

# From Strawberry Fields to the Chemistry Classroom

by

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Kelly had begun her junior year at California State University and was a couple of weeks into classes, her favorite of which was organic chemistry. She lived in California with her older brother, Kale, a farm worker on a nearby strawberry field. The profit from the harvested strawberries constituted the majority of their household income. For the past few weeks there had been a lot of excitement around the farm at both the local and corporate level regarding the pesticides used to keep the crops healthy (Guthman, 2016). By spraying the pesticides in the field prior to planting the strawberries, and eliminating any harmful organisms or insects, the company maximized its profits without rotating the crops. It was the fall of 2005 and this was the year methyl bromide, the primary pesticide used on the field, would be phased out (EPA, 2006). With financial dependency and economic stability on the front line, interest in the pesticide among community members had skyrocketed.

One afternoon while Kelly was picking Kale up from work, she saw a group in suits and ties; unusual dress for field workers.

“Who are they?” Kelly asked, as she turned to her brother, gesturing to the group.

“They are officials from the Agricultural Labor Relations Board. They came to talk to everybody about the methyl bromide pesticide and said that we shouldn’t be concerned with the business losing money,” Kale said as he got into the car.

“I’ve seen a lot of stories on the news and in magazine articles about that. They say it’s really dangerous for the ozone layer and that it can cause cancer in people who are overexposed,” Kelly continued. “It’s because the chemical  $\text{CH}_3\text{Br}$  undergoes something called an  $\text{S}_\text{N}2$  reaction.”

Kale shrugged. “Well, the officials said that the federal organizations gave orders to keep it in use until 2015 while scientists look for a safer alternative that is just as effective.”

“Okay,” Kelly muttered, “In the meantime, please be careful because I’ve heard about cases where it reacts with human DNA and produces toxic materials like formaldehyde in your body, and that’s extremely dangerous.” (Budnik *et al.*, 2012)

“Sure thing,” he assured her. “Don’t worry, they have professionals coming in tomorrow to explain the new guidelines and rules to the workers and applicators.” Kale looked at his sister for affirmation, and then added, “But they told us that this evening Santa Barbara College is holding an information session with Jessica Ramirez, if we want to know more about it.”

Kelly smiled. “Good. I think I’ll go.”

Jessica Ramirez had gone to high school with Kale and was now an environmental scientist for the National Institutes of Health (NIH) in Washington D.C. She had recently returned to California after having learned about the growing pesticide controversy. Kelly attended the talk and after the closing statement, Kelly spotted Jessica across the room and made her way over.

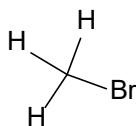
"I loved the talk," Kelly said through a smile. "You made it really fun to learn and I was wondering if we could catch dinner and you could answer some of the more in-depth questions I had."

"Of course," Jessica replied.

As the ladies conversed, they caught up on Jessica's agricultural research and Kelly's university courses. After they had ordered their meals, Jessica reached for her iPad and pulled up an online book, *Organic Chemistry*, flipping through it to the chapter titled "Substitution Reactions." "This will be a good place to start," Jessica began.

Kelly chuckled. "Okay, well, I know that the molecule undergoes something called an  $S_N2$  reaction, but I'm not quite sure what that means."

"That's a great start! To understand this, we only need to grasp a small part of organic chemistry relating to how molecules react with each other based on their structure and stability." Jessica opened a notebook page on her iPad and drew the chemical structure of methyl bromide as shown in Figure 1. "This is called a primary alkyl halide."



Methyl bromide ( $\text{CH}_3\text{Br}$ )

Figure 1. The structure of methyl bromide ( $\text{CH}_3\text{Br}$ ).

She paused to draw two more structures (Figure 2). "These are secondary and tertiary alkyl halides."

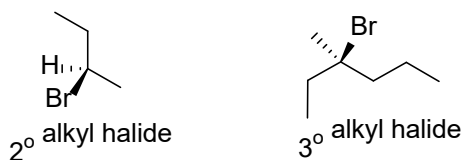


Figure 2. The chemical structures of 2-bromo butane (left) and 3-bromo-3-methyl hexane (right).

"A nucleophile, a Lewis base that is sometimes negatively charged, will attack the central carbon, the alpha carbon in the molecule," Jessica continued. "The halogen is substituted by the nucleophile."

Kelly interrupted, "But how does that happen with the bonds already intact in methyl bromide?"

"Well, there are two different mechanisms by which a substitution reaction can take place:  $S_N1$  and  $S_N2$  reaction mechanisms. In both mechanisms, the atom or group that replaces the leaving group is a nucleophile." Jessica paused and circled the Br atom in methyl bromide. "The halide connected to the carbon is called the leaving group." She then pulled up a periodic table and asked, "Can you tell which halide is a better leaving group? Bromide or iodide?"

"Hmm, not really," muttered Kelly.

"Here, take a look at Table 1. Now do you see? The bottom line is that good leaving groups are weak bases!"

"Ok," said Kelly, "but... what determines the strength of a base?"

"Strong acids have small pKa values and give weak conjugate bases," explained Jessica. "If

Table 1. Acids, pKa values and conjugate bases.

Acids	pKa Values	Conjugate Base/ Leaving Group
Hydrochloric Acid (HCl)	-6	$\text{Cl}^-$
Hydrobromic Acid (HBr)	-9	$\text{Br}^-$
Hydroiodic Acid (HI)	-10	$\text{I}^-$

we compare the acids in Table 1, we can see that hydroiodic acid is the strongest acid and it gives the weakest conjugate base.”

“I get it now, strong acids give weak conjugate bases and weak conjugate bases are good leaving groups, right?”

“You got it!” Jessica exclaimed. “The iodide anion ( $I^-$ ) is a slightly better leaving group than the bromide anion ( $Br^-$ ), and they are both better leaving groups than the chloride anion ( $Cl^-$ ).”

“Makes perfect sense,” replied Kelly. “I think I understand so far, but what is the actual difference between  $S_N1$  and  $S_N2$  reactions?”

“To start, in an  $S_N1$  reaction the mechanism occurs in two steps. First, the bromide and carbon bond (C-Br) breaks, and in doing so the electrons are given to the Br atom because it is more electronegative, meaning it has a stronger affinity for the electrons.” Jessica stopped and adjusted the iPad to face Kelly and pointed to the 3-bromo-3-methyl hexane structure (Figure 2). “What do you think happens to the carbon then?”

“It would be electron deficient and have a +1 formal charge,” said Kelly.

“Right!” Jessica handed her friend the pen to draw on the screen. “And if the carbon now harbors a positive charge, then what would happen in the presence of the nucleophile we talked about earlier?”

Kelly then drew the reaction below (Figure 3) on the iPad, with both reactants and “Nuc” to represent the nucleophile.

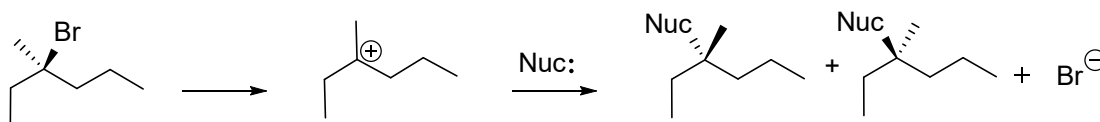


Figure 3. The  $S_N1$  reaction, showing the carbocation intermediate.

Jessica scooted forward. “Great job, but any time you do a mechanism, especially in organic chemistry, you must add an arrow, because you are showing the transfer of a pair of electrons between atoms.”

“Like this?” Kelly added arrows and finished with the mechanism below (Figure 4).

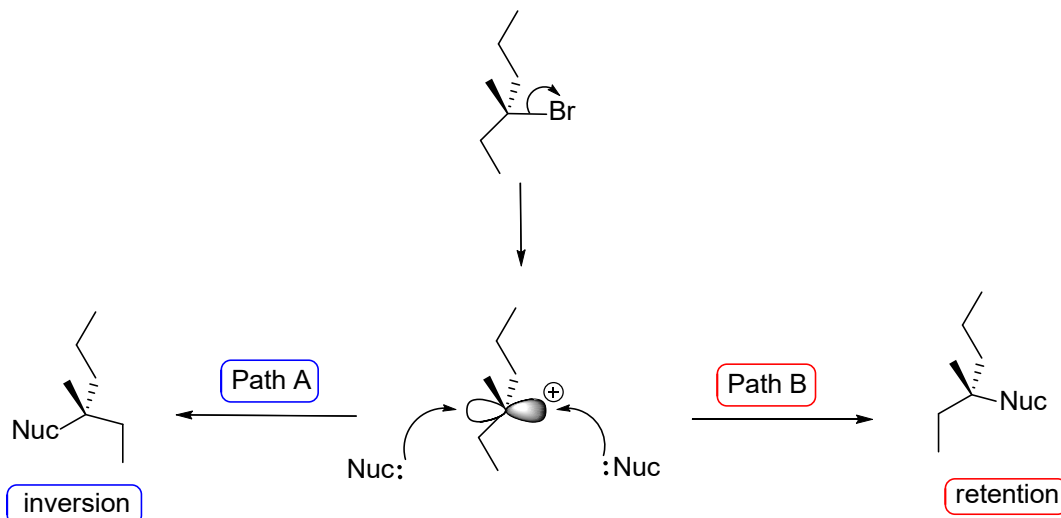


Figure 4. The mechanism of the  $S_N1$  reaction.

“Correct. What you did is the mechanism for an  $S_N1$  reaction, and the intermediate is called a carbocation. It’s more susceptible to a nucleophilic attack than the original atom, so it can react with a weak nucleophile.” Jessica paused before continuing. “This creates a tertiary carbocation, which is more stable than the secondary and primary carbocations.”

“So,” Kelly said, “in the first step of the mechanism, the carbocation intermediate is formed. The carbocation formation step is the slowest step in the reaction and therefore is considered the rate-determining step. But how does the concentration of the alkyl halide and nucleophile affect the rate of the reaction?”

“That’s an excellent question!” said Jessica. “It turns out that doubling the concentration of the alkyl halide doubles the rate of the reaction; however, changing the concentration of the nucleophile has no effect on the rate of the reaction.”

Kelly interjected, “That means the rate law for the  $S_N1$  reaction is this:

$$\text{Rate} = k [\text{alkyl halide}]$$

The rate of the reaction depends on the concentration of only one reactant and therefore the reaction is a first-order reaction.”

“Bravo, Kelly, bravo,” Jessica said while clapping. “It is just wonderful when your previous chemistry knowledge ties in nicely with new information. It’s one of the beautiful things about learning.” She then pointed to the methyl bromide structure (Figure 1) and said, “The primary carbocation is the least stable and is not likely to occur.”

Folding her arms, Kelly said, “So the reaction must occur in a single step? Concerted?”

“Yes,” Jessica replied, “the  $S_N2$  reaction requires the nucleophile to attack the carbon from the opposite side of the leaving group. This is called a back-side attack.” She proceeded with the following mechanism (Figure 5).

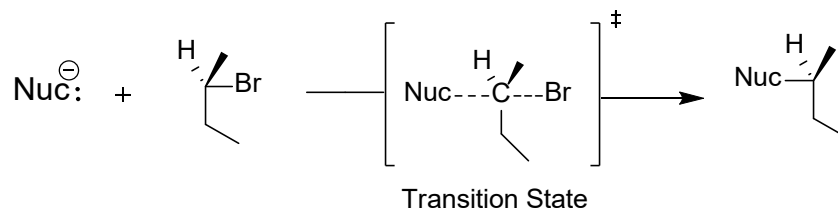


Figure 5. The mechanism of the  $S_N2$  reaction.

Jessica continued, “This mechanism shows that the alkyl halide and the nucleophile come together in the transition state of the one-step reaction.  $S_N2$  reactions only happen in the presence of a good nucleophile, as they have to be strong enough to attack the carbon and push out the halogen in the same step.”

“OK, hold on a second,” said Kelly as she put her hand on her head and tried to focus. “Based on what I know about the rate law, increasing the concentration of either the nucleophile or the alkyl halide makes their collision more probable and increases the rate of the reaction, correct?”

Jessica smiled. “Someone was paying attention in their general chemistry class! You are correct, that is precisely what makes the  $S_N2$  reaction a second-order reaction. The rate law for the  $S_N2$  reaction is written as follows:”

$$\text{Rate} = k [\text{alkyl halide}][\text{nucleophile}]$$

Kelly focused on the iPad, thought a moment, and then asked, “So, if tertiary alkyl halides undergo  $S_N1$  reactions and primary ones undergo  $S_N2$  reactions, what about secondary alkyl halides?”

“They actually undergo both reactions,” replied Jessica.

“There are several factors that influence  $S_N1$  and  $S_N2$  reactions, it’s actually overwhelming,” sighed Kelly. “What about the solvent in which the substitution reaction is carried out? Does the solvent influence whether an  $S_N1$  or  $S_N2$  reaction will predominate?”

“Yes, solvents play an important role in substitution reactions. The solvent is either a protic or aprotic solvent,” replied Jessica.



Kelly looked at her with a puzzled expression. “What does that mean?”

“Protic solvents contain a hydrogen bonded to an oxygen or to a nitrogen whereas aprotic solvents do not have a hydrogen bonded to an oxygen or to a nitrogen,” explained Jessica. “I know I’m throwing a lot of information at you but in summary an  $S_N1$  reaction of an alkyl halide is favored by a poor nucleophile in a protic solvent and an  $S_N2$  reaction of an alkyl halide is favored by a good nucleophile in an aprotic solvent.”

“Okay, I think I understand.” Kelly moved the screen of the iPad back to where they had started and scrolled through to review what she had learned so far.

“You’re doing great,” Jessica added, “You should also familiarize yourself with the terms steric hindrance and stereochemistry.”

“Those I know,” said Kelly. “Steric hindrance is the prevention of reactivity of a molecule based on the bulkiness and proximity of its attachments. The stereochemistry describes how the molecule is arranged in space in 3D.”

“That’s perfect! Steric hindrance is what prevents tertiary alkyl halides from undergoing an  $S_N2$  reaction. The carbon that the nucleophile is supposed to attack is crowded, making this reaction less feasible, so ...”

Kelly interrupted, “So, in an  $S_N2$  reaction, the nucleophile attacks the carbon from the back side only, changing the stereochemistry?”

Jessica nodded and continued, “So the product of the  $S_N2$  reaction has inverted stereochemistry. However, the molecules that undergo  $S_N1$  reactions form a carbocation intermediate. When the nucleophile attacks the carbocation from one side, that leads to inversion of stereochemistry while attack from the other side leads to retention of stereochemistry as shown in Figure 4. That’s how you end up with a pair of enantiomers.”

The server carrying the ladies’ dinner then interrupted their conversation and Jessica placed the iPad back in her bag. “I really hope that helped you understand the concept of how methyl bromide reacts and gives you more information when studying for your organic chemistry class. I’ll email you those notes and I’m sure that you’ll do well in your courses.”

“Thanks again,” said Kelly, just before taking a bite of her steak. “Wow, that’s delicious.”

“Sure is,” said Jessica. “There’s interesting chemistry behind that too, but that’s for another day.” The friends laughed and enjoyed the rest of their meal.



It was in 2010 when Kelly was on her way to the market one day that she saw a poster over the entrance to the strawberry field that read “Methyl Iodide: New Alternative to Methyl Bromide Found!” (Guthman & Barbour, 2017) The sign was a reflection of the relief the community felt that they no longer needed to worry about the pesticide. Later, Kelly thought about the poster and realized that something about this new pesticide seemed similar to the first in that only one element differed. She pulled out her organic chemistry book, flipped straight to the periodic table and found that iodide was located directly below bromide. Seeing this, she realized that a terrible mistake had been made... .

## Discussion

What does the basicity of the two atoms have to do with the two pesticides, MeBr and MeI, and their reactivity based on what you know about leaving group characteristics? Take a moment to discuss.

Due to overwhelming opposition from the general public and scientific communities, California farmers decided against regular use of methyl iodide in the fields. Despite this public outcry that included 50 scientists, several of them Noble laureates in chemistry, who delivered a letter to EPA asking them to deny registration of methyl iodide, California’s Department of Pesticide Regulation (DPR) and the EPA registered it (Guthman & Barbour, 2017). Those seeking greater government involvement in health and environmental protection moving forward must increasingly contend with the challenge of science itself too often becoming a politically partisan issue.

## References

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- United States Environmental Protection Agency (EPA). (2006). Report of food quality protection act (FQPA) tolerance reassessment and risk management decision (TRED) for methyl bromide, and reregistration eligibility decision (RED) for methyl bromide's commodity uses. EPA 738-R-06-026.

## Questions

1. What is the problem with replacing the pesticide methyl bromide with methyl iodide?
2. Alkyl halides are known to react with nucleophiles in a type of reaction called “substitution reaction.” There are two types of substitution reactions that alkyl halides can undergo. What are they and what is the main difference between them?
3. How does classification (primary, secondary, and tertiary) of an alkyl halide contribute to the type of substitution reaction that alkyl halide favors?
4. What prevents the tertiary alkyl halide from undergoing an  $S_N2$  reaction despite the presence of a good nucleophile?
5. The stereochemistry of an alkyl halide with a chiral center matters. How would it reflect in the configuration of the final product in each type of substitution reactions below (Figure 6)? Show the mechanism for the following two reactions.

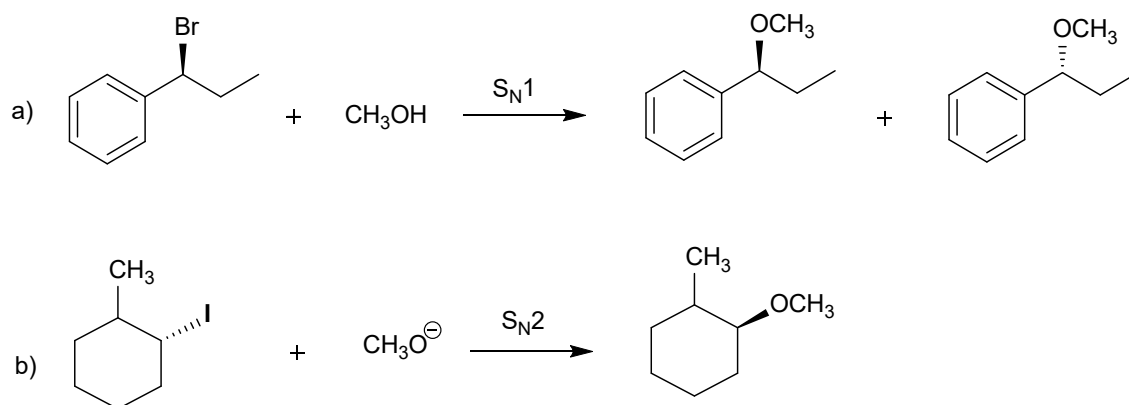


Figure 6. Substitution reactions.