Solid-phase organic synthesis

Kevin Burgess (ed.)

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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

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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: $\int h_{XC}(\vec{x}_1;\vec{x}_2)\mathrm{d}\vec{x}_2 = -1$

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