Organic Chemistry-2
Semester-2, CBCS
Course: CEMA CC-2-3-TH

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Recommended texts:
Elimination reactions:

When tert-butyl bromide is treated with ethanolic alkali, there is formed isobutene with the removal of a hydrogen and the bromine from the starting organobromide:

This is known as an elimination reaction. In this case it involves the removal of the elements of hydrogen bromide (dehydrobromination) from adjacent carbons to generate a π-bond.

This is an example of a 1,2-elimination because it entails removal of ligands from adjacent carbons. It is also called β-elimination because the hydrogen β- to the leaving group bromide is eliminated.

So, how does it happen?

Due to its high charge density, the hydroxide ion is a good nucleophile as well as a good base (conjugate acid water, pKa 15.7). When faced with an organohalide, it has two choices. Either it can directly attack the α-carbon and displace the halide to generate an alcohol - that would be a substitution reaction, or, it can pick off one of the β-protons available and simultaneously induce the removal of the bromide from the α-carbon to generate a double bond - this is the elimination reaction.

Organic Chemistry is replete with examples where one reagent sometimes acts as a base, and sometimes as a nucleophile. This is known as the base-nucleophile dichotomy. The key is to understand which behaviour would dominate in what condition.
Elimination reactions:

Both reaction proceed in a single step.

These reactions may occur together on the same substrate and generally they do go hand in hand, i.e. whenever there is some SN2, there is a chance that E2 may also accompany it.

However, in many cases, either of these two may happen in preference over the other and consequently either the SN2 or the E2 product dominates the product mixture.

One of the factors that decides which one would actually occur preferentially is the substrate structure, and in this case, a nucleophilic attack on the α-carbon of the sterically hindered tert-butyl bromide is strongly discouraged, thereby suppressing the SN2 reaction. The hydroxide ion rather attacks any one of the nine β-protons and goes for the E2 reaction here.

In this one-step mechanism, two molecules, namely the t-butyl bromide and the hydroxide ion are involved in the RDS. Therefore, the concentrations of both these species appear in the rate equation, which is second-order overall:

\[
\text{Rate} = k_2 [\text{t-BuBr}][\text{HO}^-]
\]

As the C(β)-H bond is broken in the RDS (for the single step reaction, the only step is the RDS), we expect to see a PKIE for an E2 reaction with a properly deuterated substrate where all possible β-hydrogens have been replaced with deuterium.

Ethoxide-induced dehydrobromination of 2-bromopropane was used for this purpose and as expected, a much slower elimination reaction for the deuterated analogue was observed.
Elimination reactions:

Eliminations are, however, not limited to the E2 variety. There are plenty of examples of unimolecular eliminations as well.

Consider the reaction of t-butyl bromide when it is dissolved in ethanol. We do not expect SN2 as the substrate is tertiary and we don’t expect E2 either because there is no strong base (such as hydroxide) present to abstract the proton from the β-position.

Nonetheless, over time, both elimination and substitution products would be observed! 

\[
\begin{align*}
\text{Me} & \quad \text{Me} & \quad \text{Me} & \quad \text{Br} & \quad \text{EtOH} & \quad \text{Me} & \quad \text{Me} & \quad \text{Me} & \quad + & \text{Me} & \quad \text{Me} & \quad \text{OEt} \\
\text{elimination product} & & & & & & & & & & & & & & & & & \text{substitution product}
\end{align*}
\]

How are these forming then?

In the polar, protic reaction medium that is ethanol, the tertiary bromide is slowly ionizing to afford a tertiary-butyl cation and a bromide ion via heterolytic cleavage of the C-Br bond.

This cation has two fates. It can either be captured by the solvent ethanol and eventually go over to the ether (substitution product), or, ethanol can pick off one of the β-protons and lead to the formation of the isobutene (elimination product).

The RDS is common for the substitution and the elimination reaction in this case and only the organohalide is involved in that step. These are therefore a unimolecular reactions, SN1 and E1 respectively.

As expected form the mechanisms outlined above, these reactions have a common rate law which is overall first order:

\[
\text{Rate} = k_1 [t\text{-BuBr}]
\]

It is clear then that like the SN2 and E2 pair, SN1 and E1 reactions also go hand in hand and whenever there is SN1, there is bound to be some E1 as well. Again, there are several factors that control which one would dominate in any particular case but we will deal with them later. It is also clear that formation of a relatively stable carbocation and a reaction medium conducive for ionisation are a pre-requisite for these processes to occur.

Point to note that E1 is unimolecular, but like E2, it is also a 1,2- or β-elimination as the units of H-Br are eliminated from the adjacent carbons. The timing of the bond cleavage is different in E2 and E1.

The C(α)-Br and the C(β)-H bonds are cleaved simultaneously, in concerted manner in E2, but in the E1 it is a two-step process: the C(α)-Br bond is broken in the first step while the C(β)-H bond is cleaved in the next, non-rate-limiting step and a distinct carbocation intermediate is involved here.

Unlike E2, E1 mechanism does not show any hydrogen PKIE as the C-H bond breaks only after the RDS is over. However, E1 reactions, like SN1, show SKIE.
Elimination reactions:

The third variant of elimination reaction is E1cB. As the name suggests, it is also an unimolecular process.

But the timing of the bond cleavage is different from those observed in E2 and in E1. In this case, the C(\(\beta\))-H is abstracted by a strong base (B\(^-\)) in a reversible first step, generating a carbanion through an acid-base reaction. This conjugate base (cB, don't confuse this B with B\(^-\)) of the substrate then loses the leaving group (X) from the \(\alpha\)-carbon in a second, rate-determining, slow step:

The mechanism derives its name from the fact that this elimination proceeds via formation of the conjugate base of the substrate and because only one molecule (the conjugate base) is involved in the RDS.

What should be the rate law for it?

The rate of the reaction depends upon the concentration of the carbanion (i.e. the cB) but we are not adding it directly into the reaction medium.

Rather, the cB forms in situ by a reaction with the substrate (R-X) and the base. So the concentration of the carbanion is directly proportional to the concentrations of these two species and the rate law is thus just like that of an E2 reaction!

\[
\text{Rate} = k_2 [RX][B^-]
\]

Clearly, we cannot distinguish between the E2 and the E1cB reaction just by determining the respective rate laws, something that we can do for E1 and E2 pair.

Then how may we do it?

We shall discuss this issue later. But for now, try to appreciate the fact that for an E1cB reaction to occur, not only do we need the presence of a strong base (just as in E2), but also, the substrate must satisfy the following two conditions:

i) the \(\beta\)-hydrogen must be unusually acidic (otherwise the cB won't form easily), and

ii) the leaving group has to be an unusually poor one (if it were a good leaving group, E2 will take over).

What makes a bad leaving group?

One of the factors that is responsible is the strength of the C-X bond. If it is a strong bond, one needs a higher amount of energy to break it. Thus that leaving group is bad. Case in point are the C-F and C-I bonds. The former is much stronger than the latter (why?) and thus fluoride is a poorer leaving group than iodide.

Consequently, there is much greater chance of E1cB happening for an organo-fluoride and much less so with an organo-iodide. The following is an example of an E1cB reaction:

\[
\begin{align*}
\begin{array}{c}
\text{Cl} \quad \text{Cl} \\
\text{F} \quad \text{F}
\end{array}
\text{NaOMe} \rightarrow \\
\begin{array}{c}
\text{Cl} \quad \text{F} \\
\text{C} \quad \text{=} \quad \text{F}
\end{array}
\begin{array}{c}
\text{Cl} \\
\text{F}
\end{array}
+ \text{NaF} + \text{MeOH}
\end{align*}
\]

the \(\beta\)-H is acidic, because the cB is stabilised by -

i) vacant d-orbital conjugation with Cl atoms

\([p_{\pi}(C)-d_{\pi}(Cl)]\)

ii) the -I effect of the CF\(_3\) group
Elimination reactions:

Relation between E2, E1 and E1cB mechanisms:

The relationship between the **one-step E2 mechanism** and its **two-step alternatives E1 and E1cB** can be understood using a reaction map. An elimination reaction is envisaged that can proceed via either of the three mechanisms mentioned:

Notice that the basic point of difference between the three alternatives is the timing of the C(α)-X and the C(β)-H bond cleavages.

The following table summarises these timings:

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Number of steps</th>
<th>Cleavage of</th>
<th>Nature of the intermediate</th>
</tr>
</thead>
<tbody>
<tr>
<td>E2</td>
<td>1</td>
<td>Simultaneous, concerted</td>
<td>No int. involved</td>
</tr>
<tr>
<td>E1</td>
<td>2</td>
<td>Step-1</td>
<td>Step-2</td>
</tr>
<tr>
<td>E1cB</td>
<td>2</td>
<td>Step-2</td>
<td>Step-1</td>
</tr>
</tbody>
</table>

We shall plot all three mechanisms together in a three-dimensional reaction plot where one horizontal axis (top to bottom) measures the degree of C(α)-X bond breaking, the other horizontal axis (right to left) measures the degree of C(β)-H bond breaking and the vertical third axis represents energy.

For the sake of convenience and quick drawing we shall represent the reaction plot in two dimensions where only the two horizontal axes will be seen, the third axis is imagined to stand perpendicular to the paper, projecting towards you.

This is known as the More O’Ferral- Jencks plot which looks like the following where the initial state (M, reactants - organohalide and the base) is at the top right hand corner and the final state (N, products - the alkene, conjugate acid of the base and the halide) is at the bottom left corner.

Focusing only on the substrate, we can say that the points marked in the reaction plot represents the following structures: Point M: the substrate. Point N: the alkene, Point O: the carbocation intermediate involved in the E1 pathway, Point P: the conjugate base of the substrate which is the intermediate in the E1cB pathway.

The TSs associated with each steps are designated with ± sign. Thus the diagonal path M to N represents the E2 mechanism, path M to N via O represents the E1 mechanism and path M to N via P represents the E1cB mechanism.
Elimination reactions:

Relation between E2, E1 and E1cB mechanisms:

The many shades of E2:

The E2 mechanism involves a bimolecular TS where removal of an \( \alpha \)-proton is concerted with the departure of the leaving group (X). But rarely do these two bonds break in a *synchronous* (i.e. proceed to the same extent) fashion.

In many cases of the \( \text{C(}\alpha\text{)}\)-H bond breaking *either exceeds or lags behind* the \( \text{C(}\beta\text{)}\)-X bond breaking.

Depending upon which one of these two is happening, the corresponding TSs acquire either some carbanion-like or carbocation-like appearance.

Extent of \( \text{C(}\alpha\text{)}\)-H bond breaking >

extent of \( \text{C(}\beta\text{)}\)-X bond breaking.

Extra electron density on the \( \beta \)-carbon; TS resembles a carbanion.

Extensive drawing of E1cB-like TS

Extensive drawing of E2 TS

Extensive drawing of E1-like TS

No full-blown carbocation or carbanion is formed here as by definition, the E2 mechanism is one-step and does not allow for any intermediate to form. It's only the approximate structures of the TSs that we speak of here.
Elimination reactions:

Relation between E2, E1 and E1cB mechanisms:

The pathway M to N with a slight downward curvature represents an E2 reaction which has E1-like nature.
As the E2 reaction becomes increasingly E1-like, the plot starts to shift from the diagonal towards the bottom left corner.
This pathway is encouraged by i) good leaving groups and ii) groups that stabilize the developing partial positive charge.
Therefore, if X is a good leaving group and R is an ERG the reaction will be E2 with E1-like nature.
Greater these characters, higher is the E1-like behaviour. This pathway is further promoted by use of a weak base and polar, ionizing solvents.

The TS for these reactions look like the following:

Similarly, the pathway M to N with a slight upward curvature represents an E2 reaction which has E1cB-like nature.
As the E2 reaction becomes increasingly E1cB-like, the plot starts to shift from the diagonal to the top right corner.
This pathway is encouraged by - i) poor leaving groups and ii) groups that stabilize the developing partial negative charge.
Therefore, if X is a bad leaving group and Z is an EWG the reaction will be E2 with E1cB-like nature. Use of strong base also promotes this mechanistic path.

The TS for these reactions look like the following:

Thus, with the help of the More-O’Ferrall - Jencks plot not only can we draw the E1-E2-E1cB mechanistic pathways together but it also helps us to understand that these three are but idealized situations which represent three variants of a continuum of mechanistic possibilities. The elimination reaction may proceed through transition states which are of intermediate character in terms of these limiting mechanistic types depending upon the variables discussed above.