

**As a
Second
Language™**

Organic Chemistry II

Second Semester Topics

2nd Edition

David R. Klein

*ORGANIC CHEMISTRY II
AS A SECOND
LANGUAGE*

DR. DAVID R. KLEIN

Johns Hopkins University



JOHN WILEY & SONS, INC.

SENIOR ACQUISITIONS EDITOR	Kevin Molloy
EXECUTIVE PUBLISHER	Kaye Pace
MARKETING MANAGER	Amanda Wygal
PRODUCTION MANGER	Pam Kennedy
PRODUCTION EDITOR	Sarah Wolfman-Robichaud
CREATIVE DIRECTOR	Harry Nolan
SENIOR DESIGNER	Kevin Murphy
SENIOR EDITORIAL ASSISTANT	Cathy Donovan
PROJECT MANAGEMENT SERVICES	Pam Lininger/Matrix Publishing Services
COPYEDITOR	Betty Pessagno

This book was set in 10/12 Times Roman by Matrix Publishing and printed and bound by Courier Westford. The cover was printed by Courier Westford.

This book is printed on acid-free paper. ∞

Copyright © 2006 John Wiley & Sons, Inc. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, scanning or otherwise, except as permitted under Sections 107 or 108 of the 1976 United States Copyright Act, without either the prior written permission of the Publisher, or authorization through payment of the appropriate per-copy fee to the Copyright Clearance Center, Inc. 222 Rosewood Drive, Danvers, MA 01923, website www.copyright.com. Requests to the Publisher for permission should be addressed to the Permissions Department, John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030-5774, (201)748-6011, fax (201)748-6008, website <http://www.wiley.com/go/permissions>.

To order books or for customer service please, call 1-800-CALL WILEY (225-5945).

ISBN-13 978- 0-471-73808-4
ISBN-10 0-471-73808-5

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

TABLE OF CONTENTS

Chapter 1 THE SKILLS YOU NEED 1

- 1.1 The Goal of This book 1
- 1.2 Mechanisms Are Your Keys to Success 2

Chapter 2 INTRO TO IONIC MECHANISMS 4

- 2.1 Curved Arrows 4
- 2.2 The Basic Moves 8
- 2.3 Combining the Basic Moves 16

Chapter 3 ELECTROPHILIC AROMATIC SUBSTITUTION 22

- 3.1 Halogenation and the role of Lewis Acids 23
- 3.2 Nitration 28
- 3.3 Friedel-Crafts Alkylation and Acylation 31
- 3.4 Sulfonation 38
- 3.5 Modifying the Nucleophilicity of the Nucleophile 43
- 3.6 Predicting Directing Effects 46
- 3.7 Identifying Activators and Deactivators 59
- 3.8 Predicting and Exploiting Steric Effects 69
- 3.9 Synthesis Strategies 76

Chapter 4 NUCLEOPHILIC AROMATIC SUBSTITUTION 83

- 4.1 Criteria for Nucleophilic Aromatic Substitution 83
- 4.2 S_NAr Mechanism 86
- 4.3 Elimination-Addition 90
- 4.4 Mechanism Strategies 96

Chapter 5 KETONES AND ALDEHYDES 98

- 5.1 Preparation of Ketones and Aldehydes 98
- 5.2 Stability and Reactivity of the Carbonyl 102
- 5.3 H-Nucleophiles 104
- 5.4 O-Nucleophiles 109
- 5.5 S-Nucleophiles 122

5.6 N-Nucleophiles **131**
5.7 C-Nucleophiles **139**
5.8 Some Important Exceptions to the Rule **148**
5.9 How to Approach Synthesis Problems **152**

Chapter 6 *CARBOXYLIC ACID DERIVATIVES* **159**

6.1 General Rules **160**
6.2 Acyl Halides **167**
6.3 Anhydrides **176**
6.4 Esters **179**
6.5 Amides and Nitriles **188**
6.6 Synthesis Problems **194**

Chapter 7 *ENOLS AND ENOLATES* **203**

7.1 Keto-Enol Tautomerism **205**
7.2 Reactions Involving Enols **210**
7.3 Making Enolates **213**
7.4 Haloform Reactions **216**
7.5 Alkylation of Enolates **219**
7.6 Aldol Reaction and Aldol Condensation **223**
7.7 Claisen Condensation **230**
7.8 Decarboxylation Provides Some Useful Synthetic Techniques **238**
7.9 Michael Reactions **245**

Chapter 8 *AMINES* **253**

8.1 Nucleophilicity and Basicity of Amines and Amides **253**
8.2 Preparation of Amines through S_N2 Reactions **255**
8.3 Preparation of Amines through Reductive Amination **259**
8.4 Preparation of Amines from Amides **263**
8.5 Acylation of Amines **267**
8.6 Reactions of Amines with Nitrous Acid **271**
8.7 Aromatic Diazonium Salts **274**

Answer Key **277**

Index **311**

THE SKILLS YOU NEED

1.1 THE GOAL OF THIS BOOK

There are a lot of reactions that you will learn this year. Perhaps you could try to memorize them. Some people are good at that. But rather than memorizing, you would actually be better off if you tried to focus on building your *skills*. You will need certain skills in order to do well in this course. In this book, we will focus on those skills.

Specifically, you will learn the skills that you need to do three very important types of problems:

1. Proposing a mechanism
2. Predicting products
3. Proposing a synthesis

As you progress through the course, you will soon realize that it is not enough just to learn the reactions. To do well in this course, you **MUST** learn how to approach and solve these three types of problems. You must become a master of very specific skills. These skills will guide you in solving problems. These three types of problems represent the core of an organic chemistry course. If you master the skills you need, you will do very well.

Each chapter in this book will focus on the skills that you need in order to master a particular topic. The chapters in this book are designed to map out fairly well onto the chapters in your textbook. For instance, when you are learning about carboxylic acid derivatives, there will be a chapter in this book with the same title.

We will not have enough space to cover every topic in your textbook. This supplement is not designed to replace your textbook or your instructor. Rather, it is meant to provide you with the core skills that will allow you to study more efficiently.

Although we will focus on three major types of problems, we must place the major emphasis on mechanisms. Mechanisms are your keys to success in organic chemistry. If you master the mechanisms, you will do very well in the class; if you don't master them, you will do poorly. It is hard to talk about synthesis problems if you don't know the reactions well enough (and the same is true for predicting products). That is why Chapter 2 is devoted to laying the foundation you need to master mechanisms. That chapter is important. So, even though it won't correspond to a specific chapter in your textbook, make sure to go through Chapter 2 anyway.

In Chapter 2, we will see that mechanisms follow a small number of basic themes and ideas. By focusing on these basic themes, you will see the common threads between mechanisms that would otherwise appear to be very different. This approach will minimize the need for memorization. In fact, we will soon argue that students who focus on memorization will miss problems that are trivial when you understand the basic concepts. This book will provide you with the fundamental language and tools that you need in order to master mechanisms. And while we are at it, we will work on the skills you need to solve synthesis problems and predicting products as well.

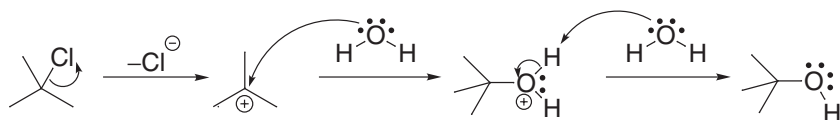
1.2 MECHANISMS ARE YOUR KEYS TO SUCCESS

What are mechanisms, and why are they so important?

To understand the important role that mechanisms play, let's consider an analogy. I recall the time that I had to teach my children how to put on their shoes. It is amazing how many steps are involved when tying your shoelaces. Next time you tie your shoelaces, think about how many individual steps your hands are doing, and think about how you would explain each of these steps to someone who never learned how to tie their own shoes. It is a difficult thing to teach. I am embarrassed to say that my first response was to take the easy road—I bought them shoes with Velcro straps. I had temporarily solved my problem because the new shoes required so few steps to put on.

The end result (a child wearing shoes) looks the same regardless of the type of shoe used. But the process of getting the shoes on is very much dependent on the type of shoe. In particular, the number of steps involved to complete the process is vastly different from one type of shoe to the other. The same is true with reactions. All reactions involve steps to get from starting materials to products. Some reactions proceed through a lot of steps, while others go through just a few steps. A detailed list of steps that a reaction follows is called a mechanism.

When two compounds react with each other to form new and different products, we try to understand **how** the reaction occurred—what are the individual steps in the process? Every step involves the flow of electron density; electrons move to break bonds or to form new bonds. Mechanisms illustrate how the electrons move during each step of a reaction. The flow of electrons is shown with curved arrows, for example:



The curved arrows in each of the three steps above show us **how** the reaction took place. You should think of a mechanism as the “book-keeping of electrons.” Just like an accountant will do the book-keeping of a company’s cash flow (money coming in and money going out), so, too, a reaction mechanism is the book-keeping of the electron-flow in each step of a reaction.

In my previous book (*Organic Chemistry as a Second Language: Translating the Basic Concepts*), we saw that bond-line drawings (the way we draw molecules in organic chemistry—see the reaction above) are the “hieroglyphics” of organic chemistry. We saw that these drawings focus on the electrons (the atoms themselves are generally not drawn, but are implied). Each line in the drawing represents a bond, which shows you where the electrons are. Look at the mechanism above, and in your mind, think of it as a sentence. The drawings of the molecules (the bond-line drawings) represent the nouns of the sentence. The curved arrows are the verbs of the sentence. So a mechanism is essentially a sentence. It is truly a language, and you need to learn how to combine the nouns and verbs, just as you do in any other language. In my previous book, we focused on the nouns of the sentences—we focused on molecules. In this book, we focus on the verbs. Imagine learning French without learning any verbs. You wouldn’t be able to get out a single sentence!!!!

So, if you want to master mechanisms, then you really need to master curved arrows, which are the verbs of our language. You need to know when and where to draw curved arrows. In other words, you need to learn to predict how electrons flow.

Once you appreciate the idea that electrons move in predictable ways, you will begin to see similarities in all of the mechanism in this course. As an analogy, consider the way water flows. You

know that, because of gravity, water flows to the lowest spot. That is true on a mountain, on a bumpy road, on a roof, and so on. In each situation, you could probably predict how water would flow on the terrain by simply inspecting it and looking for grooves that lead to the lowest point. Simple, right? Well, imagine if you had a friend who did not understand that water always flows to the lowest spot. Your friend would be absolutely amazed at your ability to predict how the water would flow in every (seemingly different) situation. After all, a roof is certainly a different situation from a bumpy road. But in fact, the situations are not all that different when you understand the one simple concept that water flows to the lowest point.

Similarly, the flow of electrons can be predicted by understanding just a few simple concepts. If you really want to make your life miserable, then you could memorize every single mechanism in the course. But that would be silly—that would be like your friend (who does not know how water flows) trying to memorize every different situation (the roof, the mountain, the road, etc.). Your friend might have a good memory, but if he does not understand how water flows, he will be completely stumped when he sees a new terrain that he has not memorized. Without knowing the one guiding principle, he would be lost. But when you know the guiding principle, it is trivial to make the prediction of how the water will flow on ANY new terrain.

When you understand a mechanism, you will understand why the reaction took place, why the stereocenters turned out the way they did, and the like. If you do not understand the mechanism, then you will find yourself memorizing the exact details of every single reaction. Unless you have a photographic memory, that will be a very difficult challenge, and as we have just seen, you will not be able to extrapolate to situations that you have never seen. By understanding mechanisms, you will be able to make more sense of the course content, you will be able to better organize all of the reactions in your mind, and you will be able to propose mechanisms in new situations.

At this point, you might be wondering why everyone always says that organic chemistry is all about memorization. Well, the truth is, they are all WRONG. Before you can master organic chemistry, you must let go of the myth that so many former students have engrained in your psyche. There is actually very little memorization in organic chemistry. And if you try to replace true understanding with rote memorization, you will not do as well.

Organic chemistry is all about taking the principles you learn and applying them to new situations. This is easy to do if you understand the rules. It is VERY hard to do if you try to memorize 200 mechanisms. So, don't memorize mechanisms. Instead, focus on *understanding* them with an emphasis on the guiding principles of how electrons flow. That way, you will be able to predict reactions that you have never seen. And when you can do that, you will feel really good about organic chemistry. It might seem like a lofty goal right now, but be patient; this book will guide you through the process, step by step.

Every year, my students ask me how many mechanisms they need to know. I always tell them that it depends how you count the mechanisms. If your strategy is memorization, then you will need to know about 200 mechanisms. However, if you focus on just a few simple principles and rules, you will see that there are only about a dozen unique mechanisms. In fact, those dozen mechanisms are just different combinations of four basic moves.

So, we will begin our step-by-step process by going over the basic moves. We will learn them and practice them. Then we will explore the various combinations of these basic moves, once again in a step-by-step fashion.

In the end, you will see that proposing a mechanism is just as simple as predicting how water will flow down your roof.

CHAPTER 2

INTRO TO IONIC MECHANISMS

Ionic reactions (those reactions that involve either full charges or partial charges) represent most (95%) of the mechanisms you will see this semester. The other two major categories, *radical* mechanisms and *pericyclic* mechanisms, occupy a much smaller focus in the typical undergraduate organic chemistry course. Accordingly, we will devote most of our attention to ionic mechanisms.

In this chapter, we will learn about the basic steps involved in all ionic mechanisms. There are only four basic moves. Let's begin with a quick review (from last semester) of curved arrows.

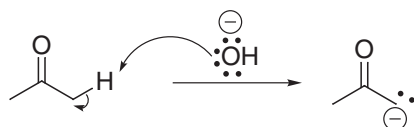
2.1 CURVED ARROWS

Before you can understand the four basic moves, you must first become a master of drawing curved arrows. These are the tools of drawing mechanisms. In the previous book, *Organic Chemistry as a Second Language: Translating the Basic Concepts*, there was an entire chapter devoted to mechanisms. The first nine pages of that chapter were devoted to building skills for drawing proper curved arrows. If you have a copy of that book, I highly recommend that you review those nine pages before continuing in this book. If you do not have a copy of that book, you should look in your textbook to see if there is any introduction to curved arrows and mechanisms.

Even for those students who feel comfortable with curved arrows, a short and quick review cannot hurt. To quickly summarize, every curved arrow has a *head* and a *tail*. It is *essential* that the head and tail of every arrow be drawn in precisely the proper place. *The tail shows where the electrons are coming from, and the head shows where the electrons are going:*

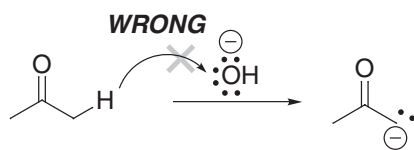


Some students confuse the meaning of an arrow. They think the arrow shows where *atoms* are moving. But this is wrong. Curved arrows actually show the motion of *electrons*. As an example, consider a simple acid-base reaction:



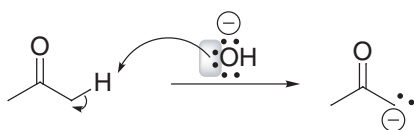
We see that one curved arrow comes from the base (OH⁻), showing the *electrons* of the base grabbing the proton. The next curved arrow shows what happens to the electrons that were originally holding onto the proton. In the end, a proton has been transferred from one place to another. So,

we call this a proton transfer. But don't let the name fool you into thinking that the mechanism is like this:

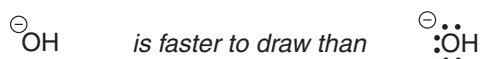


This is wrong because a mechanism does NOT show how a *proton* moves. Rather, the mechanism shows how the *electrons* move. So, for every curved arrow that you draw, you must always make sure that it is going in the right direction. Otherwise, your arrow (and therefore your mechanism) will be wrong.

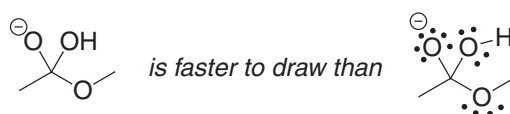
There is one more thing to clarify before we can move on. Notice that the tail of the curved arrow (coming from the oxygen) is placed on a lone pair:



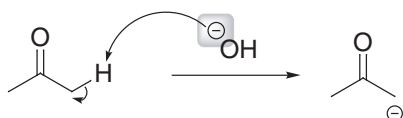
This makes sense because the tail of the arrow represents where the electrons are coming from. And electrons can either come from lone pairs or from bonds (we will see many examples very soon). In the example above, a *lone pair* is grabbing the proton. However, it is very common for organic chemists to draw compounds *without* drawing the lone pairs because it is faster that way. For example:



and here is another, more striking, example:

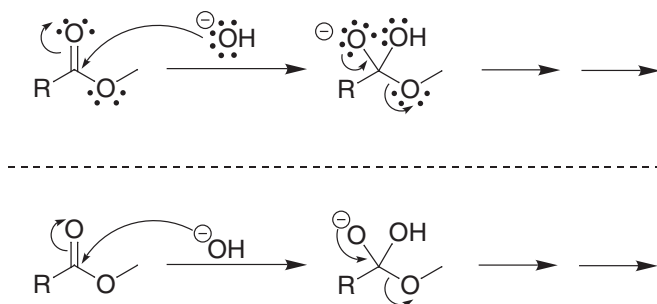


Lone pairs do not *have to* be drawn because they are implied (we saw that in the first semester). In other words, you are supposed to know that the lone pairs are really there, despite their absence from our drawing. As a result, you will often see something like this:



Notice that the tail of the curved arrow is placed on the negative charge. This is the way we must draw the curved arrow in situations where we omit the lone pairs from our drawings. But don't be confused; it really isn't the negative charge that is grabbing the proton. Rather, it is a lone pair that is grabbing the proton.

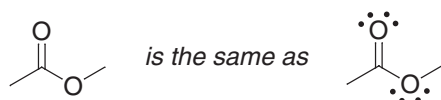
There are two reasons why chemists will often omit the lone pairs when drawing mechanisms. First of all, it is faster to draw mechanisms if we omit most of the lone pairs. But more importantly, it is a lot easier to follow a mechanism when it is not cluttered with lone pairs. Compare for yourself:



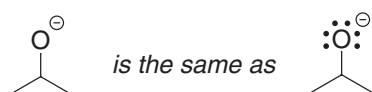
Clearly, the second way of drawing it is less cluttered and easier to follow.

Your textbook will most likely draw all lone pairs (at least the ones participating in a reaction), but your instructor might draw some mechanisms without lone pairs during the lecture (to save time). Both ways are correct. For purposes of clarity and simplicity, most drawings in this book will leave out the lone pairs. I will only show the lone pairs when their presence does not compromise the clarity of the presentation.

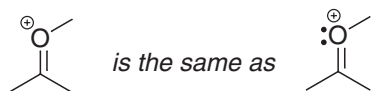
Since we will be leaving out the lone pairs very often, it is important that you get accustomed to “seeing” the lone pairs even though they are not drawn. Oxygen is the most common element that you will see in the course (that possesses lone pairs), so let’s start there. Each oxygen atom with no charge will have two lone pairs:



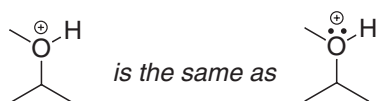
An oxygen atom with one bond and a negative charge will always have three lone pairs:



And an oxygen atom with three bonds and a positive charge will always have one lone pair:

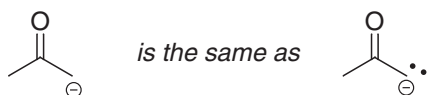


and



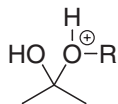
You will see many other elements in this course (nitrogen, sulfur, phosphorus, etc.), but oxygen is the most common of them all. So, you would do yourself a big favor if you would remember the rules above.

One other very common example is a carbon atom with a negative charge:

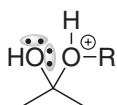


It is important that you can see the lone pairs even when they are not drawn, so let's get some quick practice to make sure that you can see the lone pairs:

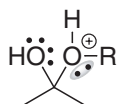
EXERCISE 2.1. In the following intermediate, the lone pairs are not drawn. Draw them.



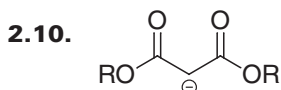
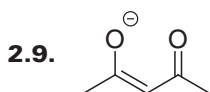
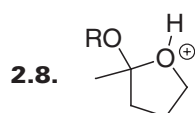
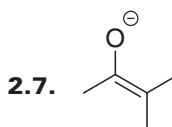
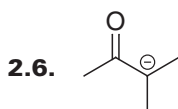
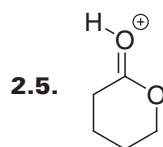
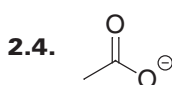
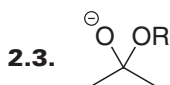
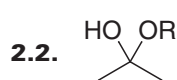
Answer: Oxygen atoms with no charge will have two lone pairs:



And oxygen atoms with three bonds and a positive charge, will always have one lone pair:



For each of the following, draw in the lone pairs that are not shown:

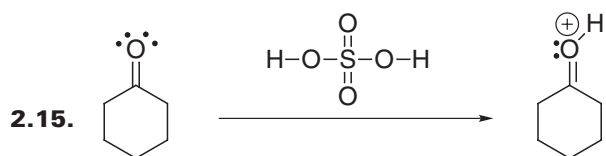
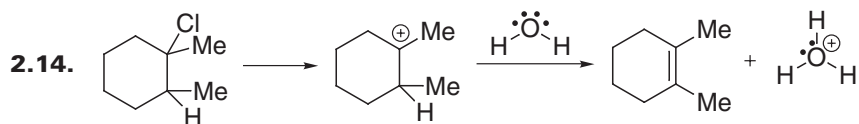
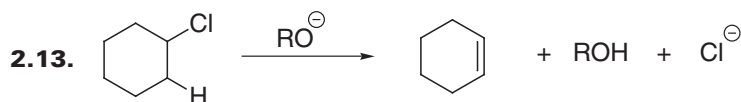
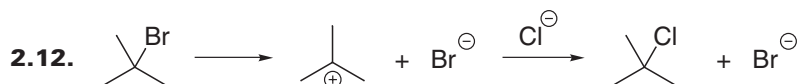
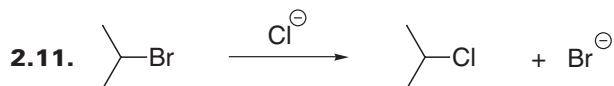


When drawing curved arrows, you must focus on two things:

1. The *tail* of every curved arrow needs to be in the right place, and
2. The *head* of every curved arrow needs to be in the right place.

Now let's make sure that you are comfortable with curved arrows. For each of the reactions below, try to draw the curved arrows *without* flipping to the answers in the back of the book. When you are finished, look up the answers in the back of the book to make sure that you drew the arrows correctly. When looking at the answers, make sure to focus on the position of every head and every tail of the arrows in your answers. If any heads or tails were not drawn in exactly the correct place, then you should go back and review the first nine pages of the mechanisms chapter from the previous book.

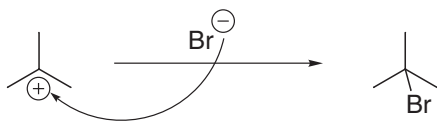
PROBLEMS. For each transformation below, complete the mechanism by drawing the proper arrows (most of these reactions are from the first semester of organic chemistry):



2.2 THE BASIC MOVES

To truly become the master of arrow pushing, you must master the “basic moves” that are at your disposal when proposing a mechanism. These basic moves are your tools for proposing mechanisms. That's what this chapter is all about: mastering the most basic moves of any ionic mechanism. It is comforting to realize that there are only four basic moves. (That will cover you for any ionic mechanism that you will see in this course.) Let's go through them, one by one:

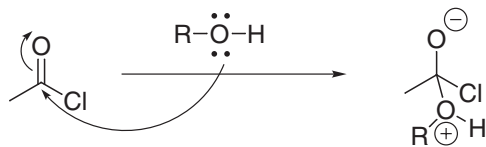
1. **Nucleophile attacks electrophile.** For example:



Remember that a nucleophile is a compound with a region of high electron density. In some cases, the nucleophile will actually have a negative charge (like the bromide ion in the example above). In

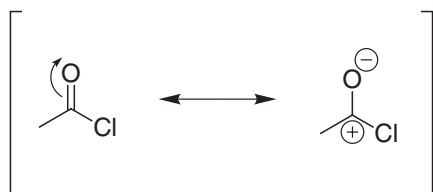
many other cases, the nucleophile will not have a charge—you must keep in mind that lone pairs and π bonds can also be nucleophilic:

Here is one example of a *lone pair* acting as a nucleophile:

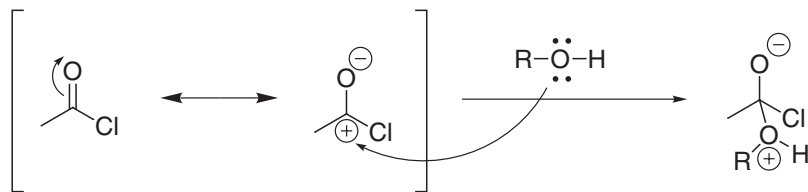


The nucleophile here is the lone pair on the oxygen of the alcohol above (ROH). This oxygen atom is using one of its lone pairs to attack the C=O bond. Notice that there is no negative charge on the attacking oxygen atom. ROH does not bear a negative charge. That's OK, because a nucleophile is just a region in space of high-electron density. And the lone pairs of the oxygen atom are regions in space of high-electron density.

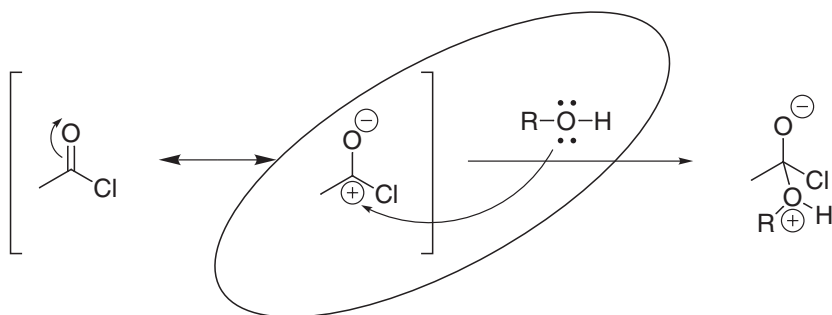
Also notice that there is more than one curved arrow on the step above. The first curved arrow shows the nucleophile (ROH) attacking the electrophile. The second curved arrow (pushing the electron density up onto the oxygen) is part of the same basic move—nucleophile attacking an electrophile. To see how this second arrow is part of the same move, consider the following: what if I were to draw a resonance structure of the starting compound BEFORE it gets attacked:



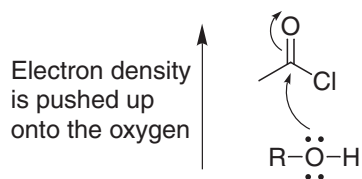
Now, I can draw the attack taking place at the second resonance structure, like this:



When we think of it like this, we realize that only one of the arrows is actually showing the attack:

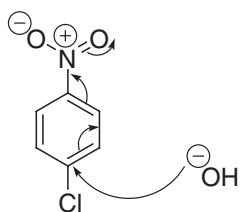


The second arrow can be thought of as resonance, or alternatively, you can think of the second arrow as an actual flow of electron density that goes up onto the oxygen when the nucleophile attacks:

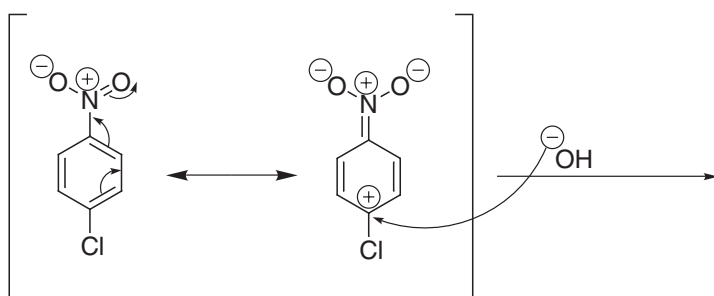


There is a subtle difference between these two ways of looking at the second arrow (either thinking of it as resonance or thinking of it as an actual flow of electron density). It is probably more accurate to think of it as an actual flow of electron density up onto the oxygen because that is the way most organic chemists think about it. However you wish to view this, you should realize that both curved arrows are used to show only one basic move: a nucleophile is attacking an electrophile.

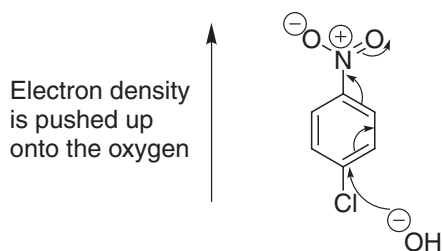
In fact, it is common to see even *more* than two arrows when a nucleophile attacks an electrophile. For example, consider the following:



All of these arrows show *one* thing happening: a nucleophile (OH^-) is attacking an electrophile. The first curved arrow (coming from OH^-) shows this attack. The other curved arrows can be viewed as resonance arrows before the attack:



Or they can be viewed as showing the flow of electron density that takes place when the nucleophile attacks:

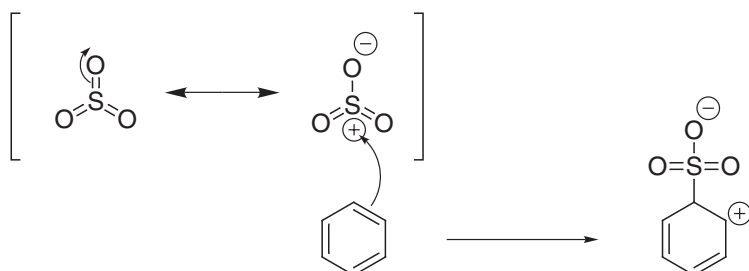


To be consistent with the way organic chemists speak, you will probably be better off if you think of it as a flow of electron density (rather than just one attacking arrow and the remaining arrows being considered as resonance arrows). I only gave the resonance argument so that we can justify in our minds that all of these arrows are really just showing one basic thing happening.

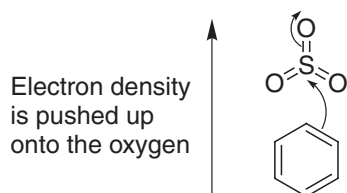
In all of the examples we have seen, the nucleophile had a lone pair that was responsible for attacking the electrophile. But we said that a π bond can also serve as a nucleophile. For example:



Once again, there is more than one curved arrow here. There are two curved arrows. The first arrow (coming from the ring to attack SO_3) is the arrow showing the attack. The second arrow can be thought of in two ways. You can think of it as a resonance arrow:



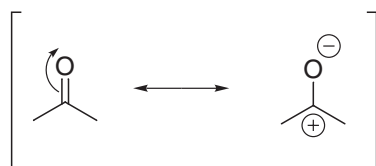
Or you can think of it as the flow of electron density when the nucleophile attacks:



Either way, you should realize that this is just one basic move: a nucleophile attacking an electrophile.

As we move through this course, we will see many more examples of nucleophiles. For now, let's just appreciate the basic feature of a nucleophile—it is a region of high-electron density (either a lone pair or a π bond). And nucleophiles always do what they are supposed to do—they attack electrophiles.

An electrophile is a compound with a region of low-electron density. In some cases, the electrophile will actually have a positive charge (as in the example we saw earlier where the bromide ion is attacking a compound with a positive charge). In many other cases, the electrophile will not have a charge. For example, a ketone is an excellent electrophile, which we can understand when we draw the resonance structures:



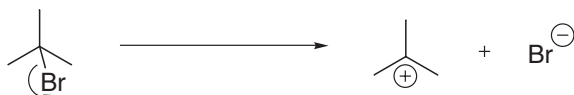
We can see from the second resonance structure that the carbon of the C=O double bond is electron-poor (a site of low-electron density). When you normally draw a ketone, you don't see a positive charge on the carbon atom:



But even though there is no net charge, there is still an electrophilic center (that is waiting to be attacked by a nucleophile). Later in this semester, we will see a lot of reactions that deal with the chemistry of compounds containing C=O bonds. Most of this chemistry revolves around the electrophilicity of the C=O group.

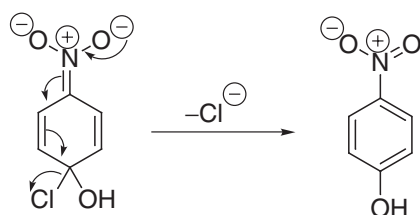
As we move through the course, we will see more examples of electrophiles. Now that we have identified the first basic move (nucleophiles attacking electrophiles), let's continue with a summary of the second basic move.

2. Loss of a leaving group. For example:

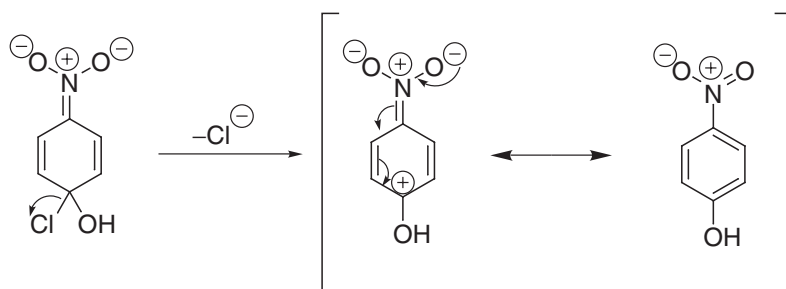


This move can be thought of as the reverse process of the first basic move that we saw. In the reaction we are showing here, a leaving group leaves to form a carbocation. If you were to imagine taking a video of this process, and then playing the video backwards (rewinding it so that you can see it while it is rewinding), you would see a bromide ion (a nucleophile) attacking a carbocation (an electrophile) to form the compound on the left above. So, in fact, the basic move we are discussing right now (loss of a leaving group) is just the reverse process of the first basic move that we saw (nucleophile attacking an electrophile).

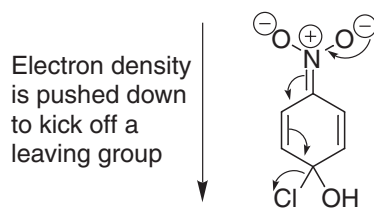
Sometimes, you will see more than one arrow being used for the loss of a leaving group. For example, consider the following:



There is one curved arrow that actually shows the Cl leaving. The remaining arrows can be thought of in two different ways (just as we saw earlier). You can think of the other arrows as being resonance arrows after the leaving group leaves:



Or you can think of this as a flow of electron density that pushes out the leaving group:



You are probably better off if you think of this as a flow of electron density that pushes out the leaving group. But however you think of it, you should realize that all of these arrows are just showing one basic move: a leaving group is leaving.

In the first semester of organic chemistry, we saw tips for identifying good leaving groups and bad leaving groups. If you are rusty on leaving groups, I recommend that you go back and review that material. You will need to be able to identify good leaving groups in order to propose mechanisms.

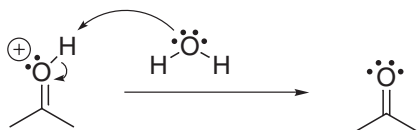
So far, we have seen two basic moves: a nucleophile attacking an electrophile and a leaving group leaving. Now let's take a look at our third basic move:

3. **Proton Transfers.** For example:

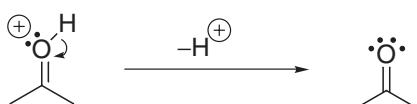


Proton transfers are just acid-base reactions. We talked about acidity (proton transfers) at length in the first semester of organic chemistry. For now, let's just focus on the fact that this basic move always requires at least two curved arrows. As an example, look at the proton transfer we just saw. The ketone is grabbing a proton, and we need *two* curved arrows to show this. One arrow goes from the ketone to the proton, and the second arrow shows what happens to the electrons that were previously holding the proton.

There are always at least two arrows, whether the compound is grabbing a proton (like the case above), or whether a compound is losing a proton, like this:

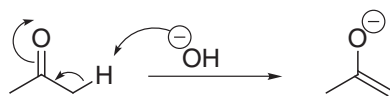


Notice that, once again, we need two arrows to show the proton transfer. When a compound is losing a proton, some textbooks and instructors will skip showing what grabs the proton. And they will only use one arrow, like this:

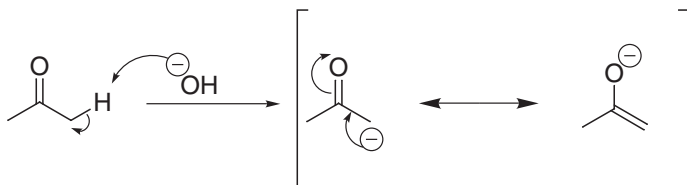


Other instructors are particular that you show both arrows. In other words, you need to show what grabs the proton. Certainly, it can't hurt to get into the habit of always showing what grabs the proton, right? So get in the habit of using two arrows.

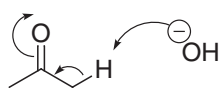
Sometimes, you will see *more* than two arrows. For example, consider this case which shows three arrows:



To explain this, we will use the same logic we used when describing the other basic moves. We can understand this in either of two ways. We can say that there are only two arrows needed for the reaction, and the remaining arrows are just resonance arrows:



Or we could argue that all of the arrows together show the flow of electron density that takes place during the proton transfer:



Electron density flows up onto the oxygen of the ketone.

For proton transfers, both arguments are equally good, and you should think of it both ways. And most importantly, you should realize that there is just one basic move happening here: a proton is being transferred.

Now we are ready to see the last basic move:

4. **Rearrangements**. For example:



When a compound has a positively charged carbon atom (a carbocation), then it is possible for the compound to undergo a rearrangement. There are other rare instances when rearrangements can take place (other than carbocations). We will point them out later in this book, when we get to them. For now, let's focus on carbocation rearrangements.

Believe it or not, that's it!!! Just four basic moves to master:

1. Nucleophiles attacking electrophiles
2. Leaving groups leaving
3. Proton transfers
4. Rearrangements

In fact, we can summarize it even better, like this:

1. Attack
2. Leave
3. Protonate (or deprotonate)
4. Rearrange

Each of these four basic moves has subtle details that you will have to learn. For example, when should you use H_2O instead of OH^- to grab a proton? As another example, if you have a reagent like OH^- that can function as a nucleophile or a base, which basic move should you use? (Should you use the reagent as a nucleophile to attack something, or should you use it as a base to grab a proton?) These questions, and many others, are the fine details of these four basic moves. As we move through the course, I will point out these details for you. Make sure to appreciate how important these details are. When you learn a new detail—for example, when you learn that proton transfers are generally faster than nucleophilic attacks—you should realize how important it is to know that. It will help you with ALL mechanisms throughout the course. You will only be able to master the mechanisms if you master the details.

The goal of this chapter was to introduce you to the four basic moves. So let's make sure that you can identify each of the four moves when you see them.

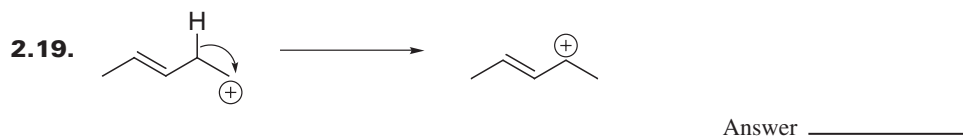
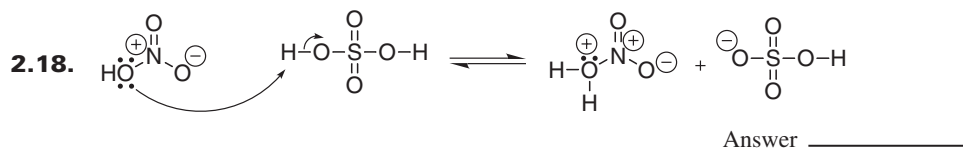
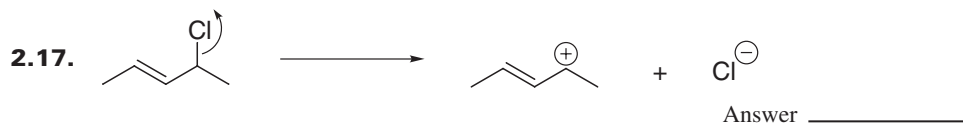
EXERCISE 2.16. Consider the following step:

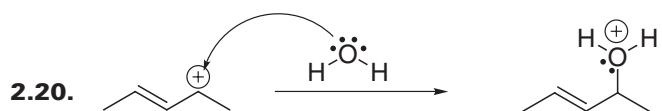


This step is one of the four basic moves. Which basic move is this step?

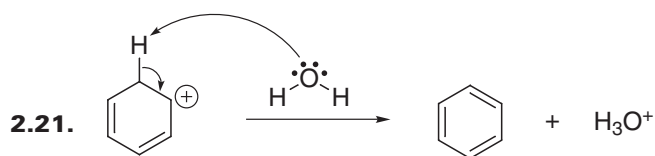
Answer: You might be tempted to call this a rearrangement because it looks like the location of C^+ is moving. But take a closer look. This is not a hydride shift, nor is it a methyl shift. If we had to describe what is happening, we would say that the double bond (the π bond) is attacking the C^+ . The π bond is acting as a nucleophile to attack an electrophile. It is an interesting case because the nucleophilic site and the electrophilic site are both contained in the same compound. So this step is called *intramolecular* because the attack takes place entirely within one molecule. This step is definitely the first basic move—a nucleophile attacking an electrophile.

PROBLEMS. For each of the following, identify the basic move that you see. Your choices are: (1) a nucleophile attacking an electrophile, (2) a leaving group leaving, (3) a proton being transferred, or (4) a rearrangement.





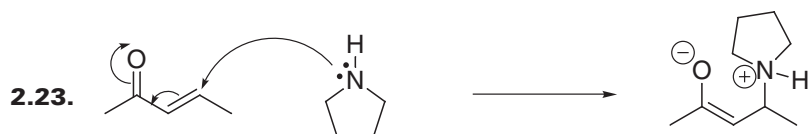
Answer _____



Answer _____



Answer _____



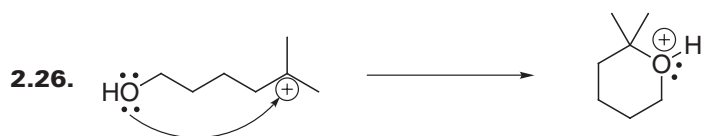
Answer _____



Answer _____



Answer _____

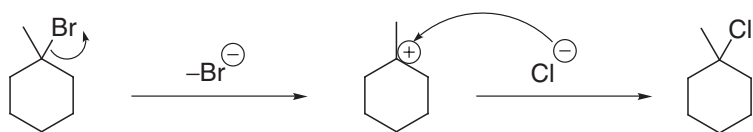


Answer _____

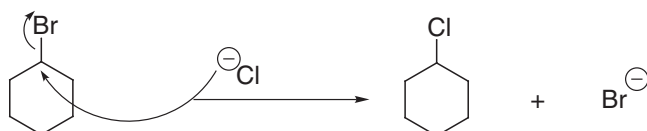
2.3 COMBINING THE BASIC MOVES

In order to conquer mechanism problems, you must have these four basic moves at your fingertips. To understand why, you must realize that all ionic mechanisms, regardless of how complex, are just different combinations of these four basic moves. Let's see a few examples.

Let's start by looking at some mechanisms that we saw in the first semester of organic chemistry (and then we can move on to a preview of reactions we will see this semester). For example, take a look at this S_N1 reaction:

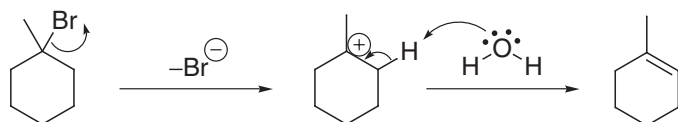


Notice that the first step is *loss of a leaving group*, and the second step is *nucleophile attacks electrophile*. So, we see that the S_N1 mechanism is just two of the four basic moves (one after the other). Now, let's look at an S_N2 reaction:

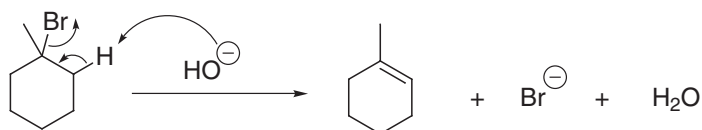


In this mechanism, we are still doing the same two basic moves as we did in the previous mechanism (*loss of a leaving group* and *nucleophile attacks electrophile*). The only difference is that we are now doing both *at the same time*.

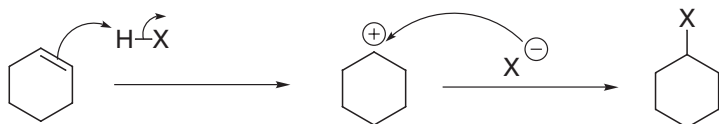
What about an elimination reaction? Consider the following $E1$ reaction:



The first step is *loss of a leaving group*, and the second step is just a *proton transfer* (which always has two curved arrows—one curved arrow is showing the base pulling off the proton, and the second curved arrow is showing where to place the electrons that used to hold the proton). If we use a stronger base, and we do all of these steps at the same time, we get an $E2$ mechanism:



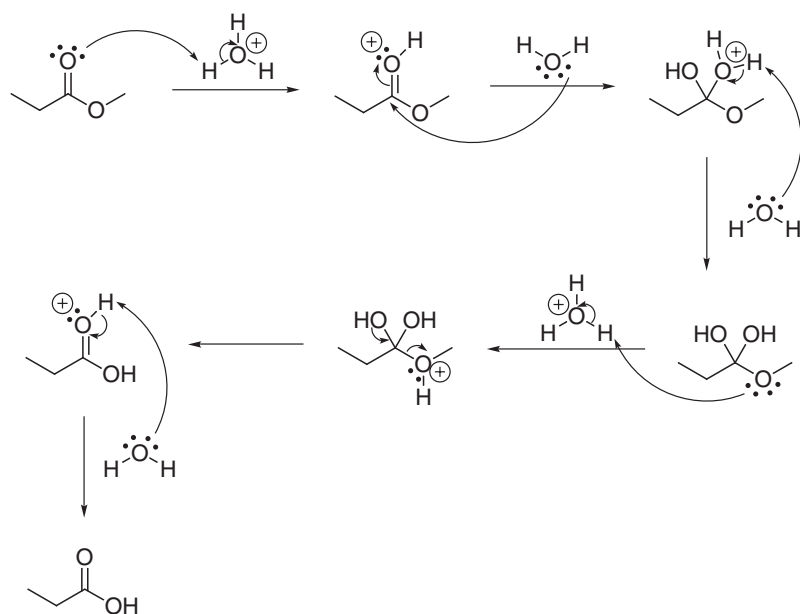
Let's do one more example. Consider the following addition reaction from last semester:



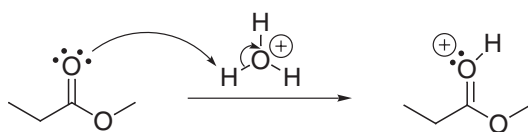
Notice that the first step is a *proton transfer*, and the second step is a *nucleophile attacking an electrophile*.

We have now seen many examples from last semester. These examples demonstrate that there are only four basic moves, and these four moves are your tools for solving mechanism problems. By mastering these tools, you will then be able to master how to use them together (one after another) to build up a mechanism. The trick is to recognize the various patterns that can arise when you combine these

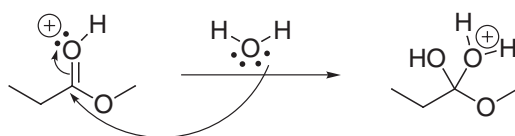
basic moves in specific ways. And that is what organic chemistry mechanisms are all about. For example, consider the following reaction that we will see later in this semester:



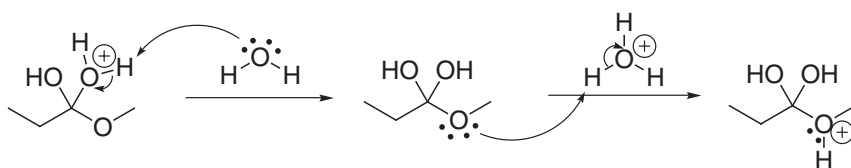
This is certainly a longer mechanism than the reactions you learned in the first semester of organic chemistry. But let's try to make sense of this long mechanism by taking a close look at the steps. Let's see if we can convince ourselves that this mechanism is just a combination of the basic moves. The first step is a proton transfer:



The second step is a nucleophile attacking an electrophile.



The next two steps are both just proton transfers:



- [Slow Man online](#)
- [download **Booze for Babes: The Smart Woman's Guide to Drinking Spirits Right** pdf, azw \(kindle\)](#)
- [Metaphors and Analogies: Power Tools for Teaching Any Subject pdf](#)
- [download *Martha Stewart's Handmade Holiday Crafts: 225 Inspired Projects for Year-Round Celebrations*](#)

- <http://reseauplatoparis.com/library/The-Bodhisattva-s-Brain--Buddhism-Naturalized.pdf>
- <http://toko-gumilar.com/books/Booze-for-Babes--The-Smart-Woman-s-Guide-to-Drinking-Spirits-Right.pdf>
- <http://aneventshop.com/ebooks/Freefall--America--Free-Markets--and-the-Sinking-of-the-World-Economy.pdf>
- <http://diy-chirol.com/lib/HTML-and-CSS-Web-Standards-Solutions--A-Web-Standardistas--Approach.pdf>