactions. This personal experience has definitely shaped the teaching philosophy of the book, and is further enhanced by the efficient way in which information can be conveyed through visuals and space. Moreover, as most individuals have a predisposition for visual learning – this book is more intuitively aligned with the way that we seem to learn the fastest. It strives to be a focused collection of the most useful, basic, and fundamental mechanisms. Started initially as a micro-blog post, the discussion, engagement, and interest it sparked indicated a clear need for a more-carefully prepared,

organized, and curated presentation in a format that could be placed in a physical library and easily internalized. The author hopes the book serves as a good starting point for the developing chemist who may need the most guidance and encouragement. No doubt it may stimulate constructive discussion, but nevertheless this will ultimately encourage and challenge everyone to learn, to search for a different answer, to think critically, and grow as a chemist and stay sharp as a scientist. Finally, knowledge is a fractal-like concept, the closer we look the more detail we see and learn. Here, we strive to reach a reasonable asymptote of precision and comprehensiveness given the purpose of the book. Further core reading [1], reference of primary and secondary sources [2–4], and on-line sources [5 and 6] as well as actual experimentation and practice will help paint the complete picture and prepare the organic chemist to be a well-rounded and informed scientist.