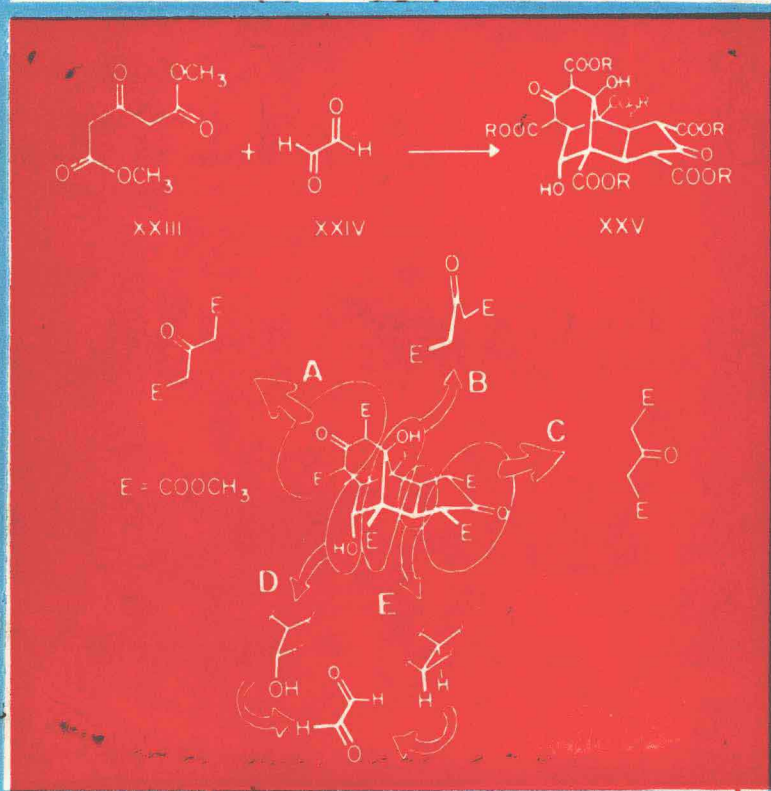


# THE ART OF PROBLEM SOLVING IN ORGANIC CHEMISTRY

Miguel E. Alonso



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Interscience Publication

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*To Adela and Gabriel  
in this world,  
Christiane and Ramon  
in the other*

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# PREFACE

“Science does not prove anything at all; rather it disproves a great deal,” asserted K. Popper in *The Logic of Scientific Discovery*. This remarkable thought has triggered a considerable amount of philosophical discussion throughout the world, and its full meaning may be debated for several years. Among other possibilities, this sentence implies that scientific discovery is more solidly developed on the basis of the experimental negation or disapproving of models or working hypotheses that attempt to explain a given phenomenon than on the basis of affirmation by experiment of these models or hypotheses.

The attitude associated with approval is generally recognized as requiring much less effort than that associated with dissent, because the latter implies a more complex thought mechanism that includes analysis, synthesis, selection, comparison, construction of opposing standpoints, and clear verbal composition to express and defend the disagreement. Therefore, Popper’s sentence may also be interpreted in terms of a desirable profile for a professional scientist. That is, a person endowed not only with high level cognitive memory or recall thinking, but also with considerable ability for *critical thinking*, which enables him or her to design hypotheses and experiments intended to negate existing models.

The latter quality has been condensed by Howard Schneiderman, Monsanto’s vice president for research, in a recent college commencement address (*Chemical and Engineering News*, June 21, 1982), as three essential abilities: development of good taste, ability to communicate in clear language, and a great deal of *problem solving capacity*.

It is clear that the system of scientific education shows inadequacies in at least these three aspects and this lack is currently the cause of deep concern among educators and theoreticians of education. Of these three abilities, problem solving is probably the most important since it should permit the development of analytical skills, synthetic reasoning, discernment in separating the important from the unworthy, and the ability to recognize valid solutions from a variety of alternatives. These qualities help considerably in attaining insight, cleverness, and even artfulness and good taste in professional practice in academic and most industrial environments.

The question then becomes, which mechanism should we adopt to educate students properly in this area and thus overcome this deficiency? There is no unique answer or magic formula. However, a good beginning is the intense practice of problem solving in specific areas of knowledge, although it would be desirable to have a more general syllabus of widespread applicability, at least in the hard core sciences.

And, there is chemistry. In the words of Robertus Alexander Todd, better known as Lord Todd, "there is no question . . . that chemistry is the center point of science." I may add that organic chemistry is perhaps the heart of this center point because it underlies so many disciplines, from agricultural production at all levels, biochemistry, industrial chemistry, polymers, pharmaceuticals, to 99% of the chemistry involved in all living systems. Furthermore, the multitude of mechanisms by which organic compounds undergo transformation offers an ideal platform on which those desirable skills mentioned previously can be developed. It is the purpose of this book to construct from this basis the educational means of achieving the development of problem solving skills in the student of advanced organic chemistry. It is also possible that practicing professionals might find this work useful if their exposure to problem solving during their college and university studies has been inadequate.

The use of a number of examples that constitute the series of 56 problems collected and discussed in the third chapter was preferred over long theoretical descriptions. Some necessary fundamental concepts are concentrated in the introductory chapters. This book may be found useful not only as a study guide but also as a source of interesting and somewhat challenging problems and as illustrations of reactions and phenomena of general interest.

I want to express my gratitude to all those who read all or parts of the rough drafts, offering helpful comments. I am particularly thankful to Professor Bruce Ganem and Professor Jerrold Meinwald for their useful suggestions and to Paul Gassman for his advice during the early stages of this work. I especially wish

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MIGUEL E. ALONSO

*Caracas, Venezuela*  
*March 1986*

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# INTRODUCTION

Few persons, if any, will argue convincingly against the premise that problem solving is one of the best means currently available to educate future professionals. It is not only a sort of athletic training of the intellect but also a very effective learning method, because of the numerous advantages problem solving offers over ordinary descriptive teaching. It allows a much more active participation of students in any instructional program,<sup>1</sup> something that has been shown recently to improve the efficiency of information transfer.<sup>2</sup> In addition, problem solving may more effectively arouse the student's interest in a particular subject, which is, needless to say, an indisputable advantage for the learning process. Furthermore, the complex mental mechanism<sup>3</sup> associated with the intensive search for solutions to given problems enhances those abilities related to critical thinking.<sup>4</sup> This does not invalidate recall thinking or what education scientists call cognitive memory. However, the classical teaching process seems to have put too much emphasis in the latter, to the point of completely ignoring formal courses of problem solving techniques. This is perhaps the consequence of the upsetting effect of the vast amount of information every scientist has to cope with every week, and feels obliged to pass on to students. The emphasis, it seems, is on information courses, leaving aside the formative aspects of teaching.

However, in essentially all branches of chemistry, problem solving is also a basic requirement for professional practice. Technicians in industry, on the

one hand, frequently confront situations whose solutions cannot be found in manuals and training booklets. Sometimes a delay in the application of the right strategy may have disastrous results: loss of feedstock, time, energy, or even the chemical plant itself. Executives also are not exempt from the risk of being unable to make a decision on the basis of the analysis of a given scenario.

Scientists, on the other hand, are sophisticated problem solvers. Not only are the proposing of hypotheses, the designing of experiments to prove or disprove them, and the drawing of valid conclusions from correlation of data complex intellectual processes that require much more than imagination and systematics, but the capacity to interpret the often circuitous and intricate data nature offers as a response to our keenly designed experiments is a challenging daily situation in the successful scientific laboratory.

It is not surprising, therefore, that interest in the study of problem solving is showing signs of renewal in recent years, and is slowly entering the classroom.<sup>5</sup> A much more serious effort will have to be made, however, to achieve a satisfactory level. In fact, at present all we regularly see in graduate level chemistry is students continuously challenging their comrades with the most fiendishly complex mechanistic problems they are able to pick up from the latest issues of chemistry journals. However, there are no regular courses on problem solving. One may be misled by the sight of students surrounded by coffee mugs late at night scrambling to find ways to explain a convoluted reaction mechanism on scraps of paper or blackboards, to conclude that these people are becoming efficient problem solvers. This is not true. A closer look will reveal that frequently their search for a solution is a disordered and confusing attempt to move electrons about until the atoms of the starting materials fall in the right place in the final product, loosely following existing chemical theories. They will never learn how to do this systematically by simply challenging each other.

The teaching of how to focus problem solving properly, so strongly emphasized in efficiency-demanding industrial environments and so little stressed in chemistry courses, might bring some balance in the formation versus information dilemma. In addition, problem solving techniques are intimately related to *analysis* and *synthesis*, two mainstays of human evaluative thinking.

Organic chemistry is there to help. The number of structures possible for a small set of carbon atoms and their means of conversion to other materials is awesome. Yet they all follow certain rules that cannot be ignored. The combination for focusing problem solving therefore seems perfect: A very large set of possibilities, situations and scenarios such as structures, reagents, and reaction conditions, all related to a number of rules—the laws and principles of

chemistry. Consequently, properly focused organic reaction mechanisms provide a very powerful tool for learning the intricate process of situation analysis, correlation analysis of available data, and the development and selection of proper criteria for choosing the correct answer.

This means that in order to communicate the *know how* and *know why* of problem solving effectively using organic chemistry mechanisms it is imperative that the rules of the game be known first; that is, the student should have a good grasp of organic reactions in general, of stereochemistry, and of physical organic chemistry. Although the latter is a "remarkably ill-defined subject" in the words of Professor N. S. Isaacs,<sup>6</sup> owing to the vast number of topics covered under that heading, its principles must be kept in mind whenever one is confronted with a reaction mechanism in order to avoid falling into the attractive field of open speculation. Of course, it is vital to be well acquainted with any particular area of knowledge in order to be able to detect the limits of the application of its principles. In terms of organic chemistry, the reader had better be familiar with reaction rates, isotopic and solvent effects, deuterium and other tracer labeling, and the trapping of reactive intermediates, in order to know when to use these powerful techniques and their underlying principles when one is left alone with one's wits trying to figure out a mechanism.

Besides being highly entertaining, the search for solutions to mechanisms embodies a highly profitable educational process of orderly thought involved in handling several concepts of varying complexity centered around a scheme. Similar to the ladder that allows one to look over the trees to see the forest, problem solving helps to develop the ability to find relationships between seemingly disparate topics. It enables us to differentiate the important from the futile, the grain from the chaff. It helps us to identify, at an early stage of development, important research subjects that may eventually evolve into relevant fields of study. This lightens appreciably the heavy burden of keeping pace with an ever expanding chemical literature. Analytical reasoning embodied in the techniques of problem solving is also a powerful aid in the design of experimental methods in new areas of research. Many reports are in effect the result of imaginative postulates put forth on a rigorous analytical basis. Finally, mechanistic problems are an excellent means of introducing named reactions or processes whose theoretical basis can be best understood by means of a good example. This particular feature has been illustrated repeatedly in many of the problems presented in this book.

It must never be forgotten, however, that the key to success is more in the hands of the reader than in the quality of the most brilliant of texts.

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# THE RULES OF THE GAME

Any self-developed method or discipline will consist of personal features and individual points of view that may or may not reflect the opinion of the majority which may not necessarily be the most valid position. One should expect, therefore, that the criteria of those readers who have already created their own systematic approach to problem solving in mechanistic organic chemistry may be in conflict with some sensitive points expressed here. In addition, there are those who feel that rules in general jeopardize their ability to create and thus to find original solutions to problems.

What follows, nevertheless, is neither a set of restricting and general laws, nor anything vaguely resembling the Philosopher's Stone. Rather, it is a collection of suggestions and techniques that have proved to be quite successful for me in problem solving as applied to organic chemistry. Those readers who will dissent from these ideas are invited to write their own book on this virtually untapped field.

## I. SLOW MOTION, DEEP INSIGHT

Modern civilization forces us to live, move, sleep, eat, and think as fast as we can, as if the human being were nothing but a sort of unmatched computer. Not so, for the computer is, as of this minute, a dumb black box incapable of intuition. These machines serve us admirably well and at astonishing speeds,

supplying us with reams of data, numbers, and calculations, but they are nothing but tools. However, we still do the thinking, press the keys, and design the programs. So, leave the speedy portion of your work to those technological wonders and dedicate yourself to careful thinking. Problem solving demands a great deal of mind churning, and unless the problem is well ruminated, mental indigestion may result. Although attentive deliberation is a time consuming operation, at the same time, it is an exceedingly rewarding one. Enjoy the chemistry of your problem much in the way an artist savors the embroidered details of his craft. One stands to learn a great deal more by solving a single problem in depth than by cranking out 10 shallow answers to as many problems in the same period of time.

In addition, it is to one's advantage to forget altogether the existence of time if full mental concentration is desired. In fact, unless undisturbed concentration is achieved, futile daydreaming, petty distractions, and the noisy manifestations of modern culture will start working against you. For those who actually cannot ignore the march of time, they will soon realize that periods of deep concentration are by far more time efficient in terms of solution output than any other clock-regulated period of the day.

So, make yourself comfortable, surrounded by as much reference material as possible, and get started. Ah!, do not forget to unplug the telephone. Nothing is more annoying than a phone call in the middle of an exothermic reaction out of control!

## II. CLEAR DRAWINGS, THREE-DIMENSIONAL STRUCTURES

If it were so ridiculously obvious and a waste of editorial space to assert that chemical structures should always be drawn as clearly as possible to simplify figuring out a problem, there would not be so many midnight horror stories of teachers and scholars trying to untangle the riddle of cumbersome molecular drawings buried under hesitating arrows and erasures while correcting organic chemistry tests.

Well shaped and elegant pictorial representations of one's ideas usually have the beneficial feedback effect of driving away the fog that surrounds vaguely stated contentions, clearing up thoughts, and even providing leads to possible solutions.

In addition to looking at clear diagrams, it is also advisable to look at compounds from several angles, not just from the most obvious. This helps in the identification of reactivity patterns other than the usual ones and in recog-

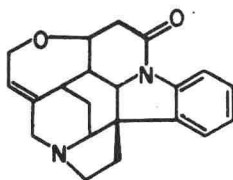


nizing a familiar fragment in a complex structure, a feature that might well be the key to a whole mechanistic scheme. For example, it will take a little longer to visualize the indole portion of a complex alkaloid such as **I** for those who follow the classical portrayal of indole with the nitrogen atom facing down on the right-hand side of the molecule, than for those who draw this compound upside down, tilted, or sideways.

The three-dimensional drawing of organic molecules, although somewhat difficult, is particularly helpful in visualizing relationships between interacting groups, steric encumbrance, conformational changes, and even the very feasibility of a reaction pathway. The two-dimensional or flat representation of the intramolecular displacement reaction that leads to a compound with the very appropriate name Twistanone (**III**)<sup>1</sup> may be thought quite absurd owing to the seemingly long distance that lies between the two reacting sites (see Scheme 1). The three-dimensional drawings **IV** and **V** of its precursor **II** show, however, that the two carbons involved interact at close range. In addition, the uncomely slash across structure **III** is nothing but a carbon-carbon bond nearly indistinguishable from the others.

Looking at molecules from different angles in their spatial picture is also a very effective means of foreseeing chemical transformations as well as simplifying drawings. Some accessible computer programs perform wonders in spinning complex molecules in space. However, doing this with pencil on a piece of paper is even more entertaining and challenging. It may take, though, some training and ability to turn an imaginary complex surface such as a molecular model around in space by manipulating it on the flat surface of a sheet of paper.

For many of the readers who glanced rapidly at Scheme 1, it may not become apparent until a second thorough examination that structures **VI-IX** all represent the very same Twistanone (**III**). Each one of these drawings seems to have a character of its own, depending on its visual relationship with more familiar molecular systems. Thus while **VI** is just a twisted maze of strained

**I**

(STRYCHNINE)