

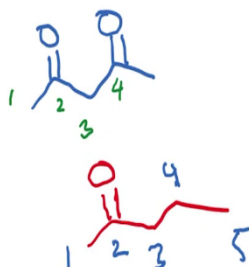
Introductory Organic Chemistry – II
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Indian Institute of Science Education and Research, Pune
Tutorial-5A

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Problem Set 5

Solutions

The pK_a of 2,4-pentanedione is 9. Draw out the equilibrium and reason out the high acidity of this compound when compared with 2-pentanone.

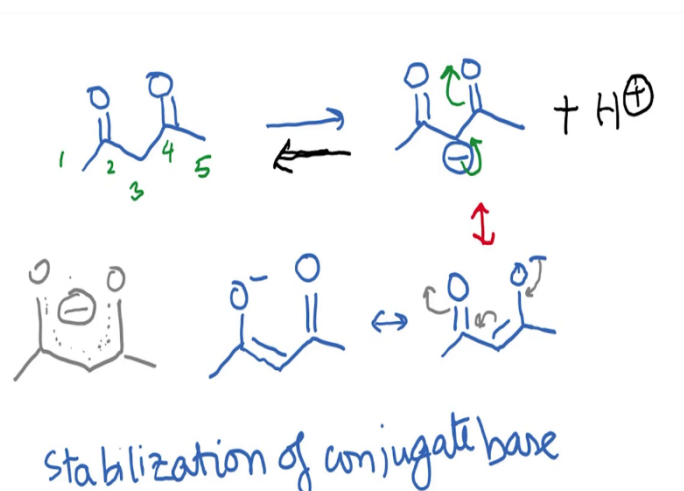


So, now let us look at the solutions to problems set 5. And as you may remember, this was something that we primarily deal with Enols and Enolates in this problem set. So, the first question here is that, the pK_a of 2,4-pentanedione is 9. So, draw the equilibrium and reason out the high acidity of this compound when compared with 2-pentanone. So, let us just draw out the structures of these compounds.

So, this is 2,4-pentanedione and 2-pentanone would be, basically the ketone is present only in position number 2, and the rest of the numbering is the same 1, 2, 3, 4, 5. So, if you see the

pKa of the carbonyl compounds, the carbonyl compounds, you have already studied this, in the past, they range somewhere between 20 and 25, and the most acidic of these would be around 18-19, or so. So, therefore, you know, there is a huge difference in the pKa levels of these two compounds. So, the question is, draw out the equilibrium and reason this out.

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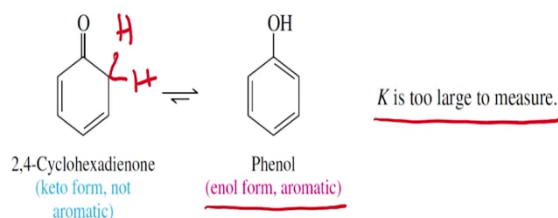
So, the way we would sort of draw out this equilibrium is in the following manner. So, this is the equilibrium arrow, and there would be H^+ that is being produced. So, you have 2,4-pentanedione, and as you can guess this is the most acidic proton. And so that is going to get deprotonated and it will form H^+ . And clearly the carbanion is not the stable form. And so, the carbanion is going to go and form the enolate.

And the important thing in this enolate is that the enolate can delocalize further and produce this other enolate over here. And so, in effect, you might have seen pictures of this in the following manner. So, you would have a dotted line, oxygen and oxygen, and you have a negative charge here. So, this is the kind of picture that we would draw out for this enolate. And therefore, the conjugate base of this acid is highly stabilized.

So, from our previous discussions, we know that the more stabilized the conjugate base, the better the acid, or we reason out acidity through measuring the stability of the conjugate base. And so here, the conjugate base being quite stable, the pKa value is quite low, which is 9. Now, let us move on to the next question.

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2. For the compound shown below, draw out the tautomer. Is the keto form more stable?

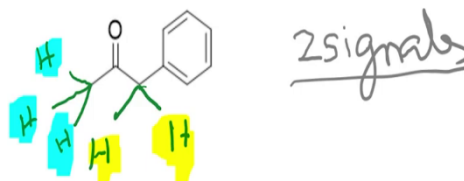


The next question here is for the compound shown below, draw out the tautomer. I think most of you could pretty much get this question very easily. So, you have these two hydrogens over here. Once the carbonyl compound tautomerizes, it is going to form the enol. And this enol is a very special enol, which is commonly known as phenol and in this enolization process, it has gained aromaticity.

And we all know that aromatic compounds are substantially more stable than their corresponding olefin counterparts. And so, when we try to detect the keto form in this compound, we are unable to detect it using a variety of experimental techniques. So, therefore, we can propose that the equilibrium constant is really, really large in favor of the phenol. So, the keto form is certainly not the stable form in this case.

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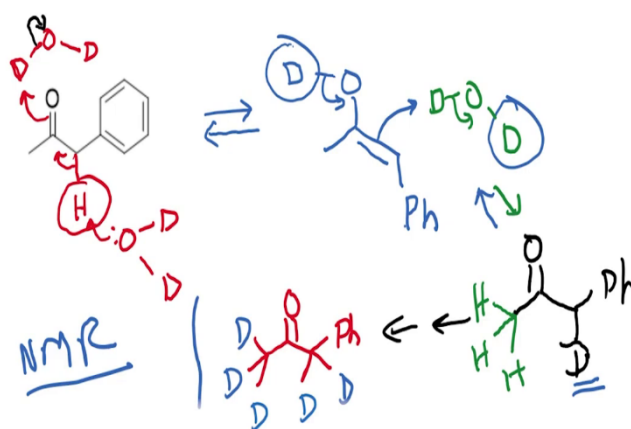
The following compound has 2 signals in the aliphatic region and signals in the aromatic region that correspond to the benzene ring. When D_2O was added to this, only aromatic signals remain. Explain



Now, the next question is basically, this compound here has 2 signals in the aliphatic region. So, therefore, if you look at it, these are the aromatic hydrogens as 1, 2, 3, 4, 5. But this is equivalent to this, this proton is equivalent to this and this is the third hydrogen, so therefore, you would have three distinct signals in the aromatic region. Now, correspondingly, the aliphatic region, you will have one, two, and these two signals are the same, because they are equivalent, these two hydrogens are equivalent.

And so, you will see one type of signal for these two hydrogens and these three hydrogens again are equivalent. And therefore, you would see another set of signals, which is what the question says is that you would see two signals in the aliphatic region. And now, when you dissolve this molecule, in D_2O . And if you measure the NMR spectrum again, you do not see a proton, you do not see any signal for the aliphatic region. And so, this is how we would reason this out.

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So, if you imagine that the molecule here has this kind of a structure, so we know that ketones can enolize, but the enol is not as stable as the ketone and therefore, we do not detect it using conventional analytical techniques. And so, you can imagine that this hydrogen can be pulled out by water, in this case D₂O. And correspondingly, even it forms the enolate, the enolate can again pick up a proton from D₂O.

And so, this is a neutral process, there is no loss or gain of H⁺ and it forms this tautomer which is shown here. Now, when the tautomer reverts to the keto form, it does not go back to this form because the dominant, you know although there is a small amount of, perhaps a small amount of H⁺ that is floating around that is derived from this, but you know the majority of the population of the solution is D₂O and so therefore, when the enol tautomerizes to form the ketone, it forms the deuterated ketone. And now, as you know this is an equilibrium.

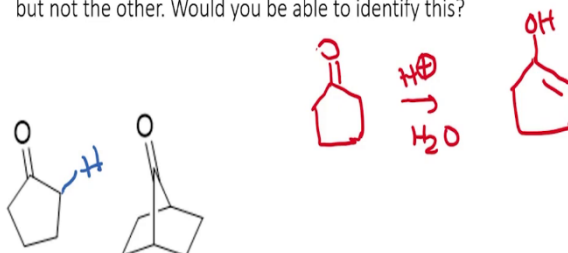
So, this is going to go back, if it goes back, it can enolize at the hydrogen or deuterium, but once in a while, if it enolizes in the hydrogen, you are going to end up, this process is going to repeat and you are going to get the di-deuterated form and then all of these hydrogens are going to get replaced by deuterium.

So, this is the product that you would expect to see in NMR. And therefore, you will not see any signal because as we discussed earlier, deuterium is NMR silent, proton NMR silent and therefore, you do not see a signal for this. So, when you add this molecule in D₂O the two

aliphatic signals completely disappear. Now, the aromatic signals do not disappear, because the aromatic hydrogens are not enolizable. And so, therefore, they remain attached to the carbon and do not dissociate. And so, the aromatic signals will continue to be present.

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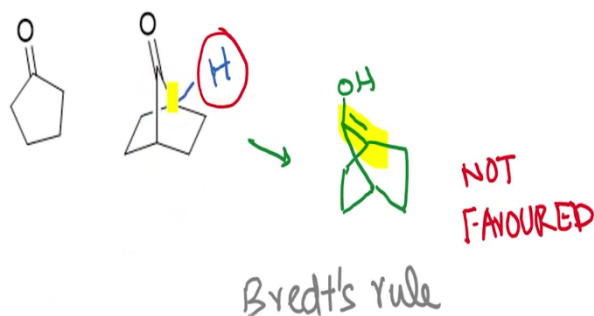
When the following compounds were dissolved in acetonitrile (solvent) and catalytic amount of H^+ was added, one of them produced an enol but not the other. Would you be able to identify this?



Let us move on to the next question. So, the question here is when the following compound is dissolved in acetonitrile and a catalytic amount of H^+ was added, and one compound you found that there was an enol produced and the other one there is no enol formation.

So, the way we would address this question is to start with cyclopentanone and when you add a catalytic amount of H^+ and H_2O , you can start detecting some level of enol that is being formed. And although it may not be in a very large concentration, but you can detect this.

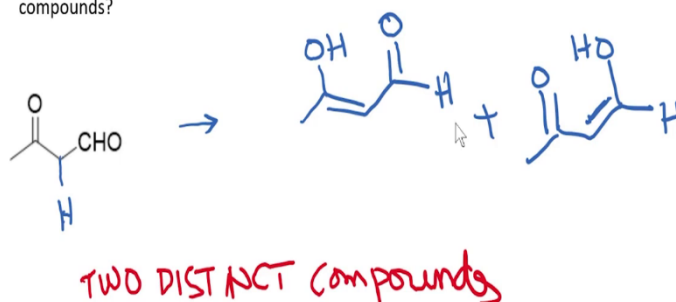
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Whereas in the other case, when you attempt to form the enol, although this hydrogen is enolizable, that is it is next to a carbonyl, once it forms the enol you produce a double bond across a bridge head and this clearly is not something that is favored. And in fact, there is a rule that sort of suggests that it is not possible and this is known as the Bredt's rule. And so, we could suggest that this compound is quite unstable and therefore it would not form. So, between the two compounds, the cyclopentanone is likely to form the enol whereas this compound here is unlikely to form the enol.

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When the following compound is dissolved in toluene, analysis reveals the disappearance of this compound and the formation of two distinct compounds. Mass spectral analysis shows no change in mass compared to the original compound. What are these two new compounds?



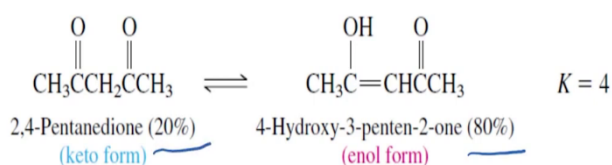
Now, moving on to the next question, here you are given this Di-carbonyl compound and analysis, when you dissolve this in toluene, as toluene is just a solvent and it shows the

disappearance of this compound, but the formation of two distinct compounds and then when we measure the mass spec of these two compounds, we find that it is identical to the starting material and so, that gives you a clue that these two compounds are tautomers.

And so, in principle, we could produce two different tautomers which is shown here. So, one is in which this ketone is going to form the enol and the other one in which the aldehyde is going to form the enol. And so, for example, you can detect this using even conventional techniques such as TLC analysis, you may form two different compounds, you will be able to see this in other techniques as well. So, these are what I think are the two compounds that are formed.

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2,4-Pentanedione exists in solution with its enol form with an equilibrium constant of 4. Calculate the % keto form in solution



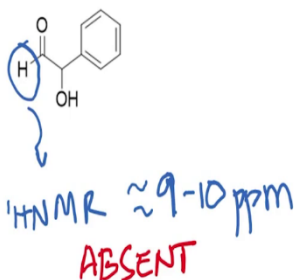
$$K = \frac{[P]}{[SM]}$$

Now, let us move to the next question. We already discussed this 2,4-Pentanedione exists in solution with its enol form with an equilibrium constant of 4. So, calculate the percentage of keto form in solution. So, this solution is fairly straightforward.

So, if you start with 2,4-Pentanedione, the equilibrium constant is 4 then from the equilibrium constant that it is the K equals concentration of product divided by concentration of starting material. So, you can do the math, and you will get 80 percent of the enol form and 20 percent of the Keto form.

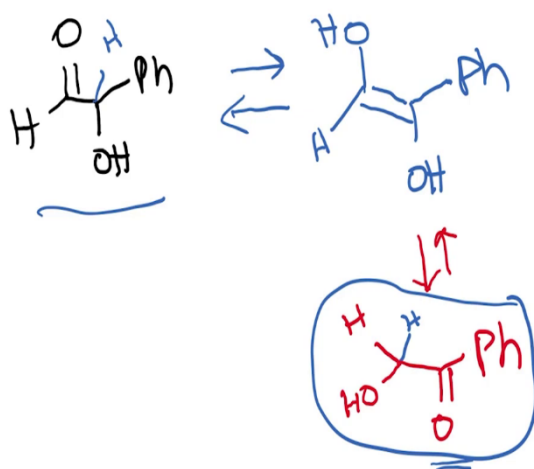
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A new compound whose structure shown below was being isolated. Mass spectrometry showed m/z was found as 136.05, which is the expected value. The compound shown below is expected to have a characteristic signal in the ^1H NMR spectrum in the range 9-10 ppm for the aldehyde. However, NMR analysis was carried out and no such signal was observed. What was the compound that was instead being isolated?



Now, let us move on to the next question. So, a new compound whose structure is shown below was being isolated. And mass spectrometry showed the m/z was 136.05, which is what is expected for the structure. But when you record the NMR spectrum, you would expect a signal between 9 and 10 ppm for the aldehyde but that was absent. So, the question is what was the compound that was instead being isolated. So, given that this proton was absent and you know, you are trying to make this compound. One possibility is that you may want to consider the possibility of enolization.

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So, let us now look at that option. So, when you start with this compound, and form the enol, let us say we start with this, and the benzene ring is over here. So, here is the hydrogen. And so, this, you can in principle propose that it can form the enol form, and the enol form is going to look something like this. Now, this is the enol form.

And now keep in mind that if this compound, this is the hydrogen over here, just to be clear. So, in principle, if you imagine that this carbon-oxygen bond is the enol, this can revert to the carbonyl over here to form this aldehyde, but you notice here on the right, you also have the same CO bond with the same enol configuration.

So, in principle, you can propose that to form the keto form where this carbon-oxygen bond can form the keto form. So, you would end up with $\text{OHCH}_2\text{C}=\text{OPh}$. So, here is the structure of the compound that you can form. And now between this aldehyde and this ketone, the keto

form has some conjugation with the aromatic ring, and you may expect that this is going to be more stable.

So, under the conditions, under which trying to isolate this compound, it is possible that it forms this enol, which can subsequently produce this ketone. And this ketone may be difficult for it to go back because this itself is quite stable. So, therefore, what we would propose as the structure over here would be this, where there is a conjugation with the benzene ring.

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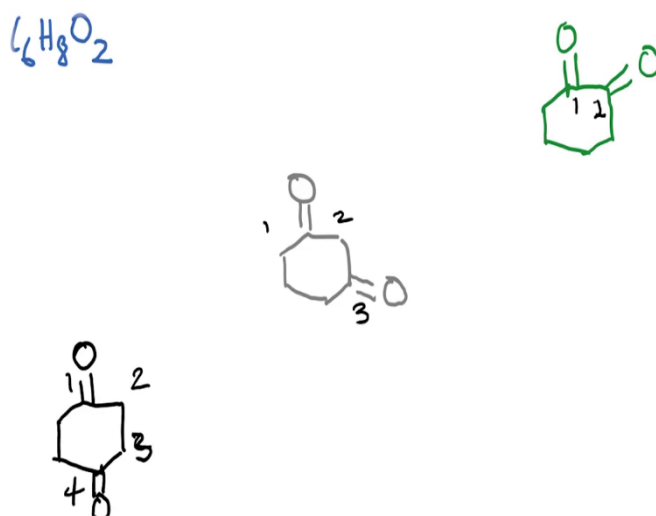
The molecular formula of a compound $C_6H_8O_2$. You have been told that it contains a cyclohexane ring. The infrared spectrum shows a distinct signal at 1700 cm^{-1} and no other significant signals. Design an experiment that will help you identify the compound.



Let us move on to the next question. So, here, the molecular formula of the compound, which is $C_6H_8O_2$. And through some analysis, it has been found that it contains a cyclohexane ring. And the IR spectrum also shows a distinct signal at around 1700 cm^{-1} , and no other significant signals. So, design an experiment that will help you identify this compound.

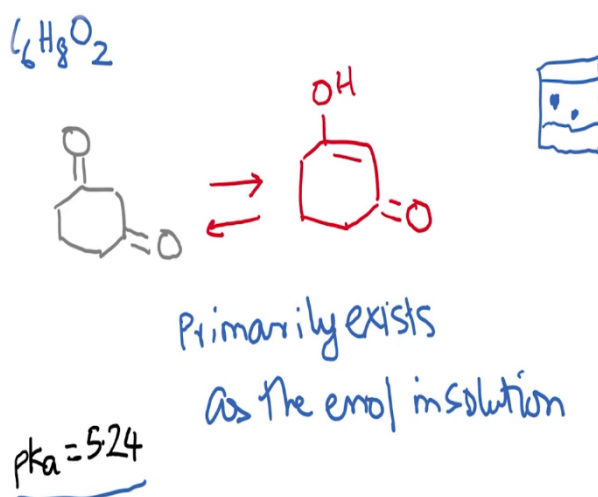
So, what we are given is that, we are given that there is a cyclohexane ring. And we know that there are 2 oxygens in the molecule. And it is not O_2 , but it is two oxygens in the molecule. And we know that there is a $C=O$. Now based on this, we can propose that maybe there are two carbonyls.

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And so, if I look at the molecular formula and draw out the various isomers, that are possible, so I would get these 3 compounds. So, this would be C_6H_8 and O_2 , so the molecular formula is correct. And now, these ketones have a very nice arrangement. So, this is a 1,2-dicarbonyl compound, this is a 1,3-dicarbonyl compound, and this is a 1,4-dicarbonyl compound. So, this is the difference between these three compounds. And then the question here is that how do you design an experiment that is going to help you distinguish this?

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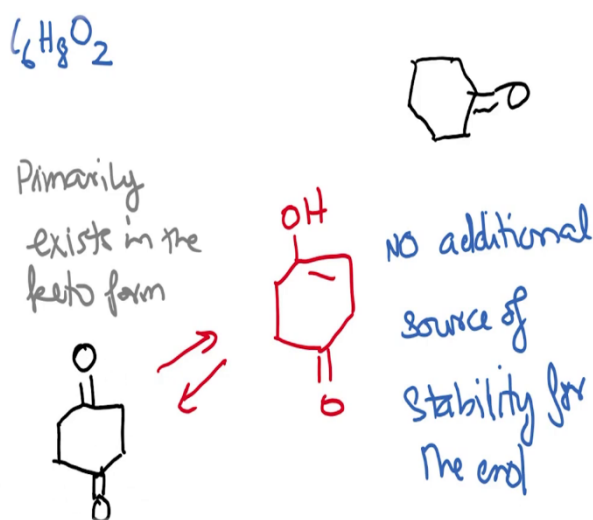
So let us consider the first case, this is the favorite case for us, because we know very well about 1,3-dicarbonyl compounds. So, when you dissolve this in solution, we know that it

primarily exists as the enol so in this case, the pKa has been reported to be 5.24. And this is fairly acidic.

So, if you put this in solution, it is going to primarily exist as the enol form. And so, the enol can be detected using many techniques, including NMR. But if you run a TLC, for example, you would see a clear disappearance of the keto form and produce the enol form. I am just drawing the enol here to be a little bit more polar.

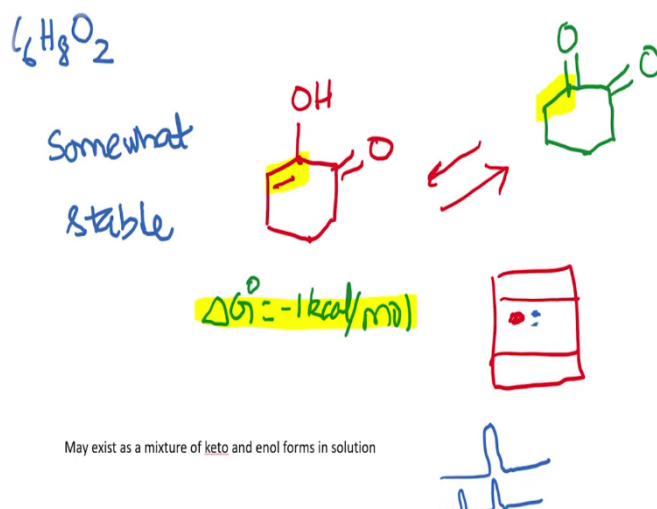
But that is just a guess. We will have to experiment to find out. So, therefore you will see a new peak that is going to be formed. And so, if you do see a new peak, or a new spot, or if you do a HPLC analysis and you find a new peak, then you may suggest that it is the 1,3-dicarbonyl compound. But we will have to also rule out the other two possibilities.

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So, when we take the 1,4-dicarbonyl compound, when we dissolve this in solution, we would expect to form this enol over here, but this enol there is no special reason for this to be stable. So, this is very much just like cyclohexanone, or even acetone for that matter. And so, when we know about cyclohexanone and acetone that there is pretty much 0 percent of the enol being formed or we are unable to detect it. So, if your solution does not produce any new peak in HPLC, or does not produce any new spot in TLC, then you can suggest that it is the 1,4-dicarbonyl compound.

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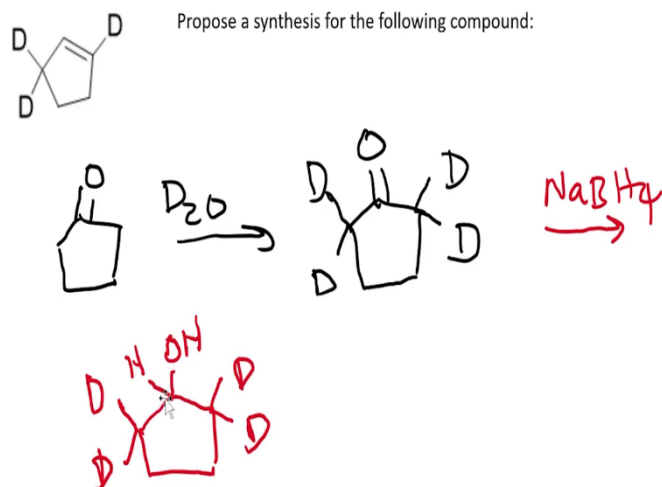
Now, lastly, you can have the 1,2-dicarbonyl compound. And so, some studies show that the enol form of this 1,2-dicarbonyl compound, this is the enol form. So, once you tautomerize this is somewhat a little bit more stable than the keto form. So, the studies have suggested that this difference is about 1 kilo calorie per mole.

So, it is not very large. So, it is certainly something that will show up in an experiment, but it is not a very large number. So, what we can suggest is that in the HPLC analysis or TLC solution. So, let us say this is the starting material. So, you may still continue to see the starting material in the TLC, but maybe a diminished spot, and you may start seeing a new spot for the enol or if you are doing an HPLC analysis, you may see the peak for the starting ketone.

But you will also see the peak for the ketone and the enol. So, this is something that we can find out using one of these techniques. So, therefore, the strategy, which we would use is to dissolve this in solution, and either do a simple TLC or to see whether there are any new products being formed.

So, in the case of the 1,2-dicarbonyl compound, which is what we are discussing right now, you may see two spots, one will be the starting material another would be the new spot. In the case of the 1,4-dicarbonyl compound, we do not expect to see any new peak or new spot and in the 1,3-dicarbonyl compound, we expect it to completely form a new spot that is the disappearance of the starting material and formation of this new enol.

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Now, let us move on to the penultimate question. So, here, you need to propose a synthesis for this compound. And so, if I look at this compound, you can imagine that this could have derived from cyclopentanone. And the reason being that we know that when you take cyclopentane on and put it in D_2O you are going to get this tetra deuterated compound over a period of time and now, all I need to do is to convert this ketone into an olefin over here. So, the way we would do this is to react this with Sodium borohydride to produce this alcohol over here.

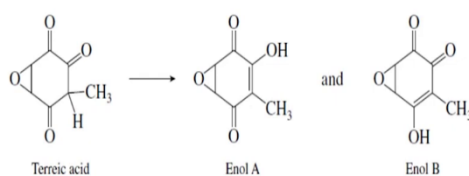
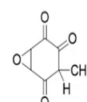
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And then maybe treatment with concentrated H_2SO_4 , you may form the carbocation, which is going to eliminate and produce this product. So, keep in mind here that this is still a hydrogen over here, so we may not be replacing that with the deuterium. And so, one of these deuteriums might fall off and give you the final product. So, you can imagine many variations for this question. And you can form a variety of products starting from cyclopentanone and D_2O .

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Terreic acid is a natural product that has the following structure. It is found to exist as an enol. Draw out possible enols and suggest which of these would be the dominant form



Of these two structures, enol A, with its double bond conjugated to two carbonyl groups, is more stable than enol B, in which the double bond is conjugated to only one carbonyl.

And the last question is about Terreic acid, it is a natural product, it is found to exist as an enol. Draw out the possible enols and suggest which of these would be the dominant form. So, this is a fairly straightforward question. So, you have this hydrogen over here, which is going to enolize. So, once it forms the enol, it is going to give you, I mean one of the enols here is this, and the other enol if it tautomerizes with this carbonyl, it is going to give you enol B.

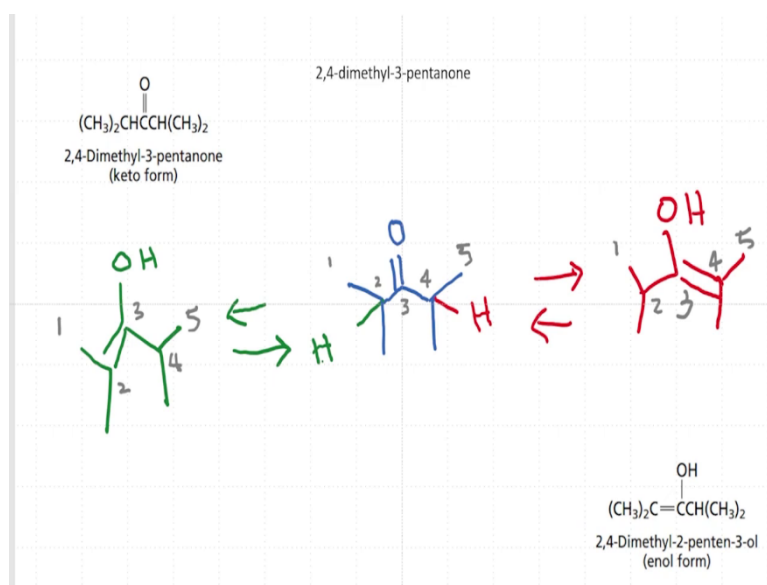
And now of these two structures enol A with its double bond conjugated to the two carbonyls. So, this double bond is conjugated to both these carbonyls is more stable than enol B which is conjugated only to this carbonyl. So, I would expect that enol A is going to be more stable.

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- Write structural formulas corresponding to
- The enol form of 2,4-dimethyl-3-pentanone
 - The enol form of acetophenone
 - The two enol forms of 2-methylcyclohexanone

The next question is, write the structural formulas corresponding to these three ketones. So, let us look at them one by one. The first one is 2,4-dimethyl-3-pentanone.

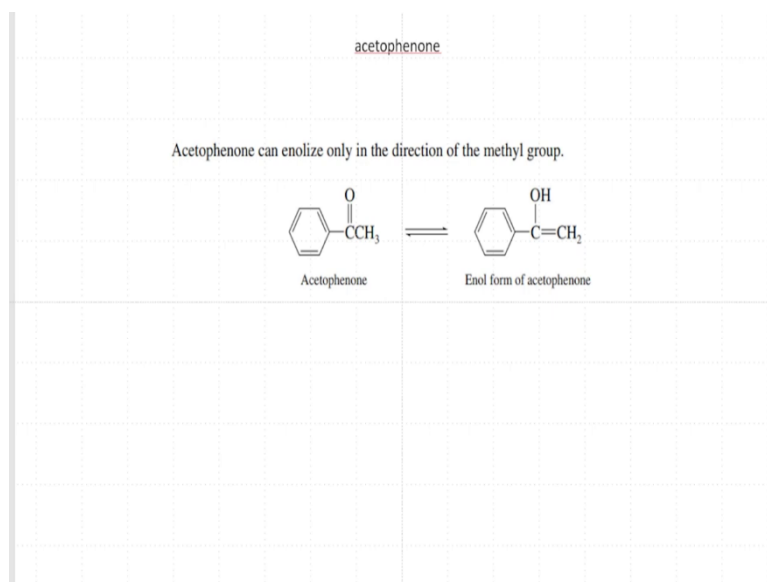
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So, I am drawing out the structure of 2,4-dimethyl-3-pentanone over here. And so, this is the keto form of this compound. So, what we would expect is that this ketone, there are two enolizable hydrogens. So, if I number it as 1, 2, 3, 4, 5 carbons, so in the carbon number 2 there is an ionizable hydrogen and carbon number 4 there is an ionizable hydrogen and either of these hydrogens can be involved in tautomerization or enolization.

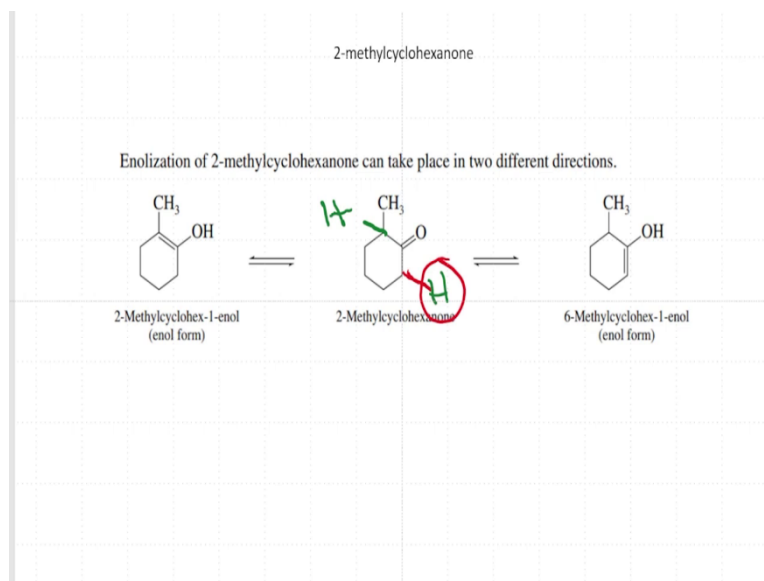
And you end up with either the enol between carbon 3 and 4 or enol between carbon 2 and 3. And of course, you will very quickly understand and realize that they are the same enol, they are identical. So, the only product that is formed, enol that is formed here is the one that is shown here.

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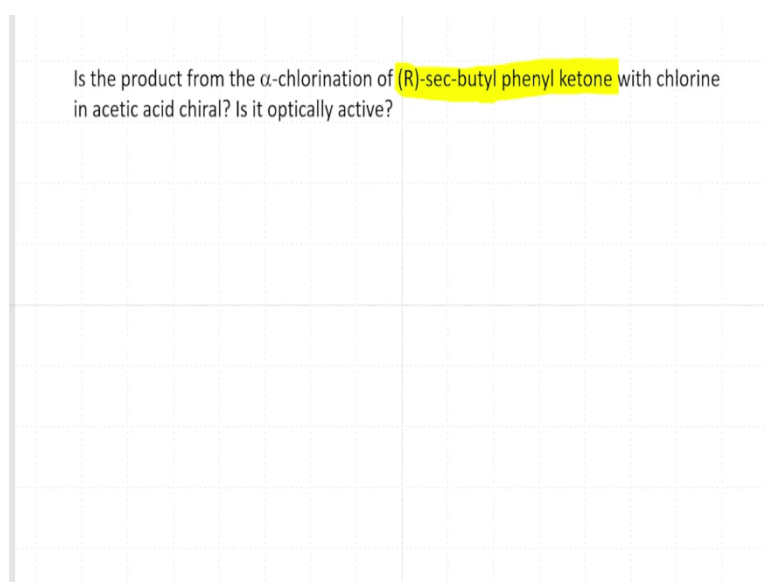
In the next question is Acetophenone. So, here in Acetophenone there are, this the benzene ring over here is not involved in enolization because the carbon next to the carbonyl does not have any hydrogens, whereas, the methyl group here has three enolizable hydrogens and so, this is the enol form of acetophenone. So, again the strategy that we would employ to address these questions is to first identify the enolizable hydrogens and then move on.

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The next question is that, the enolization of 2-methylcyclohexanone can happen in two different places and so, you have two hydrogens over here, and then there is one hydrogen over here, let me just draw it out for us to see. So, this is one hydrogen and this is the other hydrogen if either of these hydrogens can undergo enolization or can be involved in enolization and so, if this hydrogen is involved in enolization, you get the product on the right which is 6-Methylcyclohexen-1-ol and if the other hydrogen, the green hydrogen or the one next to the methyl group is involved then you get 2-Methylcyclohexen-1-ol.

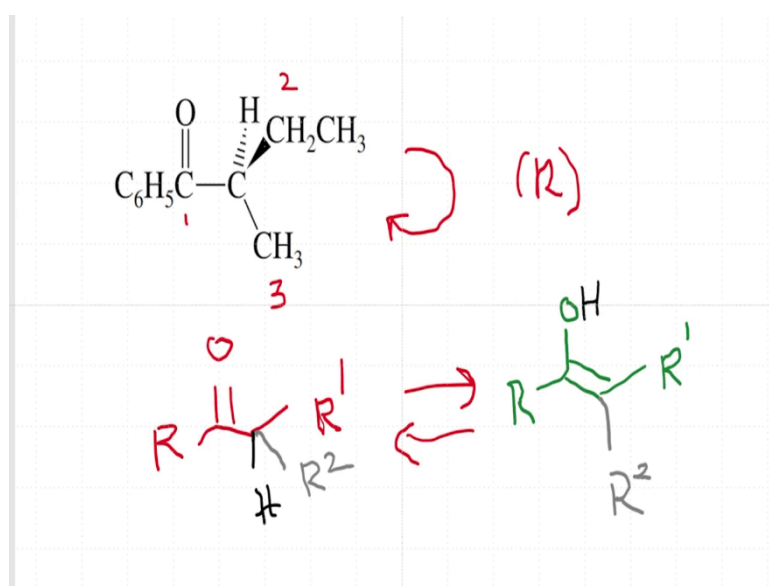
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So, the next question is, is the product from α -chlorination of (R)-secondary butyl phenyl ketone with chlorine in acetic acid chiral? Is it optically active? So, this question can be broken down into two parts. The first part is the identification of this product here and the second part is the product of α -chlorination.

So, the first thing to do is to write out the structure and then assign the stereochemistry. So, my suggestion would be that you spend some time and once you write the structure out then you can then assign the stereochemistry as (R) or (S) and then move forward with the (R) isomer. So, let me solve this problem now.

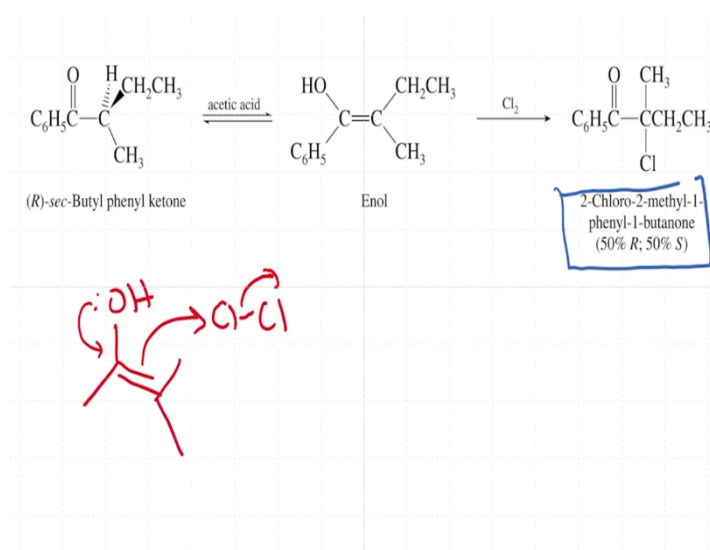
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So, this is the structure of (R) isomer of this compound. And so, if I have to look at the stereochemistry, so, hydrogen gets the least priority, the carbonyl gets priority number 1, the ethyl group gets priority number 2, and the methyl group gets priority number 3. So, this is clockwise the way it is drawn and therefore, it is (R) stereochemistry. Now, what we can sort of propose is that again if you see from the previous question, we have understood that the benzene ring does not enolize and so, the only enolizable hydrogen here is this one.

Now, when it enolizes what is going to happen is you are going to have an equilibrium between the keto form and the enol form and as you know the enol form is planar. Now, if this enol reacts with chlorine, we know that the chlorine reaction with the electrophile can occur from the top face or the bottom face and they are equally likely and therefore, it is understandable that you will get a racemic mixture.


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So, let me explain it in the following way. So, once you form the enol, then the attack of the enol to the chlorine is going to occur in the following manner. So, you have OH and it is going to attack in the following manner to Cl-Cl and chloride ion is going to be lost. So, what is going to happen is that if this is above the face of the olefin, the same reaction can also happen from below the face of the olefin.

And so, you will end up with a 50-50 mixture of *(R)* and *(S)* forms of the Halo compound. So, I would urge you to draw out both these compounds and assign *(R)* and *(S)* for yourselves. But the product itself is not optically active, because you will get a racemic mixture. But the two products that are formed are individually chiral.

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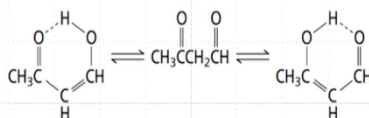
 The two most stable enol forms of $\text{CH}_3\text{CCH}_2\text{CH}$

 The two most stable enol forms of 1-phenyl-1,3-butanedione

In the next question, we want to understand what are the two most stable enol forms of the following carbonyl compounds, so, let us take them one by one.

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Enolization of this 1,3-dicarbonyl compound can involve either of the two carbonyl groups:



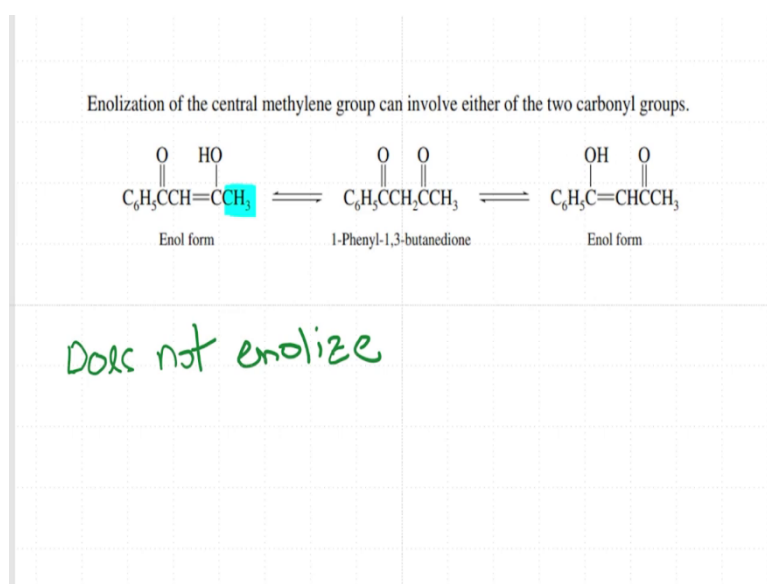
Both enols have their carbon-carbon double bonds conjugated to a carbonyl group and can form an intramolecular hydrogen bond. They are of comparable stability.

The first one is this, it is a 1,3-dicarbonyl compound. So, if you draw out this aldehyde, as shown here, again, there are two sets of enolizable hydrogens, there is this CH_2 as well as the CH_3 . But we already have discussed that the enolization of the CH_2 is far more acidic compared to the methyl group.

And so, it can form an enol much more readily than the other methyl group. So, now, if the aldehyde is involved in the enol formation, then you end up with this kind of a structure, I am

sorry, this kind of structure and if the ketone is involved in the enolization, then you get this kind of a structure. And they are of comparable stability.

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In the next problem, again, you have a central methylene group, which can undergo enolization. And there is a methyl group on the right, which clearly can undergo enolization, but does not enolize because our understanding is that the active methylene group in the center is far more reactive or far more acidic than the terminal methyl group. So, again, you have a choice of two different ketones.

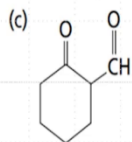
So, we are just going to write it out here. So, this is one of the enol forms where it is conjugated with the benzene ring. And this is another enol form where it is adjacent to the methyl group. So, if we have to suggest which one is more stable, it is likely or it is possible that the one with the conjugation is more stable.

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Write the structure of the enolate ion derived from each of the following β -dicarbonyl compounds. Give the three most stable resonance forms of each enolate.

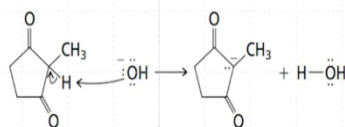
(a) 2-Methyl-1,3-cyclopentanedione

(b) 1-Phenyl-1,3-butanedione

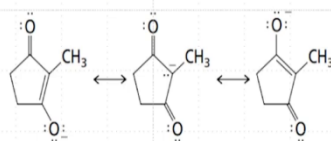


The next question is, write the structure of the enolate ion derived from each of the following β -dicarbonyl compounds and give the three most stable resonance forms of each enolate. So, let us start working on these one by one. The first question is 2-methyl-1,3-cyclopentanedione.

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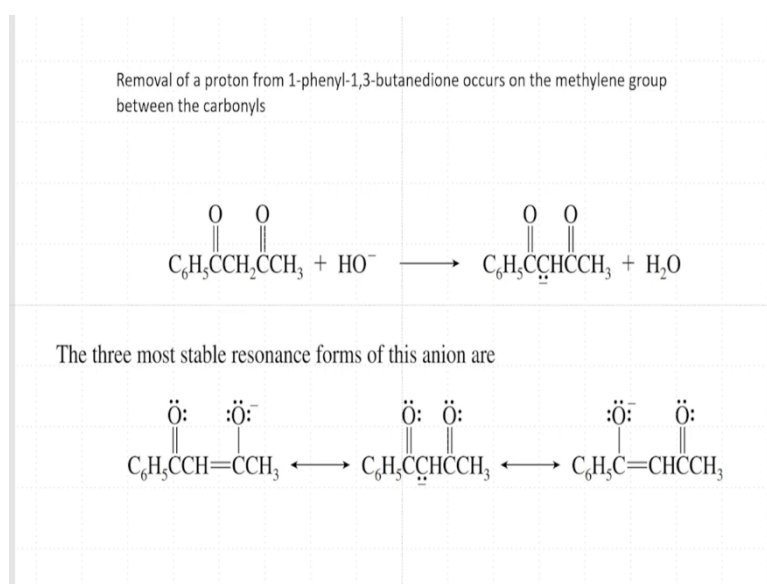
The three most stable resonance forms of this anion are



So, let us look at this answer here. So, this is the structure of the cyclopentanedione. And what we can suggest is that hydroxide ion picks up this proton and forms a carbanion and again we know that the carbanion is likely to resonate with the adjacent carbonyl compounds. And so, if one of the resonance forms is the carbanion then the other two resonance forms as

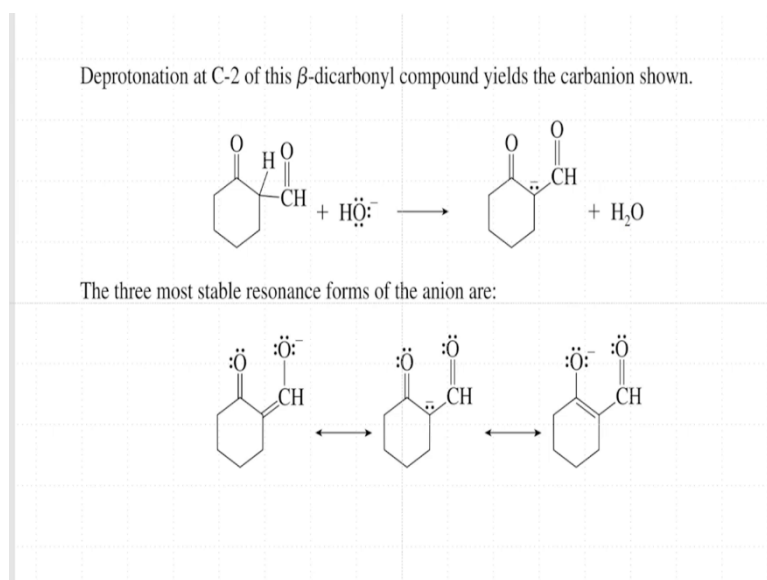
drawn here are the enolate forms. So, the answer to this question is that these are the resonance forms of the enolate that is going to be formed.

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Similarly, when you have the 1-phenyl-1,3-butanedione, then you first generate the carbanion as shown here. And that is one of the resonance forms and the other resonance form is shown here, where the ketone which is formed by the methyl group is going to be involved and the other case is where the benzene ring is involved in the formation of the enolate. So, therefore, the three most stable resonance forms are as shown here.

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Lastly, we have a similar question in that we have an aldehyde and a ketone. And again, if you push the arrows, hydroxide ion attacks the hydrogen here and generates the carbanion and the carbanion is the resonance form of these two enolates as shown here. So, I would

urge you to draw out each of these structures and convince yourselves that this is the answers to these questions.