

Chapter 7

Addition Reactions

In Chapter 6, elimination reactions were presented. In the context of elimination reactions, the formation of double bonds was noted regardless of the elimination mechanism discussed. Continuing from the concept of using elimination reactions to form sites of unsaturation, one may reason that **addition reactions** can be used to remove sites of unsaturation. Thus, elaborating upon addition reactions, this chapter provides an introduction to relevant **mechanisms** applied to both carbon–carbon double bonds (olefins) and carbon–oxygen double bonds (**carbonyls**).

7.1 ADDITION OF HALOGENS TO DOUBLE BONDS

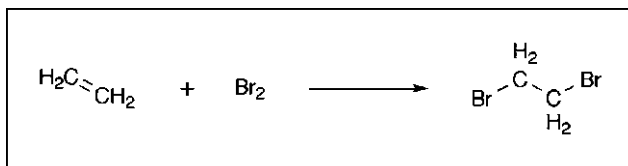
Throughout this book, the various mechanistic types driving reactions were shown to rely upon interactions between **charged species** such as nucleophiles and electrophiles. However, when looking at **ethylene**, the simplest of olefins, there are no partial charges (or steric factors) that distinguish one side of the double bond from the other. Due to its **symmetry**, there can be no pure nucleophilic or electrophilic sites. Furthermore, when looking at **bromine** in its natural form of Br_2 , there are no interactions between the two atoms other than a single and **unpolarized** bond joining them. Nevertheless, when ethylene and bromine are brought together, the reaction illustrated in Scheme 7.1 occurs.

To explain this reaction, consider the fact that, due to the overlapping *p* orbitals, double bonds are **electron rich**. This property allows olefins, under certain conditions, to act as nucleophiles. In the case of a double bond reacting with molecular bromine, the result is formation of a **three-membered ring** containing a positively charged bromine atom. This three-membered ring is known as a bridged **bromonium ion**. Concurrent to formation

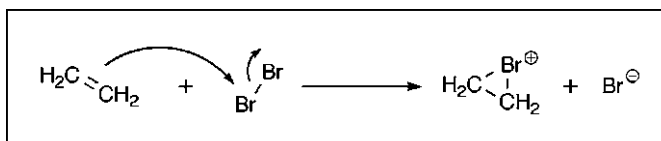
Arrow Pushing in Organic Chemistry: An Easy Approach to Understanding Reaction Mechanisms.

By Daniel E. Levy

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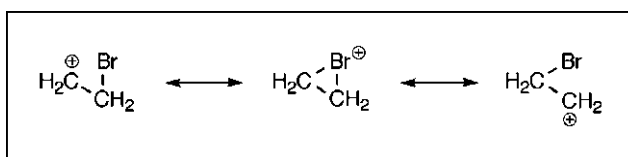
Scheme 7.1 Addition of bromine to ethylene.



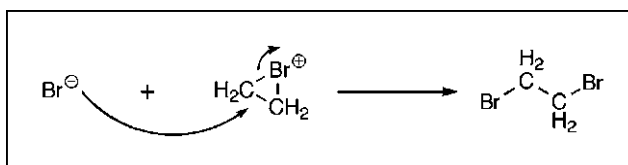
Scheme 7.2 Molecular bromine reacts with double bonds, generating a bromonium ion and a bromide anion.

of this species, a **bromide anion** is *displaced*. The initial reaction between bromine and ethylene is illustrated in Scheme 7.2 using arrow pushing.

Once the bromide anion becomes liberated from its parent molecular bromine, it is free to act as a nucleophile. Due to the positive charge residing on the bridged bromonium ion, the adjacent carbon atoms now possess partial positive charges. This is due to the positively charged bromine pulling **electron density** from the carbon atoms. The electrophilic nature of the adjacent carbon atoms is illustrated in Scheme 7.3 using resonance structures. Because the **carbon atoms** are now electrophilic, they are susceptible to reaction with the bromide anion that has dissociated as shown in Scheme 7.2. As illustrated in Scheme 7.4, using arrow pushing, this sequence of events leads to the formation of **1,2-dibromoethane**.



Scheme 7.3 Bromonium ions possess electrophilic carbon atoms.



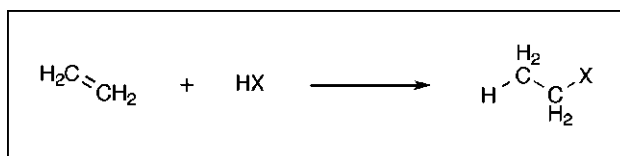
Scheme 7.4 Nucleophilic reaction between a bromide anion and a bromonium ion generates 1,2-dibromoalkanes.

7.2 MARKOVNIKOV'S RULE

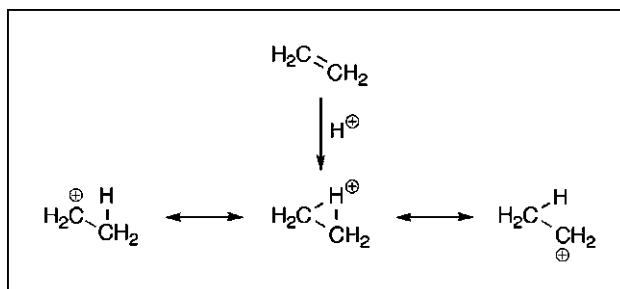
Diatomic halogen molecules such as bromine are not the only chemicals that can add across double bonds. In fact, any **protic acid**, under the proper conditions, can undergo such reactions. Specifically, as shown in Scheme 7.5, reaction of ethylene with an acid, HX, where X is OH, CN, or any halide produces a substituted ethane.

Mechanistically, the addition of acids across double bonds is very similar to the reaction of olefins with **halogens**. To understand this, it is important to recognize the electron-rich character of double bonds described in Section 7.1. With this property of olefins in mind, one recognizes that double bonds can become protonated under acidic conditions. As illustrated in Scheme 7.6, **protonated olefins** are electronically very similar to the bromonium ion shown in Scheme 7.3 and, as such, can be described with **charge-delocalized resonance structures**. Furthermore, these resonance structures are identical to those conceptually presented in Chapters 5 and 6 during discussions of hyperconjugation. Recall that hyperconjugation is the effect leading to stabilization of carbocations (Chapter 5) as well as being the driving force behind 1,2-hydride shifts (Chapter 6). Bringing these concepts into the addition of protic acids to olefins, the step following protonation (illustrated in Scheme 7.7) is no different than the second step of an S_N1 substitution reaction.

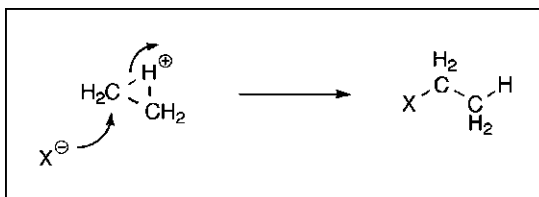
Unlike the addition of halogens across double bonds, addition of acids results in formation of **asymmetrical products**. Specifically, a different group is added to each side of the double bond. Thus, if this reaction is applied to **asymmetrical olefins** such as **propene**, multiple products might be expected to form as illustrated in Scheme 7.8. In fact, while a mixture of products is formed, there is an overwhelming presence of the **secondary substituted product** compared to that with substitution at the **primary position**. This preference of reaction products resulting from addition of protic acids across double bonds is governed by **Markovnikov's rule**.



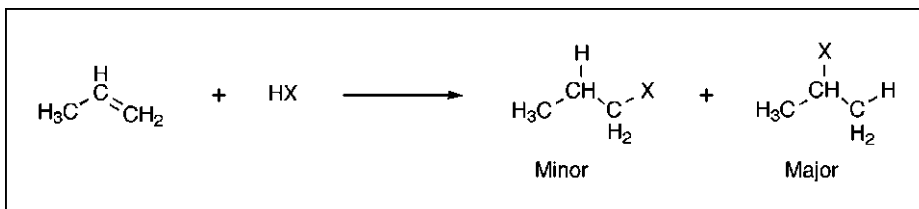
Scheme 7.5 Protic acids can add across double bonds.



Scheme 7.6 Double bonds can become protonated under acidic conditions.



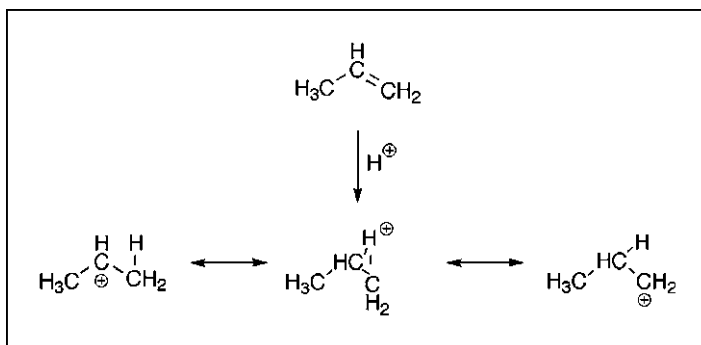
Scheme 7.7 Nucleophiles add to protonated olefins.



Scheme 7.8 Multiple potential products are possible from addition of protic acids across double bonds.

To understand the mechanistic basis behind Markovnikov's rule, it is useful to refer to the mechanisms through which acids add across double bonds. Of particular relevance are the resonance forms of the protonated olefins illustrated in Scheme 7.6. Since, for ethylene, the two carbon atoms are both primary, there is no distinction between them. However, as illustrated in Scheme 7.9, in the case of propene, protonation of the olefin results in introduction of **cationic character** to both a **primary carbon atom** and a **secondary carbon atom**.

Referring to the discussions presented in Chapter 5 regarding the relative stabilities of carbocations (and hyperconjugation), we are reminded that tertiary carbocations are more stable than secondary carbocations, which, in turn, are more stable than primary carbocations. Since, as shown in Scheme 7.9, protonation of propene results in cationic character at both a secondary carbon and a primary carbon, a greater presence of cationic character on the secondary site is expected compared to the primary. This allows



Scheme 7.9 Protonation of propene introduces cationic character to both primary and secondary centers.

a nucleophile to add, preferentially, to the secondary site generating the reaction outcome presented in Scheme 7.8. Thus, in general, Markovnikov's rule states that *when an acid is added across a double bond, the conjugate base adds to the more substituted carbon atom.*

7.3 ADDITIONS TO CARBONYLS

Olefins, in the absence of attached **polarizing groups**, generally react as described above with reactivity mediated through the nucleophilicity of the double bond. However, replacing one of the olefinic carbon atoms with oxygen results in formation of a polar carbonyl. As shown in Figure 7.1, the polarity is described through placement of a partial negative charge on the oxygen and a partial positive charge on the carbon. Discussions describing the polarity of carbonyls (and other functional groups), based on the electronegativities of the various atoms involved, were presented in Chapter 1. Addition reactions involving carbonyls are discussed in the following paragraphs.

7.3.1 1,2-Additions

Because of the inherent polarity associated with carbonyl groups, nucleophiles are drawn to the carbonyl carbon atoms in much the same way that nucleophiles participate in S_N2 reactions. This mechanism, alluded to in several problems presented in previous chapters, is illustrated in Scheme 7.10 using arrow pushing. As shown, a bonding pair of electrons joining the carbonyl oxygen atom to its associated carbon atom acts as the leaving group, placing a full negative charge on the oxygen atom. Generally, this type of reaction

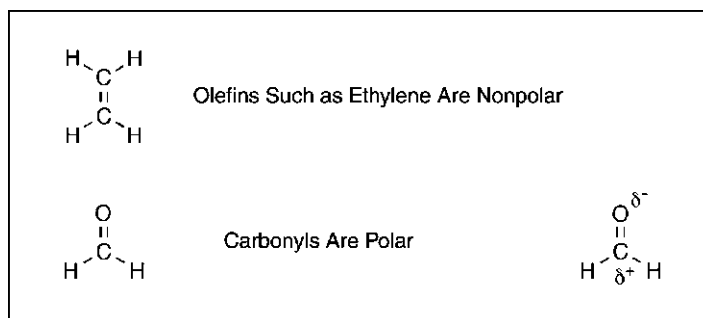
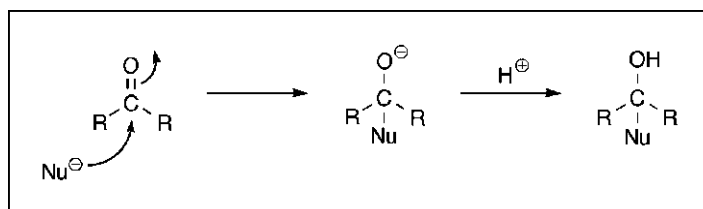
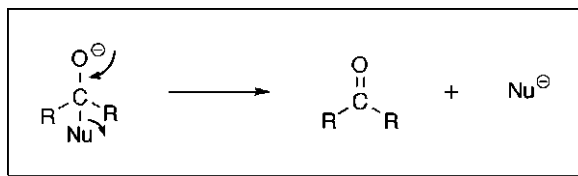


Figure 7.1 While unsubstituted olefins are not polar, carbonyls are polar.



Scheme 7.10 Nucleophiles can add to carbonyls to form alcohols.

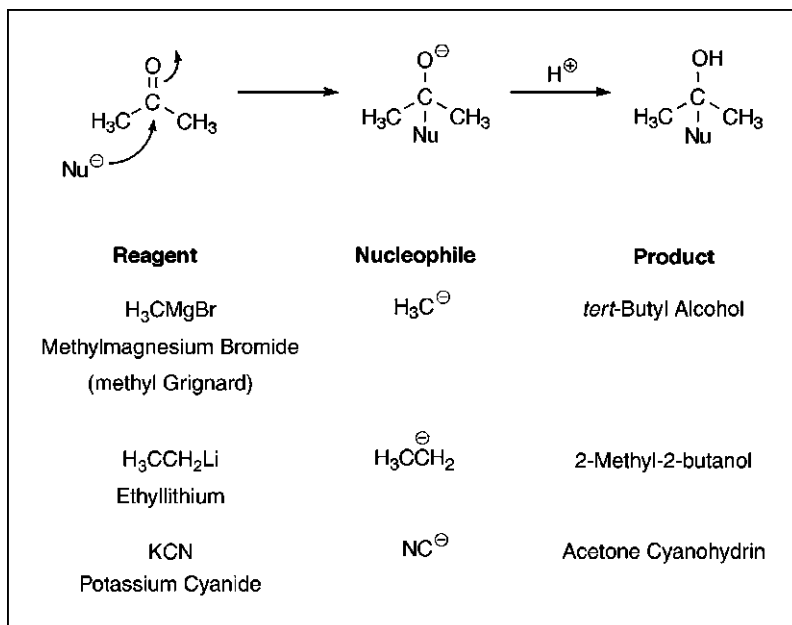


Scheme 7.11 Addition of nucleophiles to carbonyls is reversible.

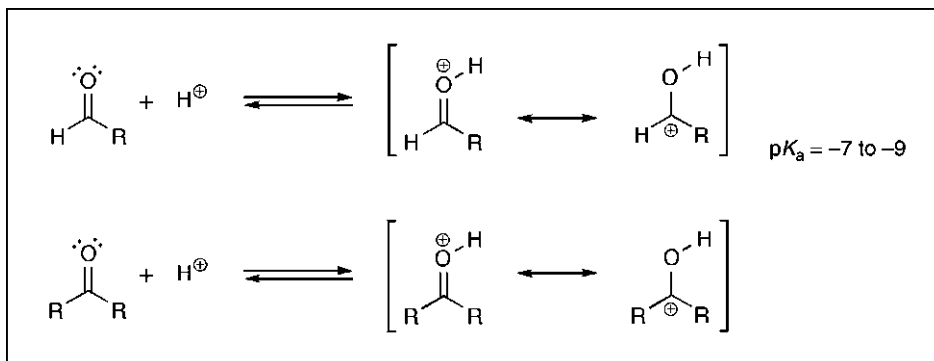
produces alcohols from carbonyls. Because of the trigonal planar geometry of a carbonyl group, there is no stereochemical preference associated with these addition reactions.

When considering reactions involving the addition of nucleophiles to carbonyls, it is important to understand that many nucleophiles can also serve as leaving groups. Therefore, to prevent the reverse reaction (elimination of the added nucleophile) illustrated in Scheme 7.11, **carbon-based nucleophiles** are generally utilized. Such nucleophiles include, but are not limited to, **Grignard reagents**, **alkyllithium reagents**, and **potassium cyanide**. In the case of Grignard and alkyllithium reagents, the result is formation of alcohols. Using potassium cyanide, **cyanohydrins** are formed. These reagents and the products of their reactions with acetone are illustrated in Scheme 7.12.

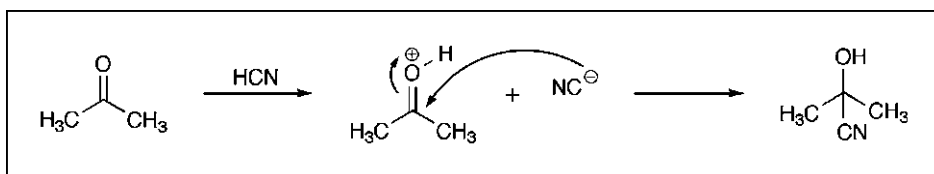
Thus far, all examples related to the addition of nucleophiles to carbonyls involve basic (anionic) conditions. However, such conditions are not required. Recalling that a carbonyl oxygen atom possesses a partial negative charge, we recognize that under acidic conditions it can be protonated. The protonation of carbonyl groups, illustrated in Scheme 7.13, was discussed in Chapter 3. Thus, as shown in Scheme 7.14 using acetone, treatment of



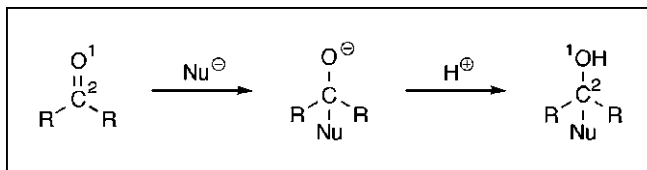
Scheme 7.12 Products resulting from addition of nucleophiles to acetone.



Scheme 7.13 Carbonyls can become protonated.



Scheme 7.14 Addition of nucleophiles to carbonyls can occur under acidic conditions.



Scheme 7.15 Addition of nucleophiles to simple carbonyls results in 1,2-additions.

carbonyls with acids such as HCN (**hydrocyanic acid**) provides another route for the formation of functional groups such as cyanohydrins.

If, as shown in Scheme 7.15, the atoms of a carbonyl are numbered with 1 representing the oxygen and 2 representing the electrophilic carbonyl carbon atom, we notice that addition of a nucleophile to the carbonyl results in the introduction of a new substituent at atom 2. Therefore, this type of addition is known as a **1,2-addition**.

7.3.2 1,4-Additions

The concept of S_N2 reactions was presented in Chapter 4. In the context of this discussion, the S_N2 mechanism was extended to allylic systems. These **allylic displacements**, because of their mechanistic similarities to S_N2 reactions, were designated S_N2' reactions. A representation of an S_N2' mechanism, compared to an S_N2 mechanism, is illustrated in Figure 7.2 using arrow pushing.

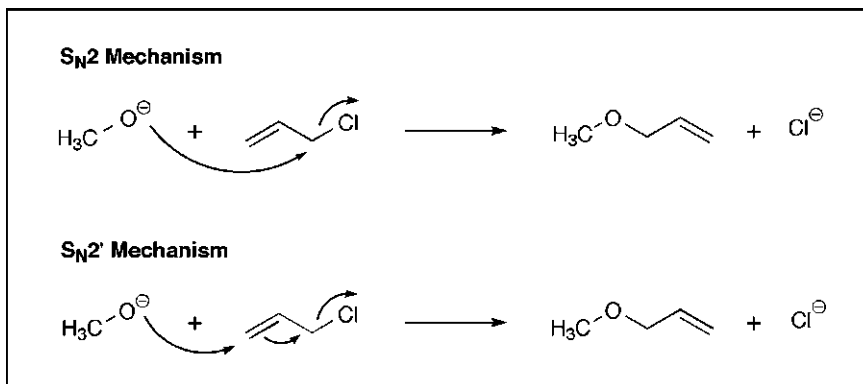
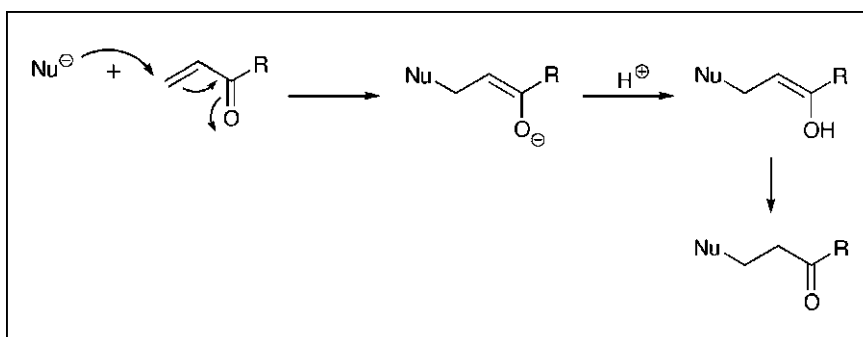


Figure 7.2 Comparison of S_N2 and S_N2' reactions as explained using arrow pushing.

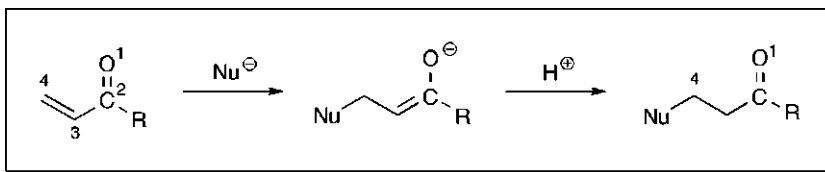


Scheme 7.16 Addition of nucleophiles to α,β -unsaturated carbonyl groups as explained using arrow pushing.

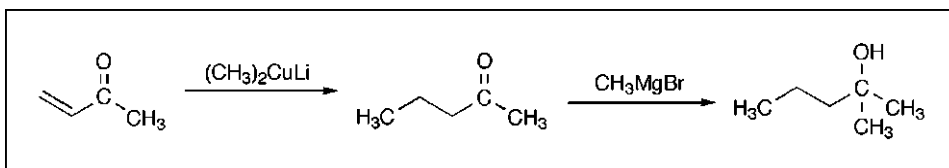
In Section 7.3.1, the addition of nucleophiles to carbonyls was directly compared to S_N2 reactions. In recognition of these mechanistic similarities, one may anticipate that nucleophiles can similarly add to **α,β -unsaturated carbonyl** systems. Such additions are, in fact, common and, as such, are illustrated in Scheme 7.16 using arrow pushing. As shown, the nucleophile initially *adds* to the double bond with delocalization of the negative charge into the carbonyl group generating an **enolate anion**. Once treated with acid, the enolate anion becomes protonated and forms an enol. **Enols**, being high-energy species, readily isomerize and regenerate the carbonyl functionality.

If, as shown in Scheme 7.17, the atoms of an α,β -unsaturated carbonyl are numbered with 1 representing the oxygen, 2 representing the carbonyl carbon atom, and 3 and 4 sequentially representing the adjacent two olefinic carbon atoms, we notice that addition of a nucleophile in the manner illustrated in Scheme 7.16 results in the introduction of a new substituent at atom 4. Therefore, this type of addition is known as a **1,4-addition**.

While 1,4-additions to carbonyls are common, it is important to recognize that the same α,β -unsaturated carbonyl systems are also subject to 1,2-additions. Fortunately, these two types of additions are highly dependent upon the form of the nucleophiles used.



Scheme 7.17 Addition of nucleophiles to α,β -unsaturated carbonyls can result in 1,4-additions.



Scheme 7.18 α,β -Unsaturated carbonyl systems can be sequentially subjected to 1,4-additions and 1,2-additions.

For example, simple organometallic reagents such as alkyllithium reagents and Grignard reagents tend to participate in 1,2-additions while **organocuprates** generally participate in 1,4-additions. These trends, however, are not absolute, and the reader is referred to general organic chemistry textbooks for broader and more detailed treatments of these addition mechanisms.

In a final consideration regarding 1,2- and 1,4-addition reactions, α,β -unsaturated carbonyl systems can be sequentially subjected to both mechanisms. As illustrated in Scheme 7.18, if **methyl vinyl ketone** is treated first with **dimethylcopperlithium** and then with **methylmagnesium bromide**, the resulting product is **2-methyl-2-pentanol**.

7.3.3 Addition–Elimination Reactions

In our present discussions, 1,2- and 1,4-additions to carbonyl systems were introduced. However, these reactions were not presented in the context of specific carbonyl-based functional groups. Expanding upon this concept, the three types of functional groups generally used in **addition reactions** to carbonyls are aldehydes, ketones, and esters.

With respect to all of the above-mentioned functional groups, 1,4-additions are generally applicable. However, of these three groups, only aldehydes and ketones are generally useful as substrates for 1,2-additions. Figure 7.3 illustrates the products resulting from both 1,2- and 1,4-additions of nucleophiles to aldehydes, ketones, and esters. As shown, while the products of 1,4-additions all result in retention of the carbonyl functionality, 1,2-additions result in conversion of the respective carbonyl groups into alcohols. However, when an ester is involved, the illustrated product is a ketone and retains the carbonyl of the starting ester.

In examining the mechanism leading to the nucleophile-mediated conversion of an ester to a ketone, initial addition of a nucleophile to the carbonyl results in formation of a **hemiacetal** intermediate. Subsequent **collapse** of the hemiacetal intermediate liberates a ketone and an **alkoxide leaving group**. This mechanistic sequence, illustrated in Scheme 7.19

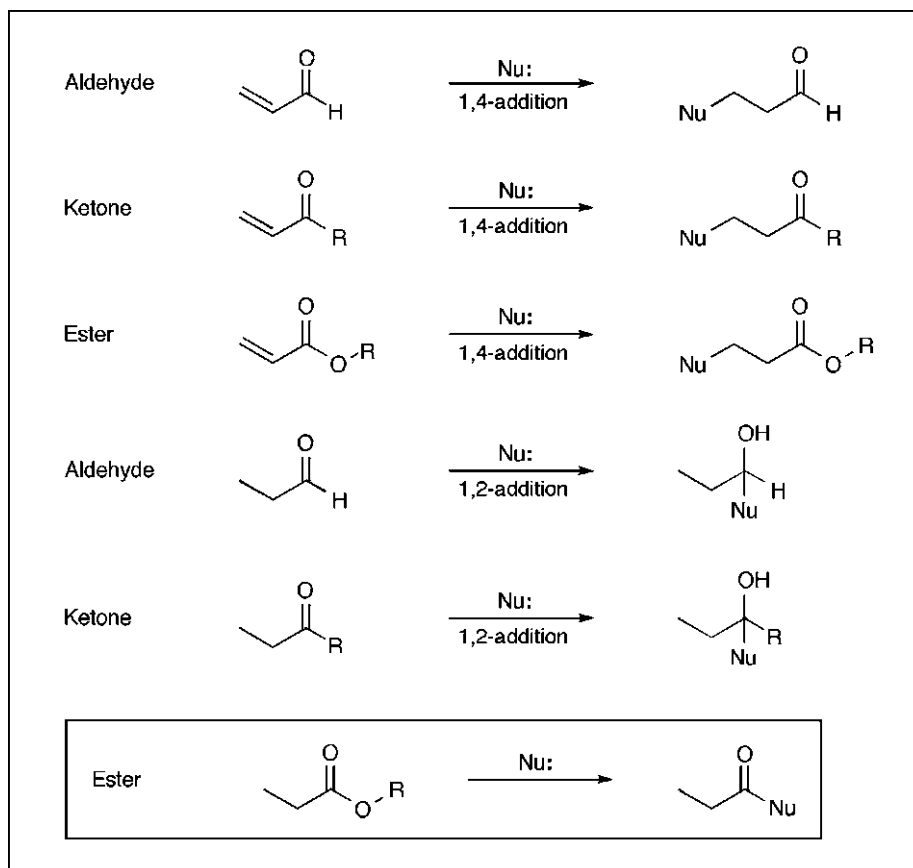
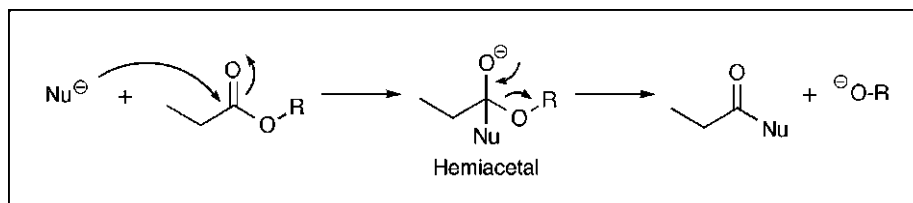


Figure 7.3 Unlike most carbonyl-based functional groups, nonconjugated esters can react with nucleophiles and retain the carbonyl unit.

using arrow pushing, is known as an addition–elimination and involves initial addition of a nucleophile to a carbonyl followed by elimination of an alkoxide leaving group. As a cautionary note, the conversion of esters to ketones can be difficult to control due to sequential reaction of the newly formed ketones with nucleophiles present in the reaction mixture.

Addition–elimination reactions are not exclusive to esters. In fact, these reactions can occur with any carbonyl-based system where the leaving group is a weaker nucleophile



Scheme 7.19 The addition–elimination mechanism illustrated with arrow pushing.

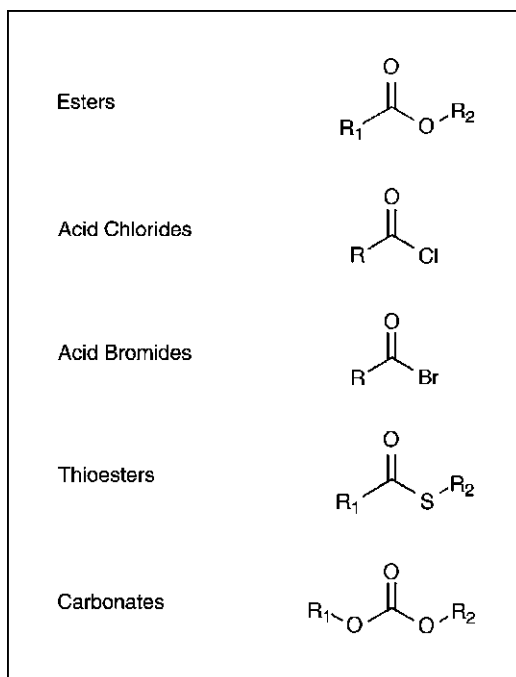


Figure 7.4 Functional groups capable of participating in addition–elimination reactions.

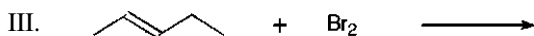
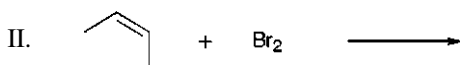
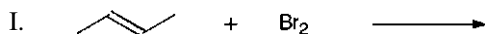
than that initially reacting. Such systems, illustrated in Figure 7.4, include, but are not limited to, esters, **acid halides**, **thioesters**, and **carbonates**. Finally, when predicting the products of potential addition–elimination reactions, guidance is readily obtained through consideration of the relative pK_a values of the respective nucleophiles and leaving groups.

7.4 SUMMARY

In this chapter, the principles presented in Chapter 4 (S_N2 reactions) were extended into olefinic and carbonyl-based systems. In exploring these areas, the electronic properties and nucleophilic/electrophilic nature of these groups were discussed. Finally, discussions of nucleophilic additions into these functionalities were extended into conjugated unsaturated systems leading to strategies for the incorporation of diverse modifications to relatively simple substrates. Specifically, this diversity of modifications becomes much more apparent when combining the principles presented in this chapter with those of Chapters 4 and 6. All of these principles will be useful when working through the problems of this chapter as well as advancing through introductory organic chemistry coursework.

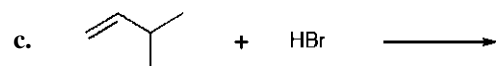
PROBLEMS

1. Predict the products of the following reactions and then answer the following questions. Consider stereochemistry.

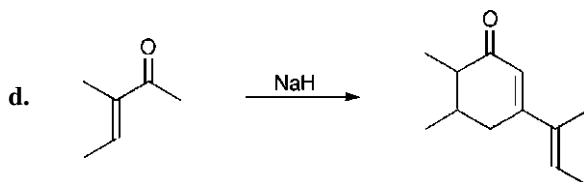
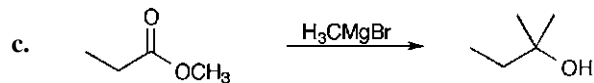
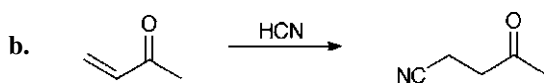
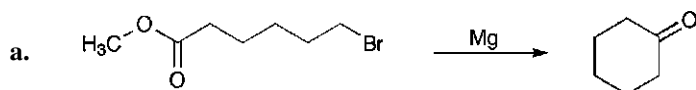


- a. Are the products of reactions I and II the same or are they different? Explain your answer.
- b. How do you account for the products of reactions I and II?
- c. Are the products of reactions III and IV the same or are they different? Explain your answer.

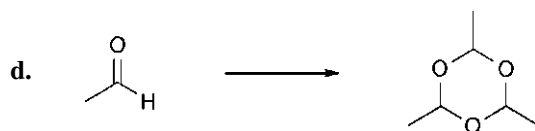
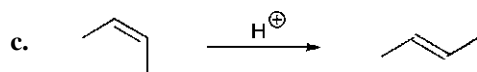
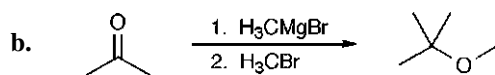
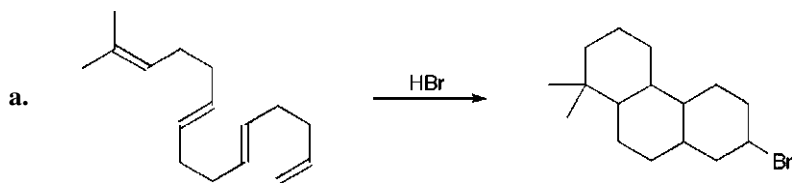
2. Predict all of the products of the following reactions:



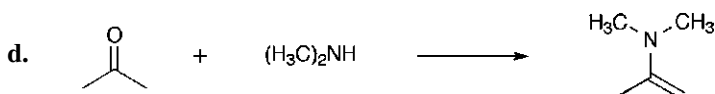
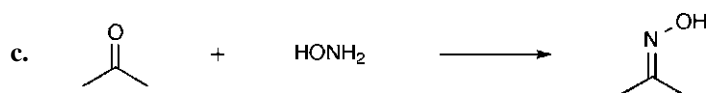
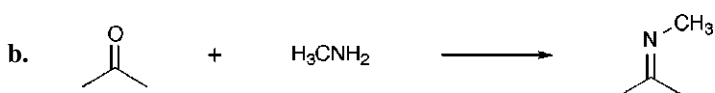
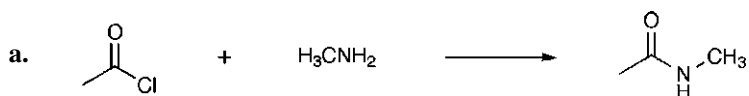
3. Explain the results of the following reactions. Use arrow pushing and specify mechanistic types.



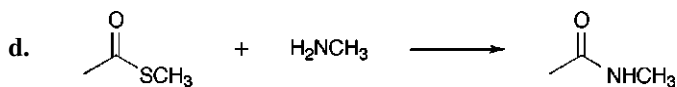
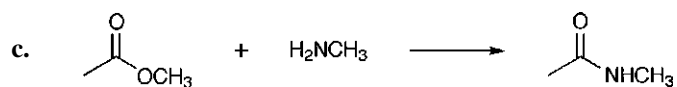
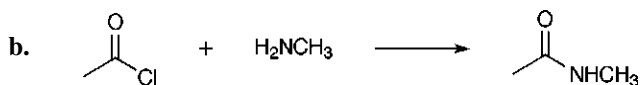
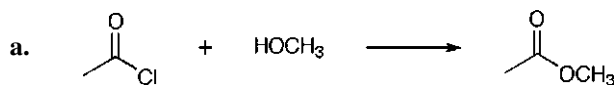
4. Explain the following reactions in mechanistic terms. Show arrow pushing.



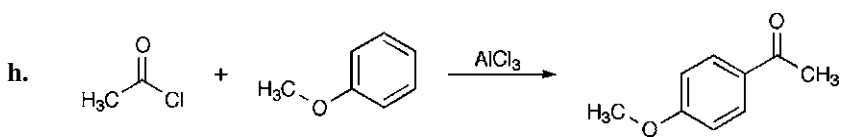
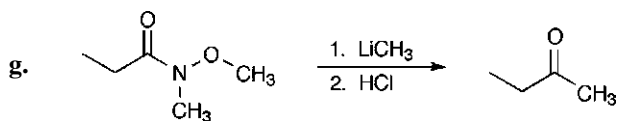
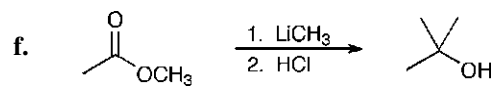
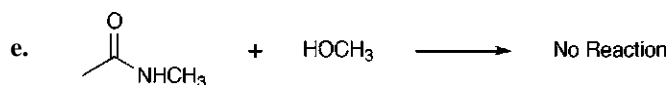
5. Explain the following products resulting from the reaction of amines with carbonyls. Use arrow pushing and specify mechanistic types.



6. Provide mechanisms for the following reactions. Show arrow pushing.



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7. Explain the following amide-forming reactions using arrow pushing. Specify the structures of **A**, **B**, and **C** and show all relevant mechanistic steps.

