

# Preface

Connecting molecular units exhibiting specific physical, chemical, or biological properties is a pivotal area of chemical synthesis. For many years, only organic units were considered worthy of this noble chemistry. Not anymore. Constructs containing inorganic or biological units are more and more common. The number of papers on coupling various moieties has been growing rapidly for dozens of years. The introduction of click chemistry was a game changer. Today, besides the original click process—the Huisgen reaction forming cyclic triazole—we have several other good coupling reactions such as the addition of thiols to various olefins, acetylenes, and isocyanates, Diels-Alder click reactions, and the newest one sulfur(VI) fluoride exchange (SuFex) [1].

While we may consider our accomplishments in the area to be wonderful, we must humbly admit that nature performs coupling better than we do and that there is a tremendous room for improving the existing chemistries. Furthermore, there is an acute need for more and better decoupling methods.

The list of methods applicable to connecting molecular units is much longer than the list of disconnecting methods. This was one of the reasons that prompted us to look at possible coupling strategies applicable to situations when decoupling will be necessary later on. We published in 2013 a relevant review article “Strategies for Coupling Molecular Units if Subsequent Decoupling is Required” [2]. In the article, we argued that there was no reason not to employ click chemistry to connect units whenever possible even when disconnection is in the cards. We just must design our coupling strategy wisely. We proposed the use of sacrificial units. The concept was called CAD (coupling and decoupling). It is worth noting that carbohydrates and their derivatives have become one of the most often used molecular units employed in the CAD processes.

Recently, Blanco, Santoyo-Gonzales et al. [3] stated in a paper published in *Advanced Synthesis and Catalysis*:

*The concept of “coupling-and-decoupling” (CAD) chemistry has been recently introduced by Bielski and Witczak as a strategy that aims at both the binding and subsequent disconnection of the target molecules, a desirable feature targeted release, the decoupling of a molecule from a solid support or a surface of interest after performing chemical*

*transformations on it (e.g., solid phase synthesis), the modification of the surface of a material or the quantification of the amount of compound bound to the surface or solid support.*

The interest in the topic prompted us to organize a symposium during the 2015 Pacificchem in Honolulu in December 2015. We hoped it would cover most important aspects of the CAD strategy. The title of the symposium was “*Strategies for Coupling and Decoupling Diverse Molecular Units in the Glycosciences*”. It attracted several prominent speakers, had a relatively large attendance and was met with a lot of interest. The symposium led to the present book. Some of the chapters in this book are based on the presentations delivered at the symposium. Other contributions are also from the leading experts in the field of carbohydrate chemistry. Some of the chapters are literature reviews, and some describe recent experiments performed in the authors’ laboratories. We believe that all articles are of very high standard and offer a novel perspective on the discussed and highly important subjects.

Since the symposium, a few wonderful papers in the area of CAD have been published. One paper by Santoyo-Gonzales et al. has been already mentioned. The authors report an exceptionally effective methodology for CAD employing vinyl sulfonates. The method is simple and yields are excellent. Another spectacular paper was published by Anslyn and coworkers [4] who developed a simple Meldrum’s acid-based reactant. It can be easily coupled to amine and thiol. What is remarkable both reactants (primary amine and thiol) can be decoupled and recovered unchanged. The authors use the words click and declick to describe the process. Additionally, it is worth mentioning two relevant reviews that were published after our symposium [5–6].

The book chapters have been written by authors coming both from the industry and academia, representing very different educational, scientific and ethnic backgrounds and perspectives. While this is probably an asset of the book, it makes creating a logically satisfying table of content a very difficult task. We apologize for this but the sequence of chapters in the book is unavoidably rather accidental.

With a growing complexity of material science and biomedical disciplines, one can expect a dramatic increase in forming and disconnecting molecular units. Moreover, it is almost impossible to find undiscovered phenomena or applications in the main areas of various disciplines. Thus, researchers will more and more look for fertile research objects in the phenomena taking place at very exotic conditions or when two or more units (that may or may not be compatible) are connected. Furthermore, it can be expected that many novel drugs will consist of two or more components. Note that often a mixture of drugs (HIV, certain cancer therapies) is significantly more effective than a single API (active pharmaceutical ingredient). All these aspects require effective methods of coupling and decoupling molecular units.

We hope that the book you keep in your hands (or watch at the screen of your computer) is what you expected and that it fills an important void. In conclusion, we believe that the present book offers a thoughtful perspective on the important area of research and will steer new ideas and solutions.

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We dedicate this book to our wives Wanda and Barbara.

Wilkes-Barre, USA

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Roman Bielski

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