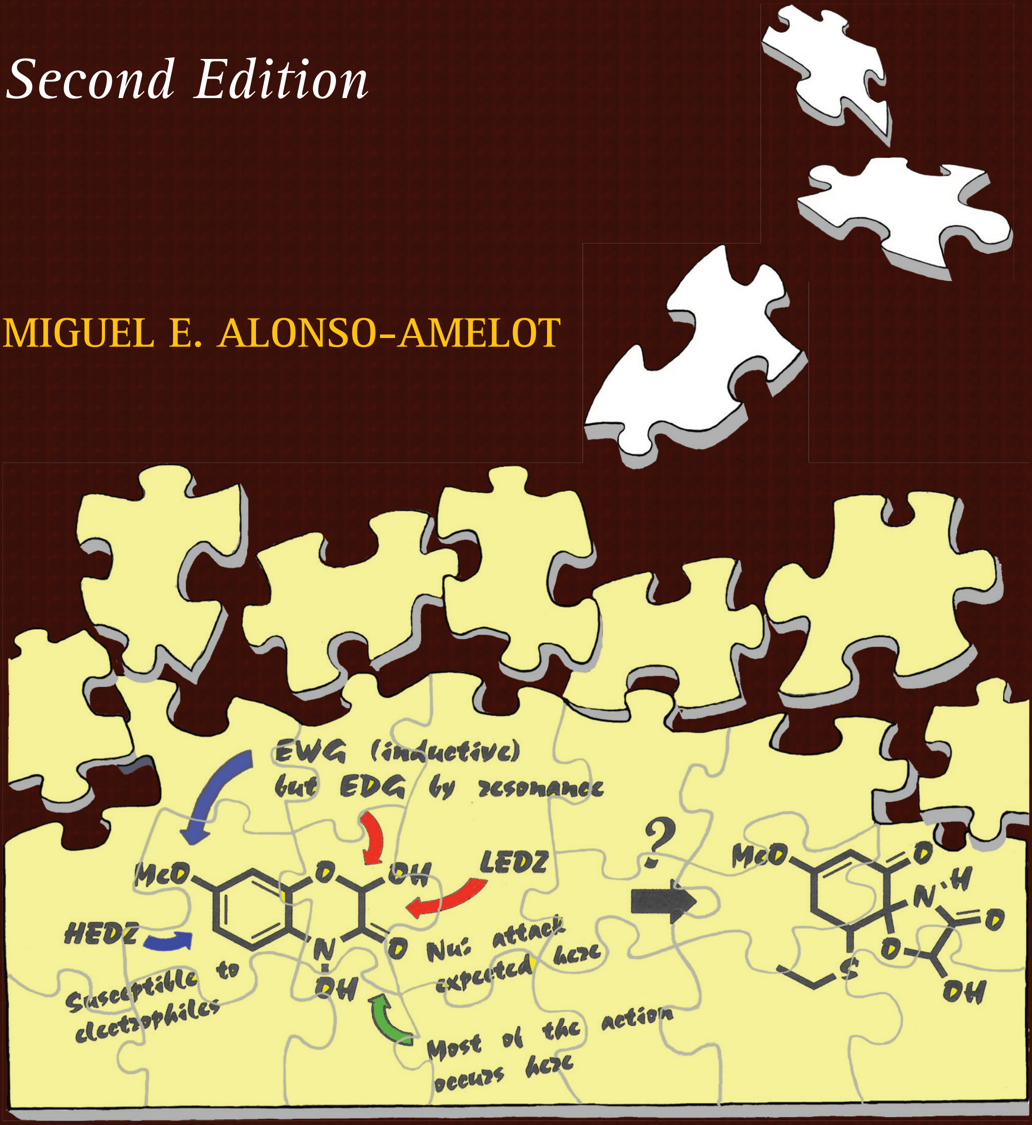
The Art of
Problem Solving in Organic Chemistry

Second Edition

MIGUEL E. ALONSO-AMELOT



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To Adela and Gabriel in this world
Christiane and Ramón, in the other

CONTENTS

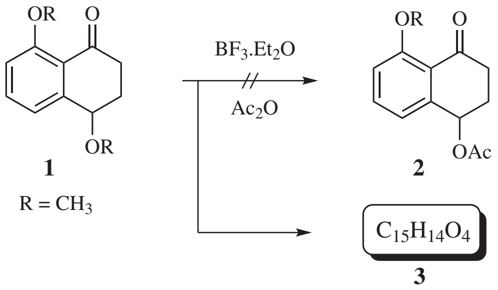
PREFACE

The book you just opened is an entirely rewritten second edition of the homonymous title, published by Wiley Interscience years ago. Growing on the success of the first edition, a set of three chapters describing time-proven techniques of problem solving and organic chemistry concepts is compounded with a new collection of 60 solved advanced-level problems of organic reaction mechanism extracted from groundbreaking research.

Proposing hypothetical solutions and contrasting them against chemical soundness and experimental evidence constitute the fundamental line of reasoning. Perhaps there is no better way to get to the bottom of things organic and extract a most rewarding learning experience. This would not have been possible without first describing a set of concepts and strategies, old and new, of problem-solving analysis applied to organic reactions. Several examples and embedded problems dot these introductory chapters in the belief that Seneca's words were absolutely right: "*Teaching by precept is a long road, but short and beneficial is the way of the example*" (Epistulae, 6, 5).

As there seems to be no end to what organic chemistry and reaction mechanism can expand and achieve, a web page has been created to lodge a large and growing body of supplementary material associated with chapter and problem discussions: http://tapsoc.yolasite.com.

To better illustrate the purpose behind this brief introduction, let me take you to the following setting. Imagine, for a moment, that you are sitting at one of those multiple-choice tests wondering where to jot your tick mark. The question might be this one: Equimolar amounts of toluene and hydrogen bromide yield a C_7H_7Br product with the aid of aluminum tribromide. Which is the reaction involved? Your choices are: A – Nucleophilic aromatic substitution; B – Addition; C – Rearrangement;



IR: 1750, 1650 cm^{-1}
^{1}H NMR (δ ppm): 2.28 (*s*), 2.50 (*s*)

SCHEME P.1

D – Addition–elimination; E – Electrophilic aromatic substitution; F – Elimination; G – Substitution.

Your answer is likely to be ciphered in the very large storage of memorized information etched somewhere in your gray matter during class or reading and deposited effectively and recoverably in your brain. Then, you plunge head on into this ocean of memorized data to identify that tiny and highly specific string, match it with a particular preselected choice in your test and finally tick that box hoping for the best.

In this sort of test, thinking as far as reasoning proper is not there but at a very rudimentary level. You may have selected choice E as a topical answer. However, if you stop and think rather than match memories, you will soon discover a high degree of ambiguity in some of the choices: electrophilic aromatic substitution involves answers D and G, as well as bits of B and F, for example.

Now, change the situation a bit as you are presented with an organic reaction like that in Scheme P.1 and asked to provide a mechanistic explanation. No multiple choices or anything to tune your mind on any particular lecture; just you and a bare bones chemical transformation: a real-life situation in which researchers expected a standard O-acylation (product **2**) but were surprised to find compound **3** coming out of the silica gel column as the only isolable material [1].

Your brain's attitude will undergo a virtual commotion as it deliberates in terms of intellectual logic, beginning by detecting and selecting *the* important issues, organizing the available data; then move on to heat up educated imagination to new highs, throw in the inevitable intuitive kink, and, oh yes, explore memory banks deep in that heavy gray mass up there in search for spectral *interpretation* and other reaction courses sufficiently resembling this one, if at all. Gradually a feasible mechanism emerges from the top of your head to be debated with yourself (who else during an exam?) until you feel satisfied enough to draw the set of sequential molecular renderings any other organic chemist can understand anywhere in the world, not just your teacher. (Is this not awesome?)

Before you read on, let me invite you to provide an answer to this problem (do not be discouraged if you cannot at this point) and then explore a full discussion in Suppl # 1 on http://tapsoc.yolasite.com.

In actual fact, everyday professional life is very much like this, unexpected daily situations with options in a scale of grays rather than black or white. Pondering, reasoning, and, why not, a bit of intuition, rather than memory alone, are the best and most efficient tools to reach a correct (or more appropriate, under the circumstances) answer. If so, why not do whatever it takes to improve these skills, so exceedingly valuable for the proficient organic chemist?

Albert Einstein was probably right when he said "*Imagination is more important than knowledge*." Coming from such a bright mind this unsettling sentence should not be taken as a cold shoulder on mnemonic learning as an outmoded teaching philosophy, a current trend by the way. After all, culture, an exclusively human trait, is almost entirely based on accumulated knowledge created by our predecessors and stored in society's *collective* memory. The individual brain takes up whatever it can and needs from this ample menu and mixes it with the daily information input, filters off the chaff (the largest portion) and retains the rest to be organized within its neuronal maze in various depth levels. Then recall these as required, sometimes in quite different forms from the original.

Memory by itself, however, cannot replace imagination but only help support it. For one reason: human knowledge is far too large for one individual to remember, and it expands at an impossible logarithmic rate growing on itself like bacteria in a petri dish without nutrient limitation. Currently, it doubles every 5 years! There is no way to stay abreast with such a deluge, regardless of electronic ultrafast databases. And yet, people who changed our way of thinking and perception of the universe, Gallileo, Keppler, Kant, Newton, Rousseau, Liebig, Kekulé, Maxwell, Freud, or Pasteur had access to few books and knew just a small fraction of what average sophomores of science careers of our day store in their mind.

How could such an "unenlightened clique" achieve such a huge goal? Because all of them put to good use the little they knew with a large dose of imagination (in Einstein's terms), reasoning, and sense of purpose to pose the right questions, tie knots between dispersed bits of knowledge of their time and persevere to get the answer. They were not only unsurpassed thinkers but great problem solvers as well. They could also live up to changing times with fresh answers. As Uruguayan poet Mario Benedetti once said: "*When we thought we had all the answers, suddenly all the questions were changed.*"

The kind of test of Scheme P.1 gauges your capacity to face this new world of ever expanding knowledge in the sciences and societal needs; that is, your ability to navigate through uncharted territory without sinking. For such steering, reasoning, and the ability to correlate apparently unrelated issues while using organized thinking and creativity are much more valuable than anything else. Although some privileged ones are born with such gifts, most of us need to acquire and develop these skills through the hardships of problem-solving training. Problem solving is not only a most powerful tool but a requisite for the good practice of the organic chemistry profession.

This is why the opening sentence of my first edition of *The Art of Problem Solving in Organic Chemistry* was: *"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."* This assertion continues to be true, perhaps more than ever.

Most textbooks covering problem solving are aimed at beginning to mid level undergraduate students of the organic chemistry trade. This is valuable information, no doubt, but limited in scope and depth for obvious and necessary reasons. Advanced students and their instructors will find them too elementary. As an alternative, students and lecturers must resort to browsing the current literature randomly in search of sufficiently challenging problems. This is not only time consuming but electronic database scanning miss many interesting reaction mechanisms deep within articles.

This book seeks to overcome these two issues by taking care of problem selection at an advanced level and describing solutions and related chemistry in detail. As such, it is a workbook rather than a text although it may still be used as such.

TEXT ORGANIZATION

It all begins with recognizing the difference between chemistry exercise and a true problem. The book opens with a set of three chapters describing problem analysis in organic reaction mechanism and special techniques of my own and others. My students and I have tested them in class and exams over the years and proved to be exceptionally commanding for problems with elusive answers, as well as for putting forward firm hypotheses and sound solutions. Although some of these topics were covered in the first edition, new ones have been added including all important electron flow during chemical transformations.

All these introductory concepts are dotted with numerous examples in problem form, which you, as a curious reader, may feel lured to solve before carrying on to the answer in the discussion of each issue. Specific links to this book's website are given at appropriate places in the text. In this manner, the subject unfolds step-by-step with an increasing involvement on your part as you work through.

The second part of the book comprises a large set of fully discussed problems in reaction mechanism. These reactions have been carefully selected from the current research literature, chiefly synthesis and organic reaction areas, and organized roughly according to level of difficulty.

The techniques described in the first chapters are applied as problems require. You are expected to cuddle up and draw your own answers and then compare the result critically with the solutions offered here. Alternatively, you may study the discussion step-by-step, stopping at suggested places to work out your own way to partial or final solutions. This is also brain material for group discussions. Gradually you will build up your proficiency as problem analyst and solver and be able to tackle ever more challenging reaction mechanisms as you progress through this collection.

In this new edition lecturers of organic reactions and synthetic methods may find inspiration for bringing increasingly demanding problems to class for students to take home and split hairs on them. Also, it should serve as a source of examples of certain sophistication from the current literature for their courses and reaction type examples. Besides, the subject of mechanism elucidation and hypothesis proposal is in itself a much-needed topic for the advanced chemistry syllabus.

Humanity will continue to face increasingly demanding challenges that may even defy its survival in this critical century. Solutions to these grave questions befall to a large extent on our scientific and ethical vision of present and future needs of us and all around us and our capacity to explore and understand the unknown. The great problem solvers will be the best prepared to tackle such responsibilities. Do you want to improve yourself in this direction? Then, read on.

This book includes a body of chemistry of considerable substance and scope and some mistakes may have escaped scrutiny. All of them are my own and not of the authors in references or the editors.

MIGUEL E. ALONSO-AMELOT, PHD.

REFERENCE

1. Banerjee AK, Bedoya L, Vera WJ, Melean C, Mora H, Laya MS, Alonso-Amelot ME. *Synth. Commun.* 2004;34:3399–3408.

PREFACE TO THE FIRST EDITION

"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 to thank Mrs. Shirley Thomas for her dedicated Production work, Ms. Cheryl Bush for her advice on language usage, and to all my students who, over the years, have provided useful feedback for many of the ideas expressed in this work. Finally, my thanks to the Tarnawiecki family of Lima, Peru. This book benefited greatly from the stimulating and highly caring environment they provided while the writing of the first draft was in progress. Two most unusual people contributed the most to this environment, Don Rafael and my wife, Adela.

MIGUEL E. ALONSO-AMELOT

Caracas, Venezuela
March 1986

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A book like this one might not have been created without the help from a number of people. My special thanks go first to my wife Adela for supporting my work so blindly and enduring the long absent-minded periods when solving organic reaction mechanisms takes precedence over other family responsibilities. My students of advanced courses in organic reactions over the years have taken their heavy load as well, providing their invaluable feedback. As many solutions here are my own, a most necessary second opinion in particularly tricky reactions was indispensable. Professors Achim Stolle and Bernd Ondruska of the Friederich Schiller University in Jena, Barry B. Snider from Brandeis University, Javier González Fernández of Universidad de Oviedo, Juan Francisco Sanz-Cervera of Universidad de Valencia, and Julia Stephanidou-Stephanatou and Constantinos Tsoleridis at the Aristotle University of Thessaloniki were kind enough to revise, discuss constructively and suggest corrections to parts of the manuscript. Likewise, my gratitude to Servicio de Biblioteca y Documentación of Universidad de Valencia, Spain, along with the Asociación de Alumnii y Amigos of this university, both absolutely essential to access the current literature and older sources of difficult retrieval, must be acknowledged.

I had the good fortune to work with Jonathan Rose and Amanda Amanullah, editors of John Wiley & Sons, Prakash Naorem, project manager of Aptara, Inc., and the assistance of a variety of unnamed reviewers as this project gained maturity. Without them, this book would have never seen light.

M. E. A.

1

PROBLEM ANALYSIS IN ORGANIC REACTION MECHANISM

1.1 OVERVIEW

Uncertain questions, in general, need to be recognized as true problems from the very beginning. This is not trivial considering that a given chemical reaction can be explained readily (not a problem, just an exercise in spite of a few unknowns), whereas another may not have any solution in sight (a true problem).

Problems are there for learning, not for troubling. One misses most of their instructive value and fun by rushing through them without first analyzing the real chemistry behind the scene. Pondering options, examining routes of action, taking decisions, and drawing a successful plan constitute a most rewarding and enjoyable experience: a game with complex rules.

This is what problem analysis (PA) is all about. This chapter focuses on the basic steps that will extract the most of each mechanistic riddle with the aid of a number of embedded mechanistic problems for you to try and then compare your solution with the one provided here. In so doing, you will begin your training as a problem solver in organic reaction mechanism from the first pages.

1.2 INTRODUCTION

Perhaps the *educated guess* to postulate a reaction mechanism is the most popular procedure among dilettante problem solvers. Starting materials and reagents are

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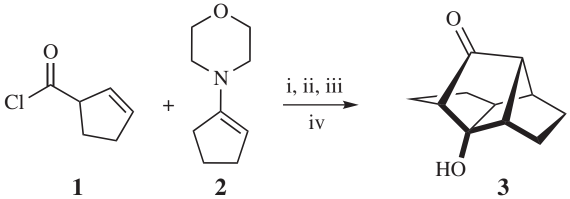
The Art of Problem Solving in Organic Chemistry, Second Edition. Miguel E. Alonso-Amelot.



1 **2** **3**

i: Et_3N, then H_3O^+
ii: AcCl, pyridine
iii: UV (254 nm), cyclohexane
iv: KOH, dioxane, H_2O

SCHEME I.1 Adapted from Reference 1. Copyright © 1978 American Chemical Society, by permission.

treated using familiar reactions to approach products. This task usually turns into a stop-and-go stepwise protocol toward the goal. Frequently enough, however, neither starting materials nor reagents look familiar enough and progress comes to a frustrating standstill.

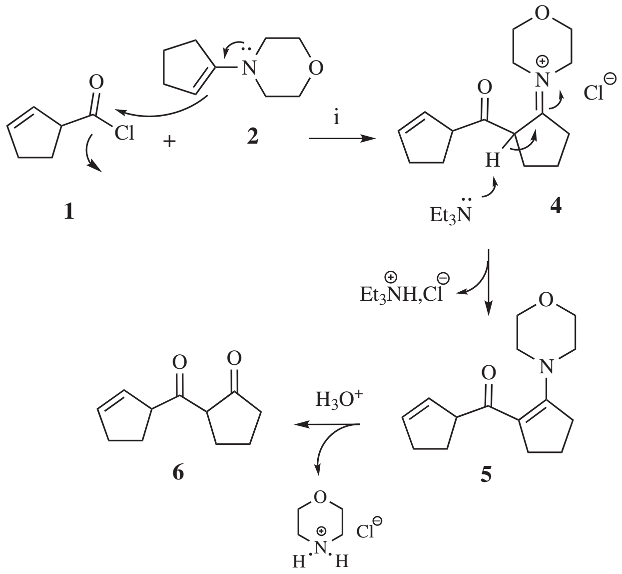
As this is a workbook, let us put to test the previous assertion with a working example. Take the reaction of Scheme I.1, extracted from a now classical transformation [1] and try to propose a reasonable mechanism. Do not be discouraged if you cannot.

This set of reagents does not involve fancy components, extravagant catalysts, or extreme reaction conditions. A good strategy at the onset is to focus your attention on the molecular hot spots: the highly active functions. Then, work your way through, supported by the chemistry you presently know. After producing an answer, compare your reactions with the *belabored* (on purpose) solution described below. It may look a bit lengthy, but keep in mind the point we want to make here: the awkwardness of this honest, exhaustive, stop-and-go educated guess approach. So please be patient if you want to learn and enjoy.

1.2.1 "Pushing Forward" a Solution in Formal and Exhaustive Terms

We shall resort to *educated guesses* in strict abidance to the rules of organic mechanism and *thoroughness* to leave no loose ends. This is not the best recommendation to proceed but good enough for what we want to demonstrate: Paying too much attention to detail is unproductive, pathway branching, and confusing.

A fast look at Scheme I.1 reveals that compound **3** appears to have many more carbon atoms than **1** or **2** taken individually, whereas the morpholine segment has disappeared. Also there are lots of new C–C connections in **3**, suggesting that bonding the starting materials is a good idea. Additional C–C bonds may be built from there as needed.



SCHEME I.2

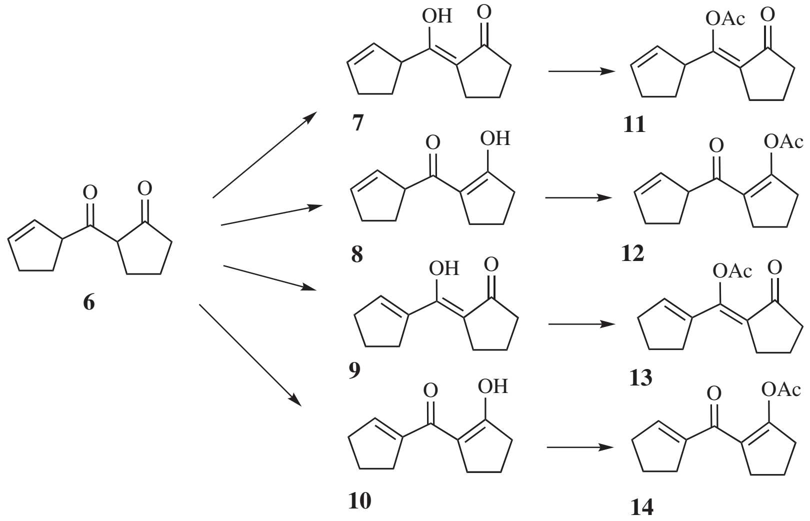
To that end, one makes use of the electronically active carbons in the starting materials: Cl–C=O in **1** and the enamine in **2**, a familiar electrophile–nucleophile combination. Expectedly, β-diketone **6** is spawn effortlessly via **5** after aqueous acid workup (Scheme I.2). Triethylamine mops up the HCl produced (leaving it alone would have blocked the enamine as the pH decreased).

Take note that there are as many carbon and oxygen atoms in **6** as in target compound **3**, so no additional moles of **1** or **2** are required. The rest of the sequence seems accessible enough, requiring only a few connections and disconnections here and there in **6.**

Well, let us see if this is so simple: Please go back to Scheme I.1 and observe the reaction conditions of Step ii. Clearly, this is a standard acetylation. Or is it really? There is no OH in sight to acylate, but one can create this OH easily by enolization of **6**. There are two firsthand enols **7** and **8** that, after acylation, will furnish enol acetates **11** and **12**. In fact, enol acetates **13** and **14** are also conceivable by C=C isomerization to the thermodynamically more stable conjugated acetates. Now we have four reaction products to submit to the next step. Our educated guess has led us to an irritating ramification of the reaction scheme (Scheme I.3).

Worse comes to worst: At this point one cannot conjecture a priori which is the most likely enol acetate, except for the stability of the conjugated systems. Hence, more educated suppositions are in order and all potential intermediates need to be considered in the next step.

Step iii: Activation comes from UV light of a high pressure Hg lamp (254 nm). Usually, this entails [2 + 2] coupling of C=C bonds located at accessible distances to



SCHEME I.3

give a cyclobutane derivative after photoexcitation of the C=C–C=O unit (denoted *). Woodward–Hoffmann rules dictate that only the suprafacial–suprafacial approach of the two π bonds would be allowed for a concerted reaction. But none of dienes **11–14** can attain this conformation (try your own Dreiding models or visit Suppl I # 1 in http://tapsoc.yolasite.com/), acquiring chiefly the supra-antarafacial configuration. This argument would have serious consequences for the stereochemistry of the resulting cyclobutanes, but not in our present case.

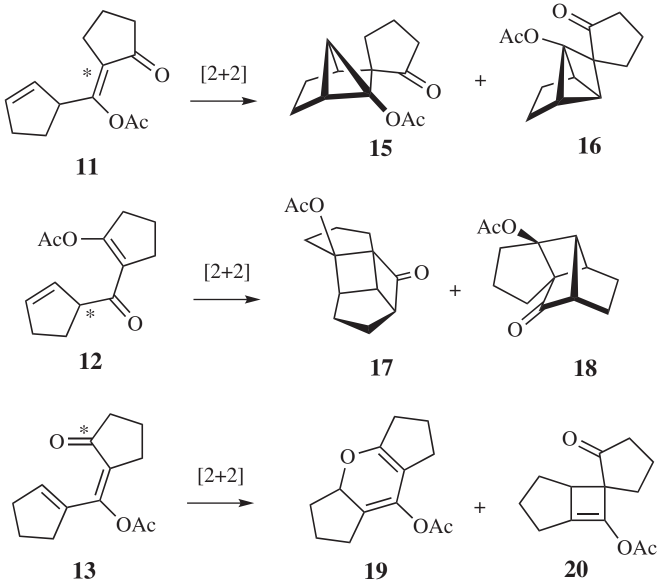
Two C–C bonds are formed in the [2 + 2] photocycloaddition, taking us closer (but we do not yet know how) to target **3**. We are driven to this blind conclusion by the increase in scaffold complexity. Rewriting enol acetates **11–14** to better observe the photoexcited π–π^* interactions, one may postulate not one but *two intramolecular* [2 + 2] *cycloaddition products for each diene* (Scheme I.4). This means that our brainchild has tragically branched out into *eight* different compounds (**15–22**), while product **3** is still as elusive as ever (none of them resembles it).

Things are getting a bit out of hand, so some clean up is due. One may discard a priori some of the photo adducts of Scheme I.4 on the basis of two criteria without resorting to Procrustean methods[1]:

(a) Resemblance to product **3** backbone, if any, and
(b) Structural incongruence.

---

[1] *Procrustes, a barbaric bandit in Greek mythology, forced his victims to fit the length of his bed by either stretching savagely their bodies with ropes if too short or amputating their limbs if too tall. So, to place an argument on the bed of Procrustes is adapting it to circumstance through arm twisting or irrational means.*



SCHEME I.4

(a) *Resemblance*: By comparing the [2.2.1] bicyclic portion of **3** with photo products **15–20**, (with some concession to additional rearrangements still to come), structures **19** and **20** may be put aside momentarily to be retaken only if exploitation of the rest does not furnish the target.

(b) *Incongruence*: While there are limits to scaffold construction of carbon [0.0.x.y . . .](multi)cyclic structures, organic synthesis has been able to produce incredibly strained compounds [2]. Therefore, it is not that simple to filter off apparently implausible structures. Besides, reaction conditions are mild (0°C) and strained compounds may survive.

In terms of intuitive (*eye-assessed*) relative probability of occurrence based on the *anticipated* relative ΔH of each compound, I would propose the following order: **18** > **15** > **17** > **16**. Do you have a different opinion? Table I.1 may help to dissipate any

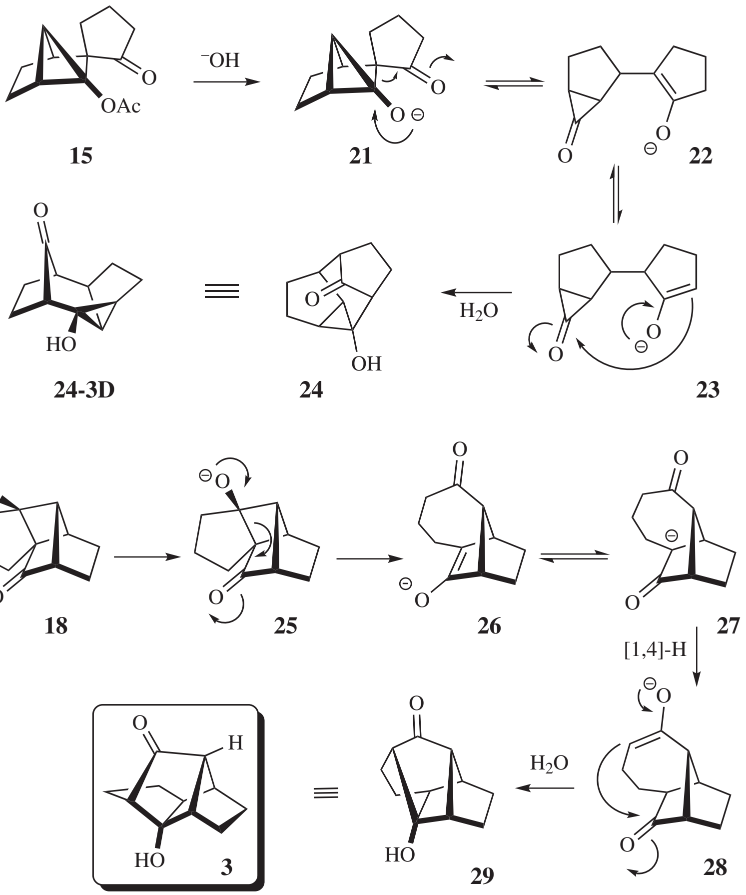
TABLE I.1 Total Strain Energy (kcal/mol) Relative to Cubane of Photo Adducts 15–18 **of Scheme I.4 (Calculated by Molecular Mechanics Methods (ChemBioDraw (CambridgeSoft) MM2 Interface)**

Compound #	*E* (kcal/mol)
15	−109.3
16	−54.5
17	−42.5
18	−49.6

handweaving controversy by revealing, after some molecular mechanics calculations, that my prediction was completely wrong. Was yours too? Mind that the more negative strain energy values imply a more stable compound. The order of stability suggested by molecular mechanics, hence the probability of the dominant photolysis, is now **15** > **16** > **18** > **17**. This order holds if we assume product-like transition states, as cyclization to such strained scaffolds are endothermic.

Although one should not take blindfolded the dictates of molecular mechanics calculations, the strain energy difference of compound **15** relative to the rest is so large that not considering it first for the next reaction would be an unpardonable gaffe. Regrettably though, basic hydrolysis and retro-aldol bond breakage followed by the reverse reaction on odd cyclopropenone **22** leads to a carbon scaffold (**24**) unrelated to target **3**. (Scheme I.5).

Acetate **17** would be next in line for scrutiny. In light of the previous discussion, it is clear that the other enolate would also give a bicyclo-cyclopropane far removed from



SCHEME I.5

3. Neither would **16** (try to convince yourself of this). All our hopes are seemingly pinned on compound **18**. Scheme I.5 describes the retro-aldol disconnection and reconnection applied to it.

At the end of the day we finally succeeded with this last minute basket, and yet it is not possible to clearly justify the chain of events leading to **18** as the most favorable conduit. It is of reassuring interest that this reaction can be stopped at the stage of diketone **27** by replacing acetate with benzyl ether, which is then removed by hydrogenolysis after UV irradiation [1]. While allowing the retro-aldol condensation, the neutral medium prevents further enolate recoupling (**27** → **29**).

1.2.2 Lessons from this Example

Although we were able to come up with an acceptable solution after treading through so many possibilities and letting our sketch reach almost unmanageable proportions, there is this residual sense of unwise application of our chemical knowledge. Exhaustiveness is not necessarily a formula for success in mechanism design and many other endeavors of professional life. Albert Einstein was once quoted as saying: "*Any intelligent fool can make things bigger, more complex, and more violent. It takes a touch of genius and a lot of courage to move in the opposite direction.*"

I dare say that you are among those who wish to move in this "opposite direction." But you will never walk this road by *pushing forward starting materials towards products without previous analysis of the problem and drawing a clever plan from it to* ***select*** *sound options and discard others*, no matter if you are well intentioned and supported by sound chemistry. As will be shown in Chapter 3, working the other way around (understanding the product rather than starting materials) may be much more creative, practical, and productive.

1.3 AVOIDING THE QUAGMIRE

A much more constructive and effective approach to reaction mechanism develops if, before throwing ourselves to scribble structures and curly arrows to convert starting materials into products, we take time first *to focus our attention on precise issues* regarding associations between all compounds, starting materials, products, and reagents in an organized way. This is so obvious, you might say, but not many people do this.

This planning begins with PA. An introductory review of PA as applied to organic chemistry reactions is the subject of the rest of this chapter. Subsequent chapters will deal with specific techniques in the search of valid solutions.

PA may be focused in many ways as the abundance of references dealing with this topic leads one to believe. In essence:

> *Problem analysis is an exercise in asking the right questions to clear the way toward the right solutions (notice the plural here).*

This assertion is probably too simplistic, but it is a good launching pad as we allow this idea to grow from this uncomplicated start. Problem solutions generally emerge *after* pondering options stemming from meticulous questioning and analysis.

1.4 THE BASIC STEPS OF PROBLEM ANALYSIS

There are three steps that may be applied not only to organic chemistry problems but to almost any situation requiring PA.

1. Recognize whether the reaction (or issue) under scrutiny is a true problem.
2. Analyze the problem by asking the right questions, discarding the irrelevant.
3. Drawing a first sketch for guidance in developing the definite answer.

These steps are now described in detail with more embedded problems for you to work out as you read.

1.4.1 Recognizing the Problem

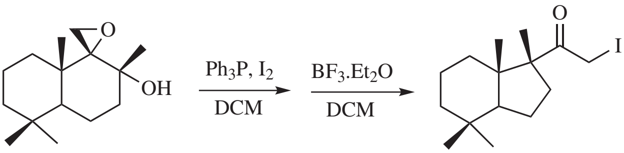
What is a problem is our first question. This is not as dumb as it sounds because many students, no matter how advanced, confuse exercises with genuine problems. A key question solves this doubt: *After a first bird's eye view, do I recognize a feasible solution right away?* If the answer is yes, then the problem does not exist; the reaction is just an exercise. A problem-example illustrates this point.

Suppose you are faced with the reaction of Scheme I.6, which I extracted from a recent synthesis sequence of (+)−austrodoral, a natural sesquiterpene [3]. We shall treat this reaction along the elementary lines described above.

Queries at the onset, once you have a superficial evaluation:

(a) Is this *really* a problem?
(b) Is it worth the effort solving it?
(c) Will I learn anything by devising and testing a mechanism?

Answers will vary depending on each one's background and attitude. Scheme I.6 may constitute a challenging problem with lots to learn from for sophomore



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SCHEME I.6