

Practical Catalytic Hydrogenation

TECHNIQUES AND APPLICATIONS

Morris Freifelder

PRACTICAL CATALYTIC HYDROGENATION

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PREFACE

Like any writer, the author of a book on catalytic hydrogenation for the working chemist is faced with many problems.

What should be included in the book and how extensive should the coverage be? Thus the theory behind catalytic hydrogenation and the stereochemistry involved in these reactions could be subjects of individual volumes. Lack of space makes it impossible to discuss them at great length in one book. Furthermore, a writer on catalytic hydrogenation must realize that not every laboratory is so well equipped as the one in which his research was carried out. Only a few catalysts may be available for immediate use; or the chemist's only interest may be in obtaining a particular compound by a working method with the equipment and catalysts on hand in the laboratory. It is for these reasons that, in addition to specific reduction procedures, I include other workable methods (or alternate ones, while pointing out the disadvantages) even when, from the literature or from my experience, it is clear that a particular method employing a specific catalyst is the best procedure.

The problem of the "best" catalyst plagues many chemists. Often there is indeed a preferred catalyst for the hydrogenation of certain functions and reducible groups, but not infrequently this designation applies only to certain subdivisions of a particular group or function. I hope to provide a better view of the specific applicability of hydrogenation catalysts by breaking down the reduction of each function, group, or ring system into subclasses.

The use of references is always a problem in a scientific book. In the present book, references could have been cited *ad infinitum*, each chapter thus becoming a lengthy review. I have tried to supply just enough pertinent and varied examples of hydrogenations in each class, so that a chemist who has not been able to find the reduction of a specific compound may come across one of a related compound. Another reason for the large number of examples is that at times there is no "best method." Furthermore, the "best method" and "best catalyst" may not work because the structure of the substrate is somewhat different from that of the substrate cited in the example. Still more important, the substrate in question may not be so

pure as the one in the example, and a less active catalyst may be more resistant to poisoning than the "best catalyst."

A primary difficulty in writing on catalytic hydrogenation is the interpretation of the work of other chemists and the decision whether a reference will be of value. Sometimes the conditions for reduction are described meagerly—the catalyst employed is noted, but the amount is not. At other times catalytic hydrogenation is only a step in the preparation of a desired intermediate with no interest in yield. The catalyst used may be one on hand; the conditions may be adapted to available equipment. When failure is cited in a reduction, the reader may not be supplied with information about the quality of the substrate or the age of the catalyst.

We also encounter other difficulties. When an investigator can carry out reactions leading to compounds to be reduced or can directly supervise these reactions, he can be confident that the substrate is in a reasonable state of purity and that one of the sources of trouble in catalytic reductions will be eliminated. Unfortunately, in some laboratories the material to be reduced is obtained from other sources. It may be purchased material that contains impurities which impede hydrogenation; it may come from another chemist who does not have or cannot supply information about its preparation; improperly cleaned equipment may also be at fault.

In the course of carrying out at least 7500 catalytic reductions, I have encountered problems from all these sources. Certain "tricks of the trade" that have been acquired through experience are imparted to the reader from time to time in the hope of aiding the chemist in overcoming difficulties. In other instances, based on this wide experience, I suggest reasons why a reaction is or is not successful and what can be done if results are unsatisfactory.

I place considerable emphasis on the use of molecular models. Some models are shown to illustrate why a particular reduction does or does not work. Although the construction of models is a fetish of mine I have tried to avoid filling the book with their pictures and, instead, often merely make the comment that a molecular model (constructed by me) does support a reported result. I hope that the examples shown in this book will encourage the reader to make greater use of molecular models. Although they are not the complete answer to the problem of catalytic hydrogenation, the construction of models of starting material and reduction products often are helpful. In some instances examination of a model of an intermediate reduction product may lead to an understanding of what is taking place.

One of the pitfalls of writing is to consider one's own work to be the best in the field. Although I have cited many of my own publications, I have tried to be objective and to point out my findings only when they seem significant. The reader will find many generalities in my unpublished work.

Abbott Laboratories, for whom I worked for many years, has generously allowed disclosure of unpublished results, but in certain instances, for security reasons, only generalities can be offered.

In the preface to his book, *Catalysis by Metals*, Dr. Geoffrey Bond points out that "One comes to see the measure of order which has been achieved in one's subject and becomes painfully aware of the many gaps and inconsistencies which exist in it." I do not search for inconsistencies, but hope that those who read this book will become inspired to fill in the gaps that exist. If my writing results in further research by other investigators into the chemistry involved in the catalytic hydrogenation of organic compounds, then the time and effort that have gone into this study will have been well spent.

Acknowledgments are due many people. First, I thank my wife, my unpaid secretary who struggled through my writing and the unfamiliar chemical names and equations. I thank also my colleagues who suggested that I tackle this task. My former co-workers at Abbott Laboratories helped in many ways, in particular Dr. John Tadanier, Dr. William Roderick, Dr. James Short, and Dr. Warren J. Close, who examined and offered constructive criticism of various parts of this book. Dr. Richard Baltzly of the Burroughs-Wellcome Company, Dr. Dale Blackburn of Smith, Kline and French, and Dr. Robert Tedeschi of the Airco Chemicals and Plastics Company were especially helpful.

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