Solid-phase organic synthesis

Kevin Burgess (ed.)
Wiley–Interscience, New York, 2000
xiv + 277 pages. £45.50
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During the last five years a mini-revolution has been taking place in organic chemistry laboratories concerned with increasing the speed and the number of compounds synthesized. These fascinating developments have been driven, in part, by commercial pressures from the pharmaceutical industry to speed up drug discovery and they have been made possible, in part, by solid-phase synthesis of compound libraries containing huge numbers of small-molecule or oligomeric structures. Hence the publication of this (and other) books on the subject of solid-phase organic synthesis and combinatorial chemistry.

This is one of the most recently published books on solid-phase organic synthesis. It has eight chapters each providing quite a comprehensive review of the literature (especially 1995–1998) on specific classes of solid-phase reactions or techniques.

The chapter that has most organometallic chemistry is Chapter 2, ‘Palladium-catalysed carbon–carbon bond formation on solid support’ (Todd and Abell). It covers Heck, Stille and Suzuki coupling reactions, which is appropriate since these are amongst the most widely studied organometallic reactions in solid-phase synthesis. The related copper-cocatalysed Sonogashira-type couplings of terminal alkynes with aryl iodides are also covered in Chapters 2 and 4.

Topics covered in other chapters are solid-phase synthesis of guanidines (Chapter 1), benzofused heterocycles (Chapter 3), phenylacetylene oligomers (Chapter 4), and natural products (Chapter 8). The overall content of the book is broadened with three chapters on relevant and useful techniques: synphase crowns for multiple parallel synthesis (Chapter 6), vibrational spectroscopic techniques for following solid-phase reactions (Chapter 7), and the increasingly popular use of polymer-supported reagents, substrates and catalysts (‘resin capture’) (Chapter 5, by Flynn, Devraj and Parlow).

The editors should be complimented on their aim of providing comprehensive reviews of narrowly defined areas by leaders in the field. The book is targeted to researchers active in the area. The corollary is that with one or two exceptions the book does not cover other more general aspects of solid-phase synthesis, e.g. experimental conditions, techniques and equipment; compound library synthesis, purification and characterization; or properties of the polymer support. Therefore it is not designed for the more general audience seeking an (under)graduate textbook.

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A chemist's guide to density functional theory

Wolfram Koch and Max C. Holthausen
Wiley–VCH, Weinheim, 2000
x + 294 pages. £70
ISBN 3-527-29918-1

Density functional theory (DFT) is very much the flavour in quantum chemical calculations. The basic idea of DFT is that for a collection of electrons and nuclei the ground-state molecular energy, the wavefunction and all other molecular electronic properties are uniquely determined by the electron probability density $\rho(x,y,z)$, a function of three variables. The ground-state energy is a functional of ρ: $E_0 = E_0[\rho]$. The authors' aim is to guide the chemist through basic theoretical and related technical aspects of DFT at an easy-to-understand theoretical level. They succeed admirably. They present and explain the basic equations of DFT and the essential quantum mechanics fundamentals. The mathematics is essential but not heavy. As ever, the challenge for the reader is to penetrate the equations. The authors, in my view, are quite outstandingly good in their explanations of the equations and the physical reality that they represent. Their half-page account of what a functional is (as opposed to a function) and why we use them is one of the best I have encountered. The literature is covered through to the autumn of 1999. Topics not covered are Carr–Parrinello methods, softness and hardness and Fukui functions, and combined DFT and force field methods.

The first part of the book (nearly half) is devoted to presenting the background quantum mechanics and the ideas and equations of DFT. The presentation is readable and attractive; the ideas are put in context and the reader's attention and interest are engaged. The important concept of electron correlation is treated through the exchange-correlation hole: correlation leads to a depletion of electron density. The exchange-correlation hole thus contains exactly the charge of one electron: $\int h_{XC}(\vec{x}_1;\vec{x}_2)d\vec{x}_2 = -1$

The discussion of the background includes an account of the electron gas model as a prelude to the Kohn–Sham treatment of the electron density. The local density and the meaning of the Kohn–Sham orbitals are discussed at length. The section ‘Do the Kohn–Sham orbitals mean anything?’ was (moderately) reassuring for chemists who worry from time to time, and I am one, whether the molecular orbital pictures generated by the graphical interfaces of our DFT programs are quite proper. After all, the business of DFT is electron density, the square of the wavefunction, and not the wavefunction itself. We are referred to the ‘many authors’ who ‘recommend the KS orbitals as legitimate tools in qualitative MO considerations.’ There is some discussion of the treatment of excited states. A chapter is devoted to the ‘quest for approximate exchange-correlation functionals’ and the local density approximation. A final chapter in the theoretical section includes discussion of the important problem of the selection of basis sets and computational procedures generally. A reader prepared to put the effort into understanding this section will be well equipped to undertake DFT calculations with a feeling for the theory and the pitfalls.

The second part of the book, ‘The performance of the model’, describes the results of DFT calculations, successes and failures, for a variety of molecular systems of interest to the chemist; it covers structure, both Main Group and transition-metal compounds and organometallics, vibrational frequencies, energies and thermochemistry, population analysis, electric properties (dipole moments, polarizabilities, infrared intensities), magnetic properties, NMR chemical shifts and NMR coupling constants. There is a chapter on water and hydrogen-bonded systems and a final chapter on chemical reactivity: exploring potential energy surfaces. Throughout this section quantities and properties calculated at various levels of theory are compared with the experimental data to provide a basis for the critical assessment of computational procedures.

This is an important book. Although I have practised DFT for some years (and by no means as a black box) I found that reading the book provided many insights and clarified concepts that had been barely understood. It is a book for practising chemists, those who recognize the value of the computational opportunities provided by today’s powerful computers and who seek and need a critical insight into what they might achieve via DFT calculations. It is strongly recommended.

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Activation and catalytic reactions of saturated hydrocarbons in the presence of metal complexes

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xiv + 536 pages. £142
ISBN 0-7923-6101-6

This book is essentially the second edition of Shilov’s earlier book, *Activation of Saturated Hydrocarbons by Transition Metal Complexes*, published in 1984. The earlier book had 203 pages, so the present work is about two and a half times as long. While the majority of the references are later than 1983, the authors have generally given a balanced view of the topic which does not assume the reader is familiar with the previous work, and the principles are set out in the first chapter. The authors had already published a review of this area in 1997.[1]

The book contains an introduction, ten chapters and an index. Somewhat strangely, the list of abbreviations is at the back of the book, and even more surprisingly in the 21st century, the authors are still using kilocalories. The treatment of the subject is very thorough and the extremely extensive lists of references (an exceptionally high ratio of references to text is a feature of the book; even the introduction has nearly four pages) make this a valuable work of scholarship.

The authors concentrate on the subject described in the title, although Chapter 2 is concerned with ‘Hydrocarbon transformations that do not involve metals or their compounds’. Anyone seeking enlightenment on heterogeneous catalysis involving saturated hydrocarbons will find a recent report[2] of the proceedings of a NATO conference to be complementary to the present work, which does, however, have a chapter entitled ‘Heterogeneous hydrocarbon reactions with participation of solid metals and metal oxides’ consisting of 34 pages of text and diagrams and 16 pages of references.

Shilov’s work on activation of hydrocarbons using platinum complexes is very well known, and a chapter (58 pages including references) is devoted to this topic. We must, however, turn to the chapter on ‘Hydrocarbon reactions with high valent metal complexes’ for a discussion of the work by Periana *et al.* on the conversion of methane to methanol involving a platinum complex in sulfuric acid.

A welcome feature of this edition is the inclusion of a chapter (55 pages) on ‘Oxidation in living cells and its chemical models’. Cytochrome P450, methane monooxygenase and metalloenzymes containing copper, molybdenum and manganese are described here, along with synthetic models which attempt to mimic the activity of the metalloenzymes.

Another chapter is concerned with ‘Homogeneous catalytic oxidation of hydrocarbons by molecular oxygen’. This covers both the commercial cobalt-catalysed oxidation of cyclohexane, and Barton’s Gif systems, which usually contain iron.

Perhaps the chapter of most interest to organometallic chemists is the account of ‘Activation of C–H bonds by low valent complexes’ (73 pages). This chapter describes the oxidative addition of C–H bonds to low-oxidation-state complexes, but mechanisms are carried over to another chapter (40 pages). In these two chapters, and indeed throughout the book, the authors focus predominantly on alkanes with some digressions into unsaturated hydrocarbons, so that the fact that the choice of metal complex for activation of a C–H bond adjacent to a functional group is dependent on the nature of the functional group is not covered here.

To summarize, this is a scholarly account of recent research on the activation of alkanes by metal complexes. It can be recommended to researchers working in the area, and as supplementary reading for advanced courses on organometallic chemistry and catalysis.