

Org. Process Res. Dev., **9** (5), 699 -700, 2005. 10.1021/op050112g S1083-6160(05)00132-5
Web Release Date: July 22, 2005

Copyright © 2005 American Chemical Society

Design and Optimization in Organic Synthesis, 2nd revised and enlarged edition Rolf Carlson and Johan E. Carlson. Elsevier: Dordrecht, The Netherlands. 2005. 574 pp (+ CD). Price: £180, \$290, 265 Euro. ISBN 0-444-51527-5.

Derek Robinson

38 Millbrook Court, Little Mill, Pontypool, Monmouthshire, NP4 0HT, United Kingdom

This is a welcome re-issue for a modern classic of the organic chemistry literature. Rolf Carlson's 1992 text provided a fresh, some would say controversial, approach to process investigation and optimization. Now, assisted by his son, he presents a revised and enlarged edition, incorporating some fresh material, updated references, and novel strategies.

The central point of the book remains encouraging chemists to use principles of statistics and matrix algebra to plan the most informative set of experiments, consistent with the goals of their investigations. This has the potential to be an extremely dry topic, but here it is presented in a lucid and provocative style, making it an accessible read even for the most mathematics-averse synthetic chemist. The examples come mostly from the authors' extensive experience in synthetic chemistry. Thus, they never allow purely mathematical aspects to dominate the discussions but always strive to relate the numerical results to real chemical phenomena.

The early chapters describe the standard methodologies of factorial design, fractional factorials, simplexes, steepest ascent methods, and response surface analysis. These are mainly useful for straightforward problems where variables are continuous and a limited number of response measurements are considered. Subsequent to the original publication, numerous software packages have become available to help the chemist use these methods effectively. However, Carlson believes that even greater insight can be obtained by canonical analysis of the data, which has largely been overlooked by software developers and thus requires a greater degree of mathematical persistence on the chemist's part. For the more difficult problem of designing experiments to choose among discrete alternatives-such as different solvents or catalysts-a number of strategies are presented in the later chapters, mainly hinging on the concept of "principle properties". There is also advice on how to deal with many different responses, such as situations in which a large number of different impurities must be minimised or eliminated. The techniques of Principle Component Analysis and Partial Least Squares modelling are strongly recommended here.

Over the past decade, the value of these chemometric techniques has become fairly well appreciated by development chemists working in industry, and regular readers of *Organic Process Research & Development* will be familiar with the many examples which have appeared in these pages. But reading the book afresh has made me realise what an untapped potential exists here for academic research also-where these methods appear to be still largely unknown. The authors recall (page 201) surveying recent literature to identify reactions for inclusion in a course on preparative organic chemistry; of over 2000 papers scrutinized, "only 4 presented methods which had been adequately optimized". This means that across the world professors are systematically selling their own ideas short-when with a modest

number of designed experiments they could obtain true perspective on the scopes of their new reactions, as well as insight into how to get them to work with the more recalcitrant substrates. This book has also shown how statistically designed experiments can provide insight into the kinetics and fundamental mechanisms of many reactions.

One useful innovation in the second edition is an accompanying CD, on which can be found the extensive tables of data which were previously printed in the book: tables which collate the measured properties of solvents, Lewis acids, aldehydes, ketones, and amines. One slight quibble I have is that the calculated principle properties, which were given in the first edition, are now missing. Perhaps we are now expected to work these out for ourselves, and indeed the CD also contains a MATLAB routine which will perform the necessary Principle Components Analyses. MATLAB routines are also supplied for canonical analysis, PLS modelling, Singular Value Decomposition, and the extraction of kinetic information from suitable studies.

The absurdly high price will make it difficult for everyone to acquire a personal copy, but I would urge all organic chemists to read this book and become acquainted with these valuable tools. To quote from the authors' concluding remarks: "Statistics is always secondary to chemistry in the domain of organic synthesis", but it "provides methods by which good chemists will be able to do even better chemistry."

1.