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Priority and Selectivity Rules To Help Students Predict Organic Reaction Mechanisms

David K. Smith*

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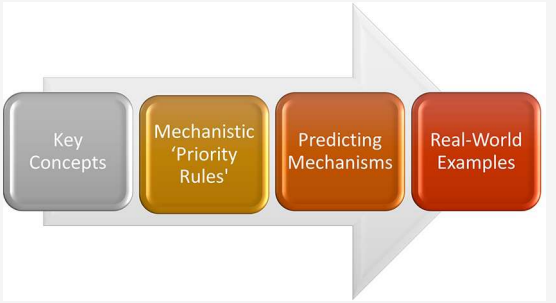
ABSTRACT: Organic reaction mechanisms lie at the heart of developing an understanding of how the molecular world functions. However, many students simply try to memorize mechanisms, or use their knowledge of the reagent and product to create a mechanism that "works". This is not helped by the content-heavy organic chemistry curriculum which focuses on rapidly progressing through a range of reaction types and functional groups. For some students, especially nonchemistry majors, OrgChem101 becomes a "rite of passage" to be endured, learned and forgotten. This paper presents an alternative way of introducing students to organic reaction mechanisms, in which mechanistic rationale and thinking is explicitly taught to students, in a simple logical way, before they meet any specific reactions. In particular, to facilitate this, a series of "priority rules" have been developed. These priority rules help students find reactive sites and predict curly arrow mechanisms, even when faced with previously unseen reagents. This approach is designed to empower students to think about organic molecules in a different way, focusing on reactivity and structure. This enables students to realize that they can predict reactions of which they have no prior knowledge by proposing plausible mechanisms from first principles. This approach to mechanistic teaching sits alongside contextualized examples and allows students to rapidly see how the principles they are learning can help them solve real-world problems—ensuring that they develop not only a mechanistic view of the molecular world but also a motivation to learn more.



KEYWORDS: *First-Year Undergraduate/General, Organic Chemistry, Curriculum, Problem Solving/Decision Making: Mechanisms of Reactions*

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INTRODUCTION

Organic chemistry underpins the way the world works, and an understanding of structure and reactivity unlocks a deeper understanding of wide-ranging subjects, from drug action to molecular machines.[1] As such, organic chemistry is an important topic of study not only for students majoring in chemistry but also in subjects like biochemistry and medicine. However, for many students, organic chemistry is one of the biggest challenges they face at university.[2] Frequently, organic chemistry is presented as a series of reactions to learn, with mechanisms for each, with these often being viewed by students as something to memorize. As a result, many students find the amount of information presented cognitively challenging and struggle to enjoy their organic chemistry studies, or see much point to them.[3] Worryingly, although it has been claimed that organic chemistry is good general training for students because it encourages problem solving and critical thinking,[4] analysis of questions actually set to students show that many fail to achieve this, and rely heavily on memorization of content.[5] Furthermore, there is some pressure from medical schools for chemistry departments to change the organic chemistry curriculum.[6]

As explored in an excellent recent review,[7] many studies have investigated the ways in which students engage with reaction mechanisms. Sadly, in many cases, students struggle to understand the electron-pushing formalism in any meaningful sense[8] and often simply use mechanisms to try and make the thing they think they want.[9] As a result, students can find it very difficult to apply cause-and-effect reasoning to explain their mechanistic thinking.[10] Indeed, even when faculty were surveyed about curly arrow mechanisms, a key conclusion was that the mechanistic process is somewhat informal, and has "back of the envelope" characteristics[11]—it is therefore perhaps not surprising that students struggle with this activity. Many researchers have innovated in trying to better engage students with mechanistic learning, using approaches ranging from card games to videos.[12] However, the basic framework in which

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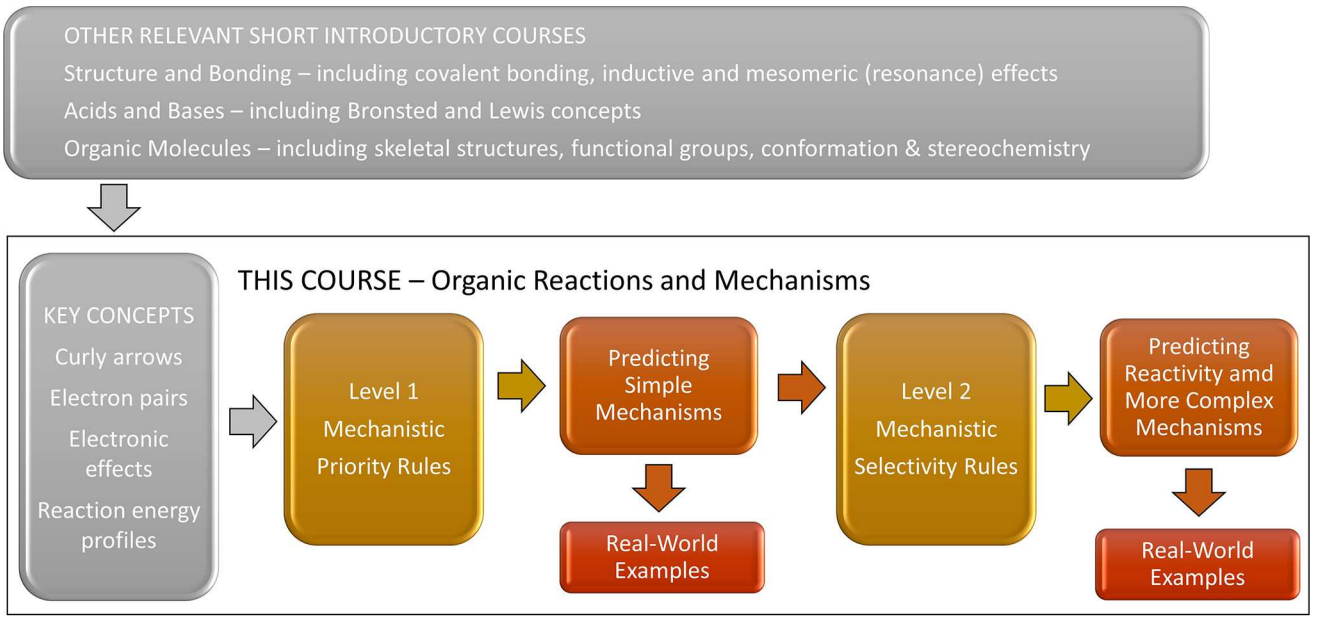

Figure 1. Schematic of the approach taken in this course on organic reactions and mechanisms and its relationship to some of the key chemistry taught to the students in other introductory first year courses at University of York.

organic chemistry is taught at many universities has changed relatively little in the past 50 years.

An alternative way of teaching organic chemistry takes an approach based on physical chemistry principles.[13] This "integrated approach" relies on the students first developing a good understanding of orbitals, and then applying this knowledge to consider frontier orbitals in organic molecules. By appreciating HOMO and LUMO shapes and energy levels, it is possible to fundamentally understand, from first-principles, why organic molecules react with one another. Although this is a logical, scientifically rigorous approach, and may be suited to those chemistry majors who are adept at physics/maths, it does not necessarily reflect how many practicing organic chemists actually think about the molecular world on a day-to-day basis. Furthermore, it can be intimidating to less mathematically minded students, or those whose interests lie primarily on the biological side of science. Notably, it requires a significant amount of physical chemistry teaching before organic reactivity can be introduced. In general, therefore, the orbital approach to organic reaction mechanisms has largely not been used in introductory organic courses, although it has sometimes been introduced in laboratory sessions to support more traditional, curly arrow mechanism teaching approaches.[14]

Within the framework of more traditional, curly arrow based approaches to organic reaction mechanisms, Flynn and co-workers carried out important and influential work to implement the teaching of mechanistic principles before students are introduced to specific reactions.[15] Curly arrow mechanisms were taught and learned, and then the teaching of reactions was organized based on mechanism rather than functional group. They argued that, in this way, students build their understanding of different reaction types on a sound mechanistic framework. Others have reported redeveloping the traditional organic chemistry syllabus to include a greater emphasis on working-out mechanisms, as well as incorporating more biological chemistry content/examples.[16] There has also been recent interest in understanding the way students solve mechanistic problems, and developing workflows to facilitate this process.[17]

At my own university, since about 2005, like Flynn and co-workers, we have also seen the value of teaching a general introductory first year course on 'Organic Reactions and Mechanisms'. This focuses on curly arrow mechanisms, prior to later courses dealing with the details and specifics of different functional groups and/or reactivity types. However, I wanted to separate the understanding of organic mechanism even more completely from the sense of "learning" different types of reactivity. I therefore decided to give the students some "rules" that would help them to think about curly arrow mechanisms in a more algorithmic way. In spite of the challenges that organic mechanisms offer to students, attempts to simplify the process of thinking about them remain few and far between,[18] and have rarely been taken up more widely in new pedagogies. I therefore developed a set of simple mechanistic "priority rules" that students could apply without worrying at all about what type of reactivity was happening. These priority rules play a key role in helping students work out plausible mechanisms from first-principles, giving them a "way into" a problem. Students find it much easier to apply a logical rubric to solve a problem, breaking it down into smaller parts, than to think about the whole problem in abstract terms. The priority rules facilitate this thinking process.

This approach therefore moves students away from learning reactions and memorizing mechanisms toward working out how molecules might behave by inspection, giving them an enhanced "feel" for organic chemistry. Furthermore, students know that the course assessment will focus on applying the rules to unseen problems, and therefore the whole emphasis of mechanistic learning gets shifted onto why the curly arrows are happening, and what the result of that is, rather than trying to learn specific examples. This also has the benefit of generating authentic and challenging assessments in which students, rather than simply regurgitating what they have learned, must apply fundamental principles to solve complex real-life problems.

In this way, students are taught, from the very beginning, the way in which experienced organic chemists view the molecular world, with the priority rules providing a simple framework to

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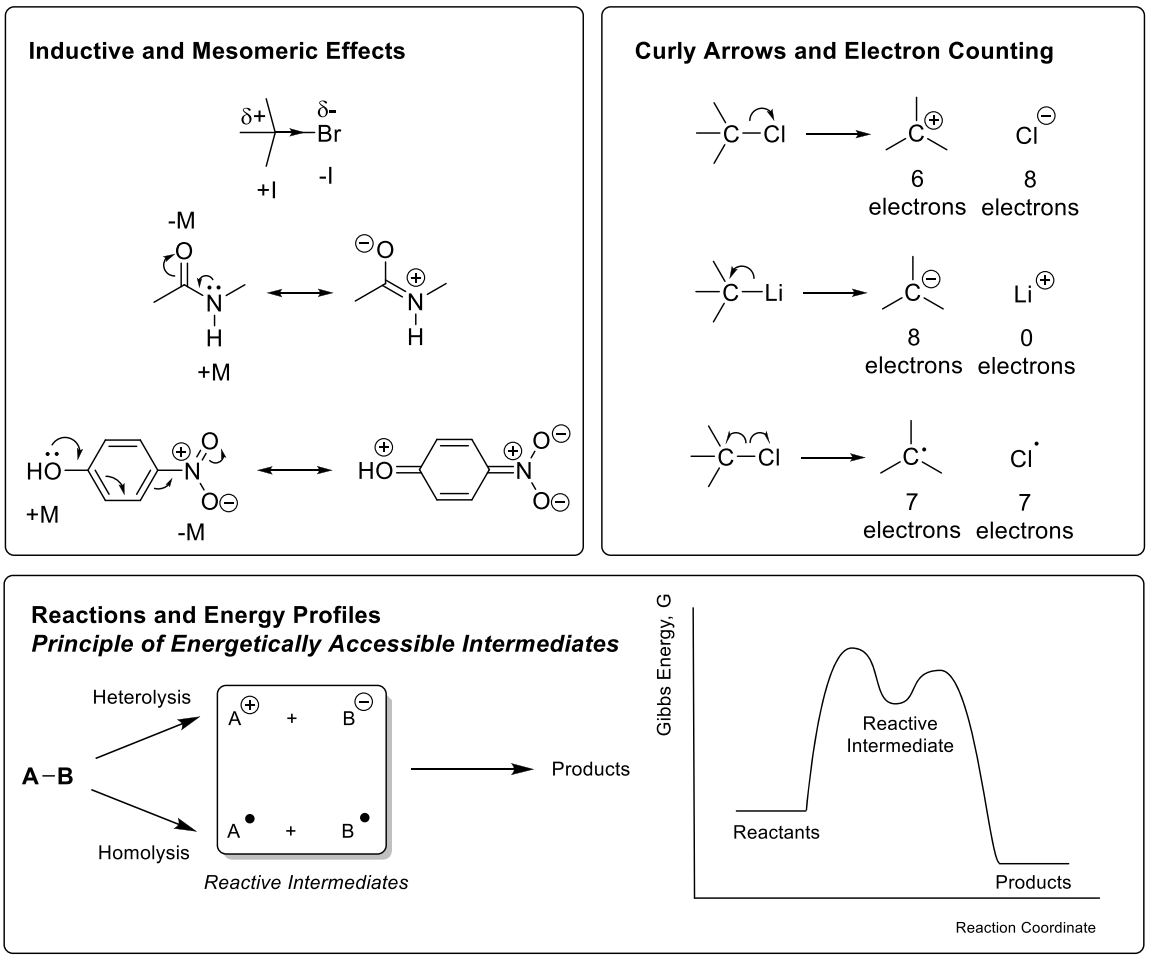

Figure 2. Some of the underlying key concepts emphasized in the first part of this course. Students will have some prior knowledge of these ideas from other lecture courses (as well as from preuniversity education).

help them access this, albeit at an introductory level. This empowers students, after very little organic chemistry instruction, to believe they can potentially approach any problem in the molecular world, rather than feeling that their only strategy is to learn and memorize a very large subject one reaction at a time.

This paper presents my general approach to Reactivity and Mechanism teaching, with particular focus on the "priority rules" and demonstrates how real-world problems are used to consolidate and/or test the learning (Figure 1).

CONTEXT

The teaching approach to reaction mechanism outlined here is delivered as part of an introductory chemistry course in the first semester of the first year at University of York, UK. In this semester, the students first receive ca. 10 lectures, relevant to organic, inorganic, and physical chemistry, which introduce key concepts of structure and bonding, electronic effects, and acids and bases. There are then ca. 10 lectures which introduce stereochemistry, conformation, functional groups, reactions, and mechanisms. It is worth noting that, within the UK context, students will have also had some limited exposure to this material during their school studies. This paper focuses on the 5 lectures dealing primarily with Reactions and Mechanism, but clearly, some of the principles students learn in other parts of this introductory module play a key role in underpinning the teaching (Figure 1).

Of course, in such a small number of teaching sessions, it is not possible to teach everything about an organic mechanism, with all its many subtleties—indeed, I have deliberately chosen to make a number of simplifications, as will become evident (see below). However, the goal is to provide a framework of thinking, and some "priority rules", such that when students go on to study other topics in more detail in the second semester of first year study (carbonyl chemistry, substitution and elimination, alkenes and alkynes, aromatic chemistry) and in later years of their degree (e.g., enolate chemistry, heterocyclic chemistry, pericyclic chemistry, physical organic chemistry, radical chemistry, asymmetric synthesis, etc.), they will be empowered to do this with curly arrow mechanisms as an underpinning conceptual framework. It is hoped that when students get stuck with an organic reaction later in their studies, they will come back to these simple priority rules, which will help them think about and rationalize the problem in a logical, mechanistic way.

Importantly, students learn very effectively through contextualization and real-world examples.[19] Using contextualized examples empowers students to see how what they are learning can be applied to solve important problems, and I therefore make extensive use of this approach, in both teaching and assessment. These real-world examples are often set as in-class quizzes/votes or discussion items, and used as "lecture breaks" to mix up the mode of delivery.[20] Some useful contextualized examples are included in this article.

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UNDERPINNING CONCEPTS

The initial part of the course on reactivity and mechanism refreshes the students' understanding of inductive effects and mesomeric[21] (resonance) effects (Figure 2), which students have learned about in more detail elsewhere. I prefer to talk about "mesomeric effects" rather than using the "resonance" language, as it unifies the nomenclature of electronic effects as ±I and ±M, emphasizing the impact each of these effects can have in terms of "adding" or "subtracting" electron density from the remainder of the molecule. It is reinforced that inductive effects are based on electronegativity and operate through the single bond (σ) framework of a molecule, while mesomeric effects are based on the movement of electron pairs operating the multiple bond/lone pair π-system of a molecule, as represented by curly arrows, each of which moves a pair of electrons. It is also noted that mesomeric (resonance) effects typically act over longer distances than inductive effects, particularly through extended conjugated systems, and are often more significant in terms of impacting the reactivity of a molecule. It is noted that, in mesomeric effects (resonance), because the curly arrows only move the π-system of the molecule, the actual bonded framework of the molecule remains unchanged.

In contrast to mesomeric effects, the lectures then explore what happens when curly arrows are used to break a single bond (Figure 2). Students are reminded that double headed arrows represent the movement of electron pairs and they are then also introduced to single-headed "fish-hook" arrows representing the movement of one electron at a time. By breaking a bond in different ways, it is demonstrated how this process can give rise to cations, anions, or free radicals (Figure 2). This is combined with electron counting and the idea of formal charge to emphasize that a carbocation (carbenium ion) only has 6 electrons and a radical has 7 electrons, while anions typically have 8 electrons in the valence shell. In the case of anions, it is noted that while there is just one "extra" electron, this is associated with a lone pair of electrons that can therefore move with a curly arrow.

In my course, students are told to draw curly arrows starting from the negative charge, rather than explicitly drawing out the associated electron pair(s). Lone pairs of electrons are still explicitly drawn if the nucleophilic atom has no formal charge. This mechanistic approach is in-line with the major chemistry textbooks used in introductory UK university-level teaching,[1,13b,22] and dates back to the classic book written by Sykes,[23] which is considered a landmark text in mechanistic teaching. Importantly, this is also the way in which mechanisms are presented in the wider scientific literature. However, it is somewhat different to what is encouraged in many UK schools prior to university, where students are expected to draw out all of the "octets" on atoms. The explicit drawing of electron pairs associated with negative charges is also used in most introductory reaction mechanism teaching in the USA, and in many of the introductory-level US textbooks.[24] In the context of the priority rules, it does not matter whether the electron pairs associated with negative charges are explicitly drawn out or not—the priority rules, and their application, remain exactly the same. However, for the purposes of this paper, I have drawn mechanisms using the approach of starting the arrow from the negative charge.

It is also worth noting that although we do not teach any more about radicals and fish-hook arrows in this introductory course, it is useful nonetheless to present them, as it helps students understand the electron counting.

Finally, in this foundational part of the course, the energy profile of a typical reaction, progressing through some sort of generic reaction intermediate (Figure 2), is presented. It is emphasized that, in general, the lower the energy barrier is, the more successful the reaction will be. The idea of "stable intermediates" is then discussed. Many textbooks and organic chemistry courses present the Hammond postulate and then use the shorthand language of stable intermediates to talk about preferred reaction pathways. In my experience, many students get confused by the idea of a "stable intermediate", thinking that if it is stable then it will somehow be unreactive, and therefore stop the reaction proceeding. This is a key misconception that leads to many problems. I therefore introduce what I call the '*Principle of energetically accessible intermediates*', and for the remainder of the course I try to talk about intermediates being "energetically accessible" rather than "stable". This simple language-change significantly helps students grasp the key principle. Of course, the Hammond postulate is folded up into this reworked discussion of intermediates and transition state energy barriers; however, in my view, describing it as the 'Principle of energetically accessible intermediates' makes it much more comprehensible than using the abstract "Hammond postulate" wording.

With these fundamentals in place, the course then moves on to define our mechanistic "priority rules". These lie at the heart of my course and allow students to work out many curly arrow mechanisms from first principles.

MECHANISTIC PRIORITY RULES

In very simplistic summary—these mechanistic priority rules can be described as, *the electrons must start somewhere electron rich, move somewhere electron poor, and end somewhere good*. Of course this is self-evident to a practicing organic chemist, but to the novice, when combined with a set of "priority rules" as a guide, it can be empowering.

1. The electrons start somewhere electron rich

As a first approximation, in order of priority (Figure 3, Box 1):

1. negative charge
2. uncharged lone pair
3. multiple bond
4. weak single bond.

The lectures then present some simple examples of species that have negative charges, lone pairs, multiple bonds, or weak single bonds, drawing appropriate curly arrows starting from the relevant point. It is also possible to present some molecules which might contain (e.g.) both a negative charge and a lone pair in quiz format and get students to draw on the most likely starting point for the curly arrow in each case. Students are told that some molecules may have two negative charges, or two lone pairs, or two multiple bonds, and it is explained that, in such cases, a more complex decision will have to be made in terms of the most likely starting point for the curly arrows. We come back to this later in the course (see Level 2 Mechanistic Selectivity Rules below).

2. The electrons move somewhere electron poor

As a first approximation, in order of priority (Figure 3, Box 2)

1. positively charged carbon/hydrogen atom
2. attached to a positively charged heteroatom

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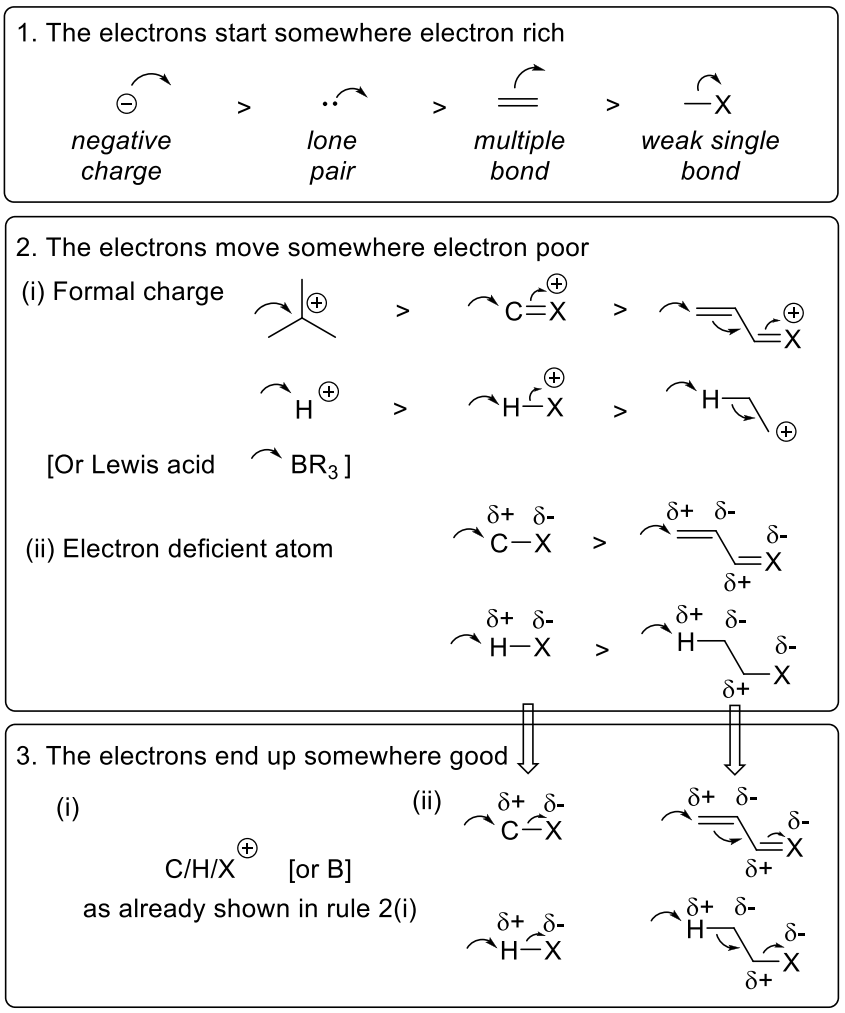

Figure 3. Priority Rules for drawing organic reaction mechanisms.

3. more distant from a positively charged atom but able to push electrons to it
4. partially positive carbon/hydrogen atom
5. partially positive carbon/hydrogen atom along an alternating conjugated pathway

Once again, in addition to the generic structures shown in Figure 3, as we work through the different priority levels, some simple concrete examples are provided to illustrate how a curly arrow moves to each of them.

First, we consider species with a positive charge (Figure 3, Box 2, (i)). It is emphasized that a positively charged carbon/hydrogen atom is electron deficient. In the case of C^+, it only has 6 valence electrons; in the case of H^+, it has 0 valence electrons. As such, the need for electron density is urgent in each case, and the formation of a bond will lead to a filled valence shell. We link this to the concept of Lewis Acids, which the students have learned elsewhere. Although I personally do not explicitly point it out in this entry-level course, the Lewis Acid could also be something like a 6-electron (but charge-neutral) boron atom, rather than a positively charged C or H. This subtlety can be included here if needed (and is included in parentheses in the figure for this reason), or alternatively, it can be easily introduced to advanced students later in their studies.

Unlike the relatively simple case of C^+ or H^+, students always find it more challenging knowing what to do with a positively charged heteroatom. Many students want to move the curly arrow directly to the positive charge (as with C^+ and H^+)—indeed, this is a major mechanistic misconception among students. The meaning of formal charges is therefore emphasized, and it is noted that the heteroatom already has 8 electrons—unlike C^+/H^+, where the valence shell was only part-filled. However, the charged heteroatom does "want" electrons and, as an electronegative site, is a good eventual location for them. The lectures also reflect on the fact that a heteroatom with a positive charge is charged because it is sharing its lone pair with an adjacent atom (something that had been discussed in the earlier revision of the mesomeric effect). As such, by attacking an adjacent atom, a lone pair can be pushed back to the heteroatom. Having explained this, we demonstrate it with a few real examples (e.g., a protonated ketone and H_3O^+).

Once students have grasped the concept of moving electrons stepwise to the positive charge, it is then noted that the electrons can also move over even further distances to potentially satisfy a positive charge, often helped by the mesomeric effect (Figure 3).

We then move on to consider cases that do not have a formal charge, but rather an electron poor $C^{\delta+}$ or $H^{\delta+}$ (Figure 3, Box 2, (ii)). It is demonstrated that a curly arrow can also be used to attack these centers. Some conjugated frameworks with alternating $\delta+$ and $\delta-$ charges along the backbone are also presented, and it is noted that it is therefore possible to attack at points further along the framework of the molecule in such cases. This discussion leads immediately onto Rule 3, as it is clear the

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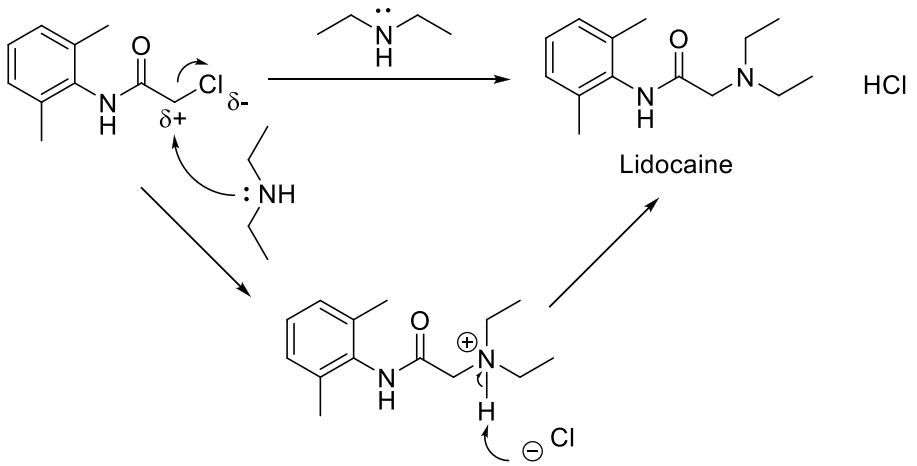

Figure 4. Key step from the synthesis of lidocaine as initially presented to the students (top), with stepwise presentation of the curly arrow mechanism (bottom).

electrons will need somewhere to move onto in order to avoid violating the octet rule.

Once again, students are told that they will often get difficult choices between reactive sites that they would initially prioritize at the same level, but that the further selectivity rules presented later on in the course will help them address such problems.

3. The electron density end up somewhere good

Depending on what happened in steps 1 and 2 this will be (Figure 3, Box 3):

1. quenched by C^+ or H^+ with a new bond being formed to the C/H
2. breaking a π bond to a heteroatom (possibly via conjugation), leaving it with a single bond
3. breaking a σ bond to a heteroatom (possibly via conjugation), disconnecting it from the molecule

In case 1, where charge has already been moved to a formal positive charge on carbon or hydrogen, no further arrows are required beyond those drawn in priority rules 1 and 2—the electron pair has filled an empty orbital, a bond has been made, and the mechanism stops. In cases 2 and 3, where there was a formal charge on the heteroatom, the electrons were, once again, already moved to the electron poor site as a part of priority rule 2, with the positively charged heteroatom gaining a lone pair.

However, when there is no formal charge, and the attack in rule 2 was on an electron poor δ+ carbon or hydrogen atom, it is *immediately* necessary to move the electrons onto the heteroatom either by breaking a π bond (case 2), or a σ bond (case 3) as appropriate. This immediate movement of electrons prevents violation of the octet rule. The heteroatom is a desirable end-point for the electrons as a result of its electronegativity—it gains a pair of electrons and a formal negative charge (see next rule).

4. Charges must be balanced

Having dealt with each step of the process separately, some simple examples are presented, such as the reaction of an alkyl bromide with the hydroxide anion. The mechanism is worked through, step-by-step, and it is emphasized that, as in any chemical reaction, students must ensure they balance charges. Most commonly, students forget to introduce a positive charge when using a neutral lone pair to form a bond in the first step of the process (see Figure 4, step 1, for a typical example of where students would find this difficult), or to remove the positive charge on a heteroatom when it regains its lone pair.

5. This may not be the end of the process

There might still be reactive sites once these mechanistic rules have been sequentially worked through once. Often, at least one of these will be charged. If so, these can potentially go on to react further according to the rules above. In such cases, students are encouraged to go back to the top of the priority rules and simply apply them again. As a simple example, when a nucleophile attacks a carbonyl group, a negatively charged O^- is generated. This reactive group will go on to react further with (e.g.) $H^{\delta+}$.

USING THE RULES IN CONTEXT

Having presented the priority rules to the students, and worked through some very simple examples, a more complex contextualized case study is then used to show how the rules work together to solve a real-world problem. A good example is the synthesis of lidocaine (Figure 4). Lidocaine is a fast-acting local anesthetic, widely used in dentistry. As such, it is a drug a number of the students have personally experienced—this personalization helps capture attention. The students are presented with a key step in the synthesis, and the mechanism is then worked out by applying the priority rules in a stepwise manner.

In the first step of the process, the most electron dense site is found. This is the lone pair on the nitrogen atom on diethylamine (PR 1.2). At this point in the course, the students are guided to using this molecule as the nucleophile and the other as the electrophile, although later on, it becomes possible for them to intuit this. In the absence of any positive charge, the lone pair is used to attack the partially positive carbon attached to the chlorine atom (PR 2.4). Although this is relatively obvious from the structure of the product, engaged students sometimes ask why the partially positive amide carbonyl is not the site that is attacked. Distinguishing between "similar" sites such as these is the focus of the *mechanistic selectivity rules* presented later in the course, and indeed we return to the lidocaine example later on (see below). The electron density is then pushed onto the chlorine atom, which is a good (electronegative) location for it, breaking the single bond in the process (PR 3.3). After this first step in the mechanism, many students fail to balance the charge appropriately (PR 4), most often forgetting to place a positive charge on the nitrogen atom. We then note that, with these

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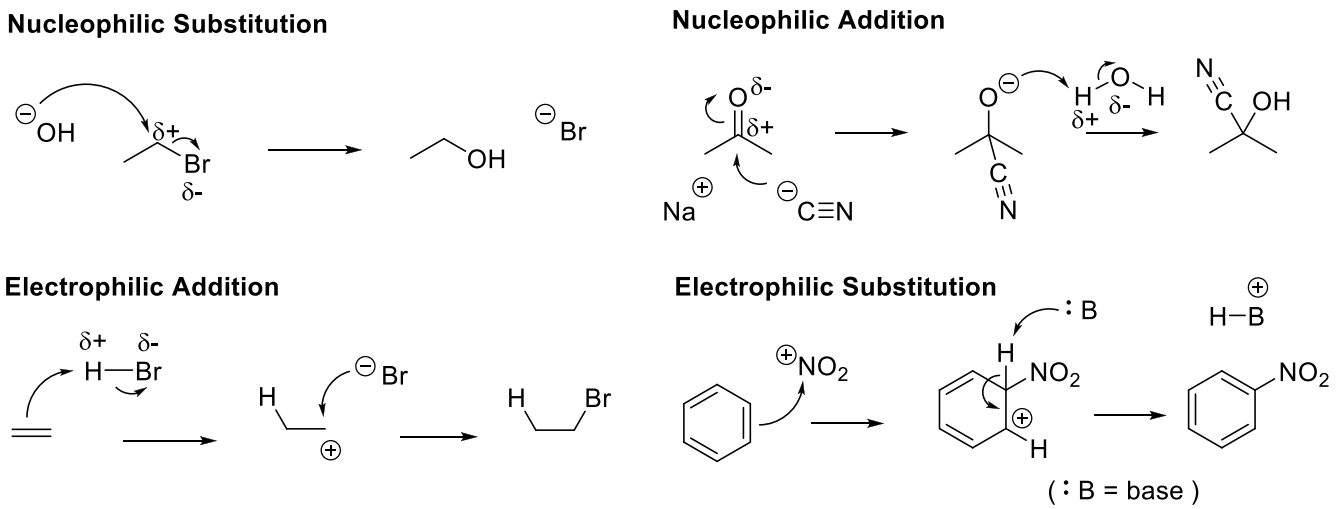

Figure 5. Four basic reaction types initially explored in the context of the mechanistic priority rules.

charges, the reaction is likely not complete (PR 5) and work through the priority rules again. This time, the most electron dense site is the negatively charged chloride ion (PR 1.1). The N^+ atom is a good final destination for the electron density, but it cannot be directly attacked; therefore Cl^- attacks the adjacent proton (PR 2.2). This pushes the electron density back onto the nitrogen, returning its lone pair, by breaking a σ bond (PR 3.3), hence completing the reaction mechanism and giving the desired pharmaceutical product.

NUCLEOPHILES AND ELECTROPHILES, ACIDS AND BASES

At this point, the terminology of nucelophiles, electrophiles, acids, and bases is formally (re)-introduced to the students and defined. It is also pointed out that when mechanistic organic chemists refer to "acids" and "bases", they usually mean Bronsted acids and bases. At this point, it is noted that, in mechanistic priority rule 2, there was the chance of attacking carbon (Figure 3, Box 2, Top Row of (i) and (ii)) or hydrogen (Figure 3, Box 2, Bottom Row of (i) and (ii)). In some molecules, both of these may be possible. It is explained that if the attacking species is a nucleophile, it will attack the carbon, whereas if it is a base, it will attack the hydrogen. This often prompts students to ask how they will know if something is a nucleophile or a base. In this preliminary course, students are always told in any given problem whether they are working with a nucleophile or a base (if this would lead to different outcomes). This is to lower the cognitive load at this point in their studies. However, students are told that electronic and steric effects will, in the future, allow them to predict this when they come to study future courses. Indeed, some of the principles allowing them to do this are touched on later in this course in the *Level 2 Mechanistic Selectivity Rules*.

WHAT ABOUT THE ORBITALS?

In reality what these simple mechanistic "priority rules" are doing, in fundamental terms, is (very) roughly estimating the highest energy HOMO, the lowest energy LUMO and using curly arrows to represent the overlap between them and the change in electron density that results. However, similar to the driver of a car not necessarily needing to fully understand how the engine works to get from A to B effectively, approaching mechanistic chemistry in terms of curly arrows and simple Lewis structures allows students to understand the basics of organic chemistry without having to look "under the hood" in terms of the underlying physical chemistry.

Importantly, however, we use one simple example to illustrate that orbitals lie at the heart of curly arrow reactivity. An example is presented in which a heteroatom lone pair (a filled p orbital) attacks a carbocation (an empty p orbital). The orbitals are explicitly drawn out, and it is explained that a new "bonding orbital" results from the overlap between the filled and empty orbitals. This gives students an important insight into what is driving curly arrow mechanistic processes, at a fundamental level, but without having to worry about deriving orbitals in every case. This also ensures students are prepared for later courses, when orbital descriptions are sometimes used to describe particular aspects of reactions to give enhanced understanding.

KEY REACTION TYPES

Once the priority rules have been presented, the course moves on to four classic types of reaction that are typically presented in introductory organic chemistry courses (Figure 5). Most importantly, it is demonstrated that, at least at a simple introductory level, such reactions can be predicted from first-principles, rather than having to be learned. In each case, rather than presenting the completed mechanism to the students and then rationalizing it, the mechanism is worked through step-by-step in the lecture. During the process, the decision-making processes that lead to each curly arrow are explained, and the effect those arrows are having on the molecules is described.

Nucleophilic Substitution

The "best" nucleophile is found using priority rule 1. This is then used to attack the best electrophile using priority rule 2. A leaving group is then displaced by breaking a σ bond (priority rule 3). In the example given (Figure 5), the negatively charged hydroxide anion (PR 1.1), in the absence of any positive charge attacks the $C^{\delta+}$ on ethyl bromide (PR 2.4), and the C−Br single bond is broken (PR 3.3) to generate the charge balancing bromide anion (PR 4). In this case, the reaction is then complete. Substitution has occurred because the attacking nucleophile has replaced the leaving group, substituting for it.

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Nucleophilic Addition

Students find the best nucleophile using priority rule 1. They use it to attack the best electrophile using priority rule 2. As a result, electron density is moved onto a heteroatom (priority rule 3), but in this case, unlike in nucleophilic substitution, the heteroatom is not disconnected/lost from the molecule. As such, the nucleophile has added to the molecule rather than substituted for a leaving group. In the example given (Figure 5), the negatively charged cyanide anion (PR 1.1), in the absence of any positive charge, attacks the $C^{\delta+}$ on the carbonyl group (PR 2.4) and the C═O π bond is broken to form a single σ bond (PR 3.4), generating the charge balancing anion (PR 4). The reaction here is not complete (PR 5), and students are explicitly told that in step (ii) the product is worked up with water (H_2O). Once again the priority rules are applied, and the negatively charged oxygen (PR 1.1) reacts with the $H^{\delta+}$ on water (PR 2.4), giving rise to the OH group in the cyanohydrin product and generating a charge balancing hydroxide anion (PR 3.3 and 4).

Electrophilic Addition

In this reaction, students apply the priority rules to find that an electrophile adds across a multiple bond. In the specific example given (Figure 5), the doubly bonded alkene (PR 1.3) is the most electron rich site in the reagent (in the absence of any negative charges or lone pairs). In the absence of any positive charge, this attacks the $H^{\delta+}$ on HBr (PR 2.4), pushing an electron pair onto the bromine to create a bromide anion (PR 3.3). The result of these arrows is that a new C−H bond is formed, and the double bond is lost, leaving the other carbon atom positively charged to balance charge (PR 4). This system has a negative and positive charge and can react further (PR 5). The bromide anion is the best nucleophile (PR 1.1) and directly attacks the carbocation (PR 2.1) to form a new bond (PR 3.1) and complete the reaction.

Electrophilic Substitution

In electrophilic substitution, an aromatic ring attacks an electrophile, and then in the second step a base removes a suitable proton to generate the product. This is distinct from electrophilic addition in which the second step involved the attack of a nucleophile. For the purposes of this course, students are told that a base is present in the second step to emphasize the only role it can play here is to remove a proton. It is also noted that the regeneration of aromaticity provides a driving force that helps favor deprotonation over simple nucleophilic attack in the second step.

In the specific example given (Figure 5), the best starting point for a curly arrow is one of the multiple bonds in benzene (PR 1.3) and this attacks the positively charged electrophile (PR 2.1). Obviously, in more advanced courses focusing on aromatic chemistry, the students will be expected to work out how this type of eletrophile is generated from actual reagents, but that is not the point here. The formation of the C−N bond (PR 3.1) and the breakage of the C═C leaves a positive charge on the aromatic ring (PR 4). The students are then explicitly told to use a base. As such, they simply have to decide which hydrogen to remove. A common mistake here is to attack C^+ directly with the base—students are reminded of the meaning of the word "base". A second common mistake is to remove the hydrogen attached to C^+. However, this is not one of the cases allowed by the priority rules. To convince students this is not allowed, it is explained that such a curly arrow simply gives the positively charged carbon atom a pair of electrons which it was already sharing—its electron count therefore remains at 6. As such, students are convinced the base reacts with the other hydrogen atom, which is able to move the electrons to the positive charge through resonance (PR 2.3). This regenerates the aromatic ring (PR 3.1) and completes the reaction.

LEVEL 2 MECHANISTIC SELECTIVITY RULES

Having demonstrated how the basic priority rules work, and allow prediction and understanding of key reactions, the course then moves on to consider cases where a greater degree of judgment is required. Often, when looking at molecules in the real world, students will be faced with a difficult choice, because when they apply their priority rules to molecules, they will find a number of possible reactive sites at the same "priority level". With this in mind, some Level 2 'mechanistic selectivity rules' are therefore presented (Figure 6). Of course, these could have been presented previously alongside the priority rules; however, it is beneficial for students to gain some fluency with the basic rules, before having to move on to consider more subtle effects, avoiding cognitive overload at an early stage. A key pedagogic challenge of organic chemistry is that students often have to weigh a number of different factors in their decision-making (some of which will sometimes conflict). Taking a stepwise approach to exploring why things react and how to draw curly arrows enables students to build an understanding at their own pace.

Obviously, it is not possible, in an introductory course, to present every possible example of selectivity in organic reactions. Indeed, understanding such effects is a process that will take much of the time and effort spent learning organic chemistry. However, it is possible to give some key pointers that enhance the level of mechanistic sophistication.

1. Where the Electrons Start

Electronegativity. When comparing two different atoms as a starting point for a curly arrow, as a general rule, the less electronegative atom will be more reactive (Figure 6, Box 1). Therefore, generally, in the absence of steric constraints, the reactivity of the halide anions is $I^- > Br^- > Cl^- > F^-$. In terms of lone pair reactivity, S > O and *N* > O > F. Students find this intuitively very surprising, as they associate electronegativity with charge and hence with reactivity. Indeed, this is a significant misconception in mechanistic chemistry. It is therefore important to emphasize that the curly arrow represents electrons being given away—if atoms are more electronegative, they hold on to the electron pair more tightly and are less effective donors. Conversely, less electronegative atoms with a pair of electrons are much more able to donate them to form a new bond, sharing them with another atom. This is a good point to link back to the idea (in qualitative terms) that curly arrows are representing orbitals, and that it is vital that the orbitals can overlap effectively if a bond is to be made efficiently. Electronegative elements lead to small contracted orbitals which suffer from poor orbital overlap

Mesomeric Effects (Resonance). Having emphasized the importance of the electron pair being given away, the detrimental effect of mesomerically withdrawing groups is then discussed. The resonance stabilization that can be provided by such groups delocalizes the electron pair across the molecule and, therefore, means it is much less able to act as the starting point for a reaction mechanism. Examples are given, such as the nucleophilicities of alkoxide and phenolate anions, and the basicities of amines and amides (Figure 6, Box 1).

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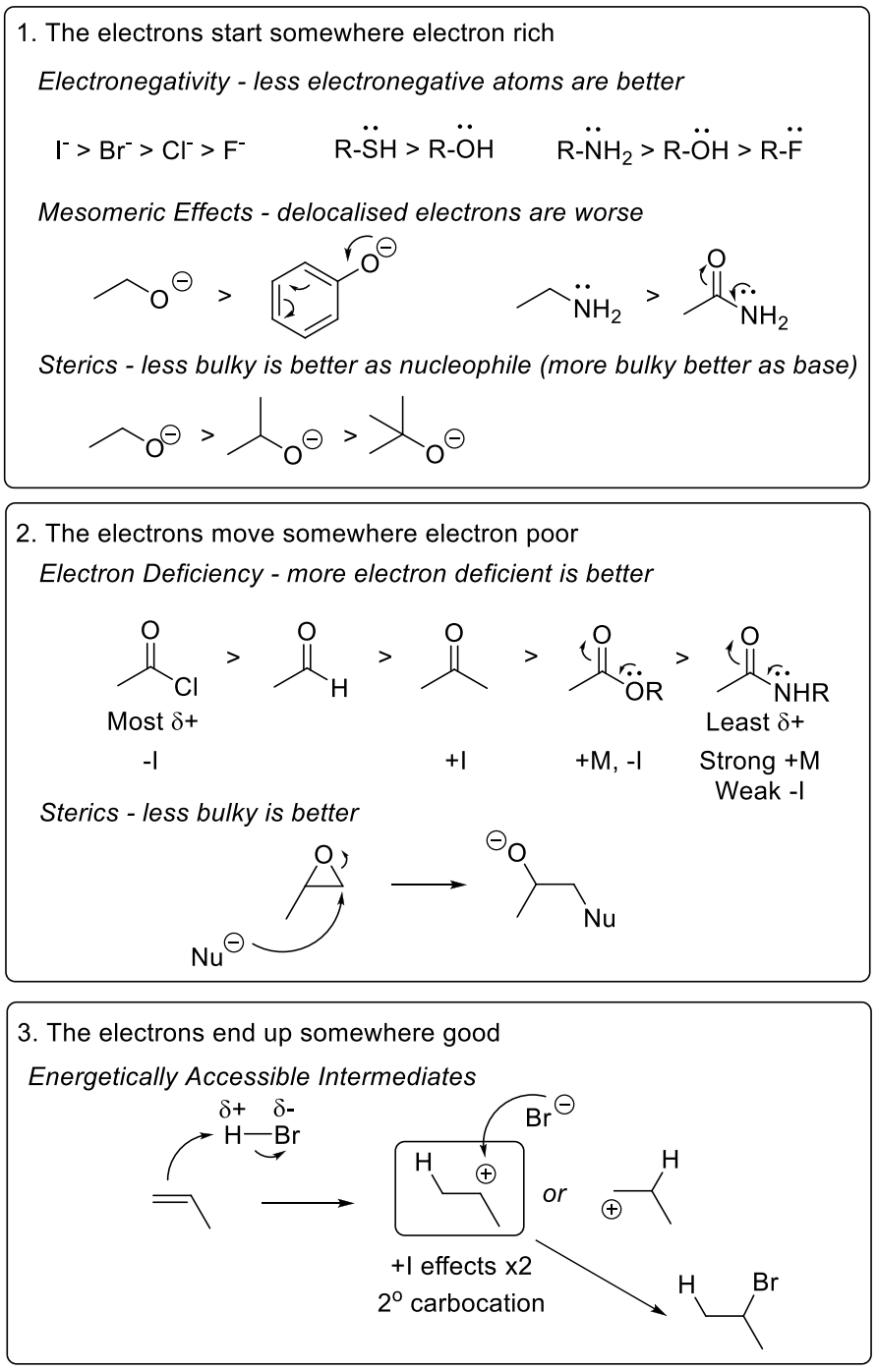

Figure 6. Level 2 mechanistic selectivity rules.

Sterics. When comparing two equivalent atoms with similar reactivities, steric bulk often plays a role in determining which will react as a nucleophile and which will not. In general, less bulky reagents will be better able to donate a pair of electrons at the start of a mechanism. A good example is provided by the different reactivities of primary, secondary and tertiary alcohols acting as nucleophiles (Figure 6, Box 1). It is noted that the reasoning here is different for bases, which do not suffer from steric effects when accessing a small hydrogen atom (as the process is thermodynamically, rather than kinetically controlled). As such, bulky electron rich systems are more likely to act as bases than nucleophiles. This is the first time students consider structural features that control whether something acts as a nucleophile or base, and whether it will therefore attack a carbon or hydrogen atom. They return to this principle in a later course when they learn about substitution and elimination reactions in more detail.

2. Where the Electrons Move to

Electron Deficiency. In many reactions, there are multiple $\delta+$ carbon atoms. To exemplify how it is possible to differentiate between them, the order of reactivity of a carbonyl group toward a general nucleophile (Nu^-) is discussed, based on inductive/mesomeric effect arguments (Figure 6, Box 2). These electronic effects make the carbon atom more or less $\delta+$ and hence strongly influence its reactivity. This reinforces the idea that less

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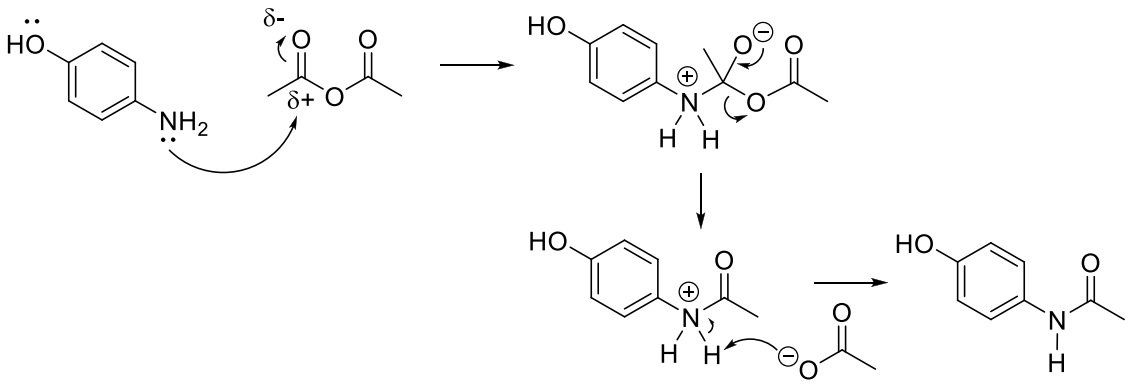

Figure 7. Mechanism for the synthesis of paracetamol (acetaminophen, Tylenol).

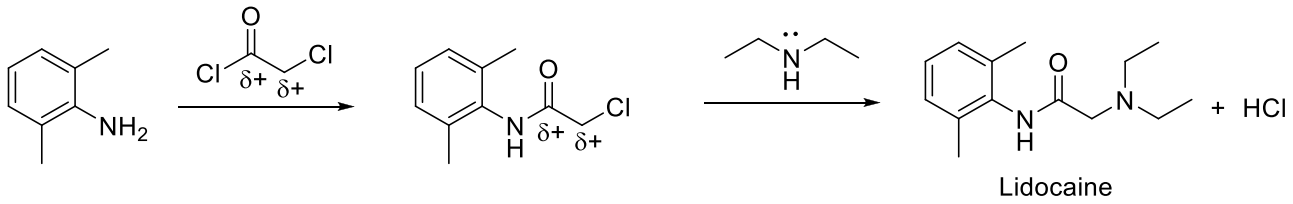

Figure 8. Full synthesis of lidocaine, highlighting the choice between electrophilic sites in the sequential nucleophilic substitution reactions.

electronegative atoms are better electron pair donors (i.e., an amide is significantly less reactive than an ester). It is noted that this explains the reason proteins, the machinery of life, evolved to use amide linkages rather than esters—amides are stable enough to survive in water, but esters are not. Simple electronic effects, and their impact on reactivity, directing the way life itself evolved is something students find fascinating.

Sterics. When comparing the relative reactivity of ketones and aldehydes in the section above, sterics as well as electronics play a key role in making the ketone less reactive, which is highlighted. The reaction of an epoxide is also used to explore the impact of both steric hindrance (and electron deficiency). In the form of a vote, students predict which end of an epoxide they would choose to attack with a general nucleophile (Figure 6, Box 2). Here, the steric and electronic effects reinforce one another and lead to attack at the less-substituted carbon. A nice analogy is that the epoxide is like the "perfect bar"—not only is one end of the bar less crowded, meaning you can get served straight-away, but the beer at that end of the bar is cheaper! It should be noted that this reaction occurs under basic conditions with the reagents as drawn. Under acidic conditions, the process will be different. The students should be able to recognize that, in the presence of H^+, the epoxide will be converted into a different species using the priority rules; however, the subtlety of acid-mediated epoxide openings is not introduced here, and is left for a later stage of study.

3. Where the Electrons End up

Energetically Accessible Intermediates. In some cases, there will be a choice of product based on exactly the "same" curly arrows. This is best exemplified by electrophilic addition to an alkene, and provides the opportunity to revisit the 'principle of energetically accessible intermediates'. In the example illustrated (Figure 6, Box 3), there is a choice of primary or secondary carbocation intermediates, depending on which end of the double bond becomes bonded to the hydrogen. Electronic effects (in this case, +I/hyperconjugation) favor the secondary carbocation intermediate and hence give rise to one product selectively. This is a good opportunity to set some quiz questions where students predict the regioselectivity of reactions of different alkenes.

PREDICTING COMPLEX MECHANISMS

The ultimate goal of this approach to teaching organic reaction mechanism is to allow students to use the simple priority rules to predict reactivity and hence solve contextualized problems. Ideally, students will realize that without actually having 'learned' any reactions, they can now make sensible predictions about some quite complex processes just by pushing arrows. We exemplify this in a range of different ways—a few selected examples are given here. Some of these are taught in the course, and some of them are the basis of homework or past examination problems.

The synthesis of paracetamol (acetaminophen, Tylenol) provides an effective contextualized introduction based on a pharmaceutical that most students in the class will have taken at some point in their lives (Figure 7). Students are only provided with the starting materials (not the product) and asked to vote on the best place to start the curly arrows. They hopefully apply the selectivity rules to determine the amine as the most reactive lone pair on account of its lower electronegativity. On working through the curly arrows, after attacking the $C^{\delta+}$, there are two electronegative atoms in the molecule onto which the electron density could be moved—two oxygen atoms. The electrons are initially moved onto the C═O oxygen to yield the tetrahedral intermediate, but ultimately, the electron pair can then move back to regenerate C═O and break the C−O bond, a process favored by the creation of the resonance stabilized CH_3COO^- leaving group. This is a good opportunity to emphasize that intramolecular movements of electron density are facile and rapid processes in comparison to intermolecular ones and that electrons can easily "explore" the different options. The final step of the process is just a deprotonation, but it is pointed out that it logically follows the priority rules and allows the structure of the product to be worked out.

The acetaminophen problem described above revolves around a choice between nucleophiles. For a choice between

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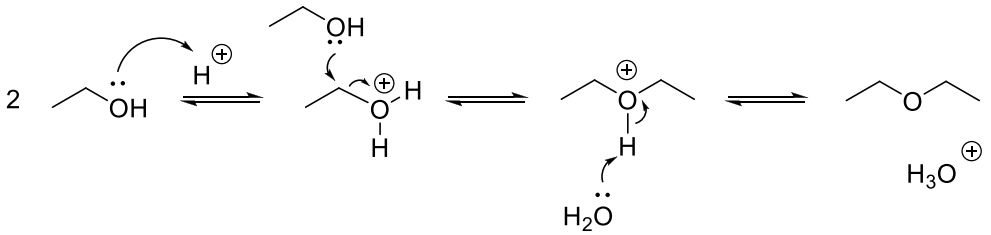

Figure 9. Mechanism of the acid-catalyzed synthesis of diethyl ether from 2 equiv of ethanol.

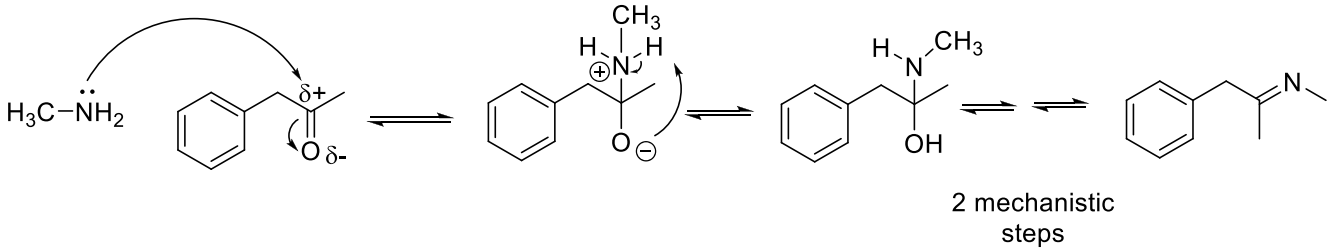

Figure 10. Initial mechanistic chemistry of the "Walter White" synthesis of methamphetamine as presented in the TV show Breaking Bad, which can be simply derived using mechanistic priority rules.

electrophilic sites, the local anesthetic lidocaine, discussed earlier (Figure 4), provides an excellent example. In this case, the full two-step synthesis of lidocaine is now presented, and students are asked to rationalize the reactivity in each step (Figure 8). In the first step, the acid chloride is more reactive than the alkyl chloride, because of the additional −I inductive effect provided by the C═O group. Hence a nucleophilic substitution reaction proceeds to form an amide. In the second step, the amide is less reactive than the alkyl chloride because the +M effect of the nitrogen lone pair acts to push electron density toward $C^{\delta+}$, making it significantly less reactive. The second reaction therefore proceeds via nucleophilic substitution at the alkyl chloride to yield the amine product.

The mechanistic priority rules are then applied to work out what is, to the students, a completely unknown reaction. The students are initially asked if they know what happens if ethanol is boiled in a strong acid. Invariably they do not, and this therefore allows us to decide to work out the answer mechanistically (Figure 9). The problem is carefully framed as 2 equiv of ethanol reacting with 1 equiv of H^+ (this helps the students significantly). The mechanism is then worked out step-by-step (rather than being presented in complete form), with each step being explained using the priority rules.

Initially, the best place to start an arrow is the lone pair on the alcohol oxygen (PR 1.2), and this attacks the positively charged hydrogen atom (PR 2.1). The protonated product (PR 3.1) now contains a positive charge (students are reminded about the charge balancing rule, PR 4). It is then pointed out that 2 equiv of ethanol are being used, and are given a vote on what will happen next. They are reminded that a positive charge on a heteroatom cannot be attached directly (some students often suggest this), and therefore they must attack adjacent to it. Some students want to attack the hydrogen, but obviously, this does not progress the mechanism forward; it simply shifts a proton between two ethanol molecules (it can be noted in passing that this will be happening all the time—there is no need to draw it out). Thus, the students are convinced that attacking the carbon is the "productive option". Pushing electrons to the positive charge breaks the single bond, and the students realize water has left. Once again, the organic product here is positively charged, and the rules of mechanism say that the best place to start a curly arrow is the lone pair on water (PR 1.2), which can now attack the H attached to the positively charged oxygen (PR 2.2), generating a neutral ether product. Some students ask why water cannot attack the carbon atom—it is pointed out that in principle it can, but that would simply reverse the previous mechanistic step, so does not move the reaction forward. As such, it is understood that this is a reversible reaction, proceeding with the loss of water, and also that it is catalyzed by H^+, with H^+ being regenerated at the end of the reaction.

In this way, students learn, from first-principles, that they can dehydrate an alcohol to synthesize a symmetric ether. The goal here is to convince students that reaction mechanisms are an underlying theoretical predictive framework to organic chemistry, in the same way quantum mechanics underpins physical chemistry and the periodic table plays a central role in inorganic chemistry.

The first step of the synthesis of crystal meth presented in the TV show, Breaking Bad (Figure 10), provides an eye-catching entry into slightly more complex reaction mechanisms based on fundamental carbonyl chemistry. Any fans of the show will know that the availability of methylamine (or lack of it) becomes a major plot point in some of the later series of the show (no spoilers). This reaction is one of the key-stone mechanisms in organic chemistry, and is taught to our students in detail in their carbonyl chemistry course. However, there is real power in demonstrating here that the rules can be applied in a stepwise manner to understand processes such as this. Initially, the amine nucleophile (PR 1.2) attacks the $\delta+$ carbonyl (PR 2.4), with the electron density moving from the π bond onto the oxygen atom (PR 3.2). Balancing charge (PR 4) generates an intermediate with two charges. Students generally realize that this is not the end of the reaction process (PR 5) and, using the rules, suggest that the most electron dense site (O^-, PR 1.1) attacks the $H-N^+$ bond (PR 2.2). It is discussed that this process will be assisted by transfer of the proton with solvent (not shown here)—indeed, it is important that students realize that protons are very easy to move in mechanistic processes, because they are often in rapid exchange with solvent and can "hop" on and off solvent molecules. I anticipate that, in later courses, students will revisit

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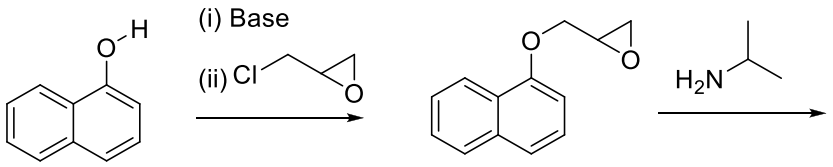

Figure 11. Scheme presented to the students for the synthesis of propranolol.

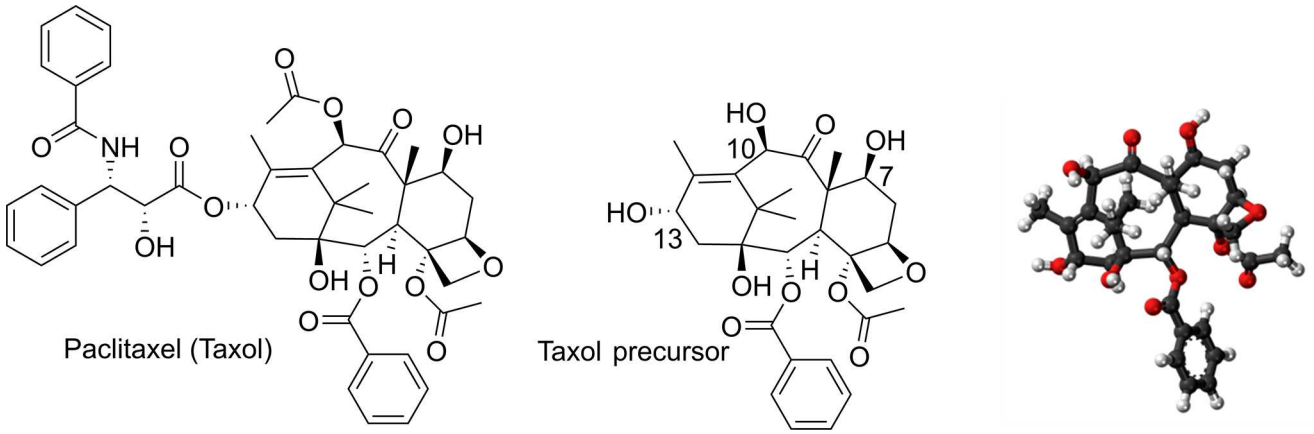

Figure 12. Structures of paclitaxel (Taxol) and taxol precursor (10-deacetyl baccetin), as well as the 3D structure of 10-deacetyl baccetin.

this and will then draw out the explicit role of solvent, but at this stage, I prefer to emphasize the simple driving forces behind the process and not confuse the mechanistic picture with solvent. This generates the neutral hemiaminal, which students are broadly happy with as looking like a stable species.

This is an effective point to tell students that the reaction can actually continue further, and note that there is normally an H^+ catalyst present to facilitate this kind of chemistry. This can encourage a number of further discussions, such as how C═O can be protonated by H^+ at the start of the mechanism to enhance its reactivity, as well as how the OH group in the hemiaminal can be protonated to generate a positively charged H_2O leaving group, moving the reaction toward the imine product as shown. This also requires the use of intramolecular curly arrows (using the priority rules)—something the students find challenging at this introductory stage of mechanistic learning (see further discussion below). Working out these further steps makes a nice homework exercise for the more proficient students, but is beyond what I would formally assess at this stage.

The synthesis of propranolol, an important β-blocker drug used for patients with heart problems, provides another good example of selectivity which is useful for interactive problem classes. Students are presented with the partial reaction scheme shown in Figure 11, and asked to provide plausible curly arrow mechanisms for each of the three steps. Step (i), which specifies the use of base, simply requires the students to find the most δ+ hydrogen on 1-naphthol, which is obviously the one attached to the electronegative oxygen atom. They then have to provide appropriate curly arrows to remove it, generating a negatively charged oxygen. This then becomes the most reactive nucleophile and the starting point for the curly arrows in step (ii). In reality, the step (ii) arrows are tricky, as each of the carbon atoms has δ+ character and it is not easy to distinguish between them. The two terminal carbons are the most reactive on steric grounds. The students here are guided by the product, and usually elect to attack the C−Cl bond leaving the epoxide intact. In reality, it does not matter which carbon is attacked, as the same product is obtained in each case. This is because if the epoxide is opened, it can close again (intramolecularly) displacing the Cl atom. In reality, this is the way the mechanism proceeds, but for early stage students this subtlety is not too important. However, it can open useful discussions with the more proficient students about how they could possibly tell the difference, which may even lead them to think about isotopic labeling. This can usefully help make the point that mechanisms are always based on experimental evidence—not just theoretical hypothesis. After the challenge of step (ii), the third step is relatively simple. The amine acts as nucleophile and, under basic conditions as shown, attacks the terminal carbon atom of the epoxide (on both steric and electronic grounds). This opens the epoxide ring, generating O^-. The reaction is not complete, and this O^- removes H from the positively charged nitrogen atom to synthesize the target drug.

A final example, which also makes for fun discussions, helps the students see how they could use these simple rules to begin to consider even extremely complex molecules. The structure of the anticancer drug paclitaxel (Taxol) is presented (Figure 12), and it is explained to the students this compound is found in the bark of the slowly growing Pacific yew tree. Harvesting paclitaxel for medical use generally leads to destruction of the tree, making it practically not possible given the amounts of drug required. The structure of 10-deactyl baccetin (Figure 12) is then also presented. This compound is available relatively abundantly from the needles of the European yew tree, meaning it is much more accessible, as the needles can be harvested. Students are asked to consider how, in general terms, 10-deactyl baccetin could be converted into paclitaxel.

First, students are encouraged to find the most nucleophilic site(s) on 10-deactyl baccetin. They usually correctly deduce the alcohols are the most reactive sites—however there are four of them. One of the alcohols is tertiary and will be less reactive on steric grounds. The other three sites (7, 10 and 13) are secondary, and on paper, it is difficult to know which will be

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more reactive. Clearly, one of these alcohols is the site that has been modified to create paclitaxel.

For fun, students are then shown the 3D structure of Taxol, and it is explained that one of the secondary alcohols (C-7) is exposed on the convex side of the molecule, while C-10 is slightly hindered, and C-13 is relatively buried on the concave side. The students correctly deduce that the exposed convex secondary alcohol in the C-7 position will be more reactive as a nucleophile as it is less sterically hindered. Unfortunately, this alcohol is the one that does not have to be modified to make Taxol! This leads to a discussion (with no further details at this stage) of the idea that the convex C-7 alcohol could be reacted with something to 'block it off'. Then C-10 could be reacted with ethanoyl chloride to make an ester, and finally, the concave C-13 alcohol could be reacted (with something like an acid chloride) to create the desired paclitaxel 'tail' modification. Finally, unblocking the convex C-7 alcohol (i.e. removing the blocking group) would yield the target molecule. Although the details are not worked through, this introduces students to the concept of a protecting group strategy, to which they will return much later in their degree. Importantly, this demonstrates how new strategies can emerge from a simple consideration of reactivity and priority rules, allowing students to see how even their basic understanding of the molecular world enables them to access some really challenging problems—hopefully motivating them to study further so that they can discover all of the details to solve such problems fully.

SUBTLETIES AND NEXT STEPS

Beyond this introductory course, students will encounter examples in which they have to consider the mechanism in a more subtle way. In each case, these simple priority rules provide the framework for an effective starting point; however, it is important to note that students will find some mechanisms that appear to diverge somewhat from the simple priority rules.

An example of a case where priority rules need a little more consideration is where a reactive species has different resonance forms. In such cases, which are beyond the context of this introductory-level course, students should draw out both resonance forms to find the most reactive site. A good example would be the reaction of an enamine with methyl iodide (Figure 13), where simple priority rules reasoning might predict the lone pair on the nitrogen as the reactive site. However, the enamine resonance form clearly indicates the presence of a negatively charged carbon atom, which would be much more reactive as an electron donor. Indeed, the resonance form also emphasizes that the nitrogen atom is somewhat electron poor with a degree of positive charge. As such, the priority rules still hold, but on first inspection of the reagents, without considering mesomeric effects, students could intuit the wrong answer.[25]

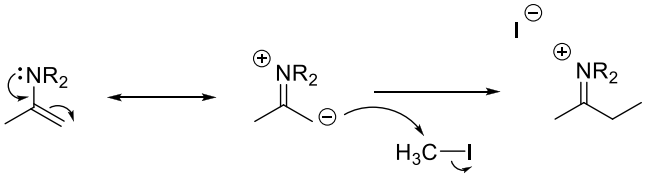

Figure 13. Structure of enamine, illustrating how considering resonance forms reveals the reactive site, followed by reaction with methyl iodide.

As a further "problematic" example, students will meet both S_N1 and S_N2 reaction mechanisms later in their organic chemistry course. If faced with the reagents and conditions for an S_N1 mechanism, the priority rules would predict a plausible mechanism and the correct product, but would always suggest an S_N2 mechanism (attack of nucleophile and loss of leaving group) rather than S_N1 (loss of leaving group then attack of nucleophile). At this point it becomes important to add another layer of subtlety—the order in which mechanistic steps occur can, in exceptional cases, with good reasons, vary. In this particular case, if the nucleophile is not very good (low in the priority rules), the bond to the leaving group is easily broken and (most importantly) the resulting carbocation is stabilized (principle of energetically accessible intermediates), then the mechanism will change from the predicted S_N2 to the variant, S_N1. Similar considerations apply to the E1 and E2 mechanisms. Interestingly, the pedagogic "difficulty" of teaching these "unusual" carbocationic mechanisms aligns with the views of Goldish.[26] Over 30 years ago, in a particularly far-sighted commentary, Goldish argued for a mechanistic-led approach to organic chemistry teaching, in which mechanisms would not be taught for the sake of mechanisms, but rather because they helped develop students' understanding. Furthermore, this article advocated focusing on ionic reactivity, introducing carbonyl chemistry quite early, and suggested that the exceptional nature of carbocationic mechanisms such as S_N1 meant they should be taught to students somewhat later in the program.

Although this might seem like a weakness of the priority rules approach, the existence of the rules actually provides students with a very good framework for reflecting on the reasons why certain substrates will subvert the predicted mechanism and give rise to a different mechanistic outcome. By thinking stepwise about a mechanism using the priority rules, it becomes obvious why certain strengths or weaknesses of the reagents may lead it to happen in a slightly different way.

STUDENT EVALUATION

Versions of this course have been taught for a number of years with outstanding student feedback (e.g., most recently: 2020−21, 4.90/5.00; 2021−22, 4.71/5.00 on a five point Likert scale). The course is currently taught to ca. 300 students a year, including chemistry majors, as well as students studying on Biochemistry and Natural Sciences degree programs. Importantly, a significant number of students reflect positively, and unprompted, on the way the subject is taught, i.e. taking a conceptual approach to reaction mechanisms. Many students also reflect positively on the real-world examples, many of which are used as "You Do The Work" homework examples (comments from 2021/22).

- "I liked how we were given simple rules that can apply to most molecules rather than being told to commit certain mechanisms to memory. I also enjoyed the "you do the work" parts as it showed how the chemistry we were learning can be applied in real life as some of the other lecture courses appear to have no real life implications."
- "The approach that Prof. Smith takes (emphasizing a learning of method, not specific examples) is one that I wholly agree with."
- "He made what seemed like a hard topic very easy to approach."

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- "I thought it was very good that he allowed us to think for ourselves and try to understand why things would happen, rather than just stating what would happen and spoon feeding the content."

It is noted that all testing on this subject is carried out in terms of unseen problems based on molecules and syntheses with applications in the real world. This approach is quite different to many introductory organic chemistry courses which rely heavily on recall of material and "classic" examples, many that have been explicitly taught in lectures. Students perform well in this type of authentic problem-solving assessment and in general go on to achieve good marks in later organic chemistry assessments. However, for students to become really proficient in curly arrow mechanistic chemistry, it is vital to continue this type of approach beyond just the introductory module, rather than returning to the 'mechanisms as something to learn' method. In the future, it would be desirable to formally assess any learning gain associated with this approach to mechanistic teaching using standardized tests and control groups. However, it is important to remember that some benefits may be experienced further down the educational pathway, as students become more proficient 'organic chemistry thinkers', and will be more difficult to test for. It is worth noting as anecdotal evidence of our students becoming 'organic chemistry thinkers' that, of the three traditional areas of chemistry at my own institution, students are most likely to express a preference for organic chemistry and select final year modules and projects based on organic chemistry.

CONCLUSIONS

In summary, this paper presents a simple introductory approach to teaching mechanisms, including some mechanistic priority rules, which allows students to predict plausible mechanisms from first-principles, consider complex molecular structures and begin to think about how different molecules might react with one another. This encourages students to think in terms of mechanism, with an understanding of why they draw the curly arrows they do, rather than simply trying to learn reaction mechanisms as an "additional burden" of studying organic chemistry. Indeed, thinking mechanistically is actually an excellent way of students lowering the cognitive load of organic chemistry, as a few fundamental principles can allow students to understand much of the subject.

By teaching this material in a real-world context, student motivation to understand mechanistic behavior is harnessed. Furthermore, by approaching challenging questions, students see that although they cannot yet solve every problem, the skillset they are developing in mechanistic thinking will go on to be used further in their studies of organic chemistry, hopefully encouraging them to look forward to further studies of the subject. By teaching curly arrow mechanisms as a conceptual approach, rather than simply using them to rationalize reaction outcomes, students begin to see organic chemistry as a coherent whole with an underpinning philosophical framework.

The priority rules presented here are simple to understand and use, and allow students to solve many problems. They capture the essence of mechanistic thinking used by proficient organic chemists and lead to plausible curly arrow mechanisms which can act as a good starting point for further discussions. Furthermore, the teaching methods employed are very well received by our undergraduate students, including those nonchemistry specialists studying biochemistry and natural sciences.

If curly arrow mechanisms are the language of organic chemistry, it is hoped that these priority rules, rather like the "phonics" approach to breaking down words for reading, will allow students to make the first steps to literacy in a more logical manner, and build their confidence, which ultimately leads to fluency.

AUTHOR INFORMATION

Corresponding Author

David K. Smith − *Department of Chemistry, University of York, York YO10 5DD, U.K.;* orcid.org/0000-0002-9881-2714; Email: david.smith@york.ac.uk

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.jchemed.2c00950

Notes

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