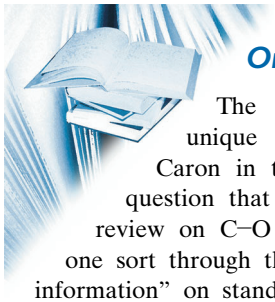


Practical Synthetic Organic Chemistry

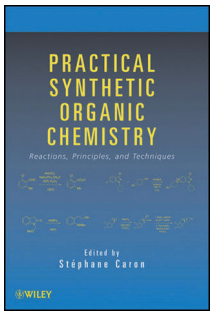
The raison d'être of this unique book, as stated by Caron in the introduction, is the question that he raised in writing a review on C–O oxidations: "how does one sort through this incredible wealth of information" on standard methodologies, i.e., how to separate the good from the bad and from the "don't try this". The result is a compilation of proven methodologies of value to practicing synthetic chemists. The authors are all enthusiastic Pfizer chemists (apart from two exceptions with regard to their affiliation, not their enthusiasm). The chapters describe how to select conditions to test out first for a given transformation with the experienced eye of a med or process chemist, to highlight to scale-up procedures, and to make the book modern (literature $>$ 1980). The result is a refreshing book which, as a hard copy and not an e-book, should be on the shelf of every practicing synthetic chemist.

A thoughtful and well-written foreword by Steve Ley sets the stage: "*the achievements of the pharmaceutical industry are underpinned by … synthesis of all the healing substances that are currently on the market, …*" and "*… synthesis of complex … architectures is not a trivial or routine process.*" The titles of the chapters reflect the careful selection of methods based on the bench and pilot-plant experience of the Pfizer chemists. For example, who has not worried about choosing the best conditions (solvent, leaving group) for an S_N2 reaction or an electrophilic addition to a double or triple bond? These topics receive about 140 pages of coverage in total. S_NAr and S_EAr are bread-and-butter topics of chemists in the pharmaceutical industry. For S_NAr-type syntheses, examples of both intramolecular and intermolecular reactions in heteroaromatic systems are described; here, quite appropriately, mention is made of the usefulness of benzyne species. For S_EAr tactics, which are usually better appreciated in industry than in academia (aside from the well-known Friedel–Crafts reactions) instructive examples of Claisen and the less common thioalkylation and Fries rearrangements are given. Another bread-and-butter set, eliminations, receive authoritative coverage in a chapter that ends with a useful table of dehydration reagents and conditions.

The now widely active area of cross-coupling reactions, which is difficult to summarize, is treated by describing selected highlights of process chemistry, e.g., Losartan (now a BMS drug), and an Alzheimer's disease mediator drug (Lilly), among others. Showing scales of reactions under the arrows would have been appreciated, although it is understood that this information might not be accessible. The Nobel-Prize-winning Suzuki reaction has a dominant position in this chapter; in addition, the Sonogashira, Migita–Stille (with the problems of removing the residual tin), Kumada, Negishi, and Heck (to complete the Nobel triumvirate) reactions receive ample coverage. The increasingly used C–N and C–O and the less common C–S cross-coupling methods are well illustrated, and well-chosen examples of the metathesis methodology are given. The Tsuji–Trost allylic substitution, mainly catalyzed using Pd, is also not neglected.

Rearrangement reactions are sometimes the purview of teachers who love the convolutions of molecules to trap students in examinations. Here, instead of examples of familiar classical rearrangements such as Wagner–Meerwein, pinacol, Favorskii, diazomethane homologation, and Hofmann–Curtius–Loessen, and Beckmann and Baeyer–Villiger reactions, the emphasis is on the less widely known Fritsch–Buttenberg–Wiechell, Stevens, and Brook rearrangements, among a multitude of others—a veritable feast for setting problems at lunchtime. Seven Pfizer chemists heroically take on the ""Reductions" chapter, while a single author deals with the corresponding "Oxidations" chapter. In the former chapter, all the oxidation states of carbon, as well as those of C–N, C–O, C–S, and C–halogen are covered, and in the latter one oxidations of N– and S–groups, C–H, C–C, C–O, and C–N bonds are described, with the cautionary note that many oxidants release large amounts of energy, sometimes uncontrolled, and a surprising footnote stating that oxidations comprise as little as 3% of preparative-scale reactions in the pharmaceutical industry. Although free-radical reactions receive fewer than 20 pages, there are surprising illustrations of their industrial application, e.g., Barton nitrite ester C–H functionalization for carbacephems, and Keck allylation for synthesizing carbohydrates. For this reviewer, it is pleasant to see mention of the Minisci process, which has a greater potential than is currently exploited.

Quotation marks are appropriately used for the term "nucleophilic" organometallic reagents, in view of the lack of distinction, at times, between polar and covalent organometallics, as discussed by Schlosser in a reference that is cited. Although the book is not fully comprehensive, much of what the industrial chemist needs to know is here, from the routinely used Li to the still not widely adopted Bi. A section on heteroaromatic ring metalation provides only bare coverage of the directed *ortho*-metalation (DoM) strategy, which has had a major influence on how bioactive molecules are prepared on mg to kg scales. The chapter on the synthesis of common heteroaromatic compounds, which of



Practical Synthetic Organic Chemistry
Reactions, Principles, and Techniques. Edited by Stéphane Caron. John Wiley & Sons, Hoboken, 2011. 872 pp., softcover, € 87.90.—ISBN 978-0470037331

necessity is brief, has some well-chosen examples of pyrroles, indoles, pyrazoles, pyridines, and other N-, O-, and S-containing heterocycles.

The rest of the book is a jewel. As editor Caron states in the preface, "*We have tried to provide … some information that may not be common knowledge outside of process chemistry groups.*" Topics such as the most effective routes for access to chiral building blocks, solvent favoritism, the definition of the fragile term "green chemistry", information about pK_a values, and insightful advice that is mainly privy to process chemists ("things they don't teach you in school") are difficult to find in any other book or compendium. The section on "risk phrases" associated with dangerous substances and preparations is useful for graduate students. The section on IUPAC nomenclature is perhaps less valuable in view of the present ability to name molecules on the basis of an entry in Google or SciFinder.

The last sentence by editor Caron is an appropriate conclusion: "*Building each chapter … served as an excellent chemistry refresher course for the authors, and we learned a lot of new chemistry in the process.*" Chemists everywhere will applaud their efforts and make use of their knowledge and advice.

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