Essentials of Oxidation, Reduction and C – C Bond Formation
Application in Organic Systems
Prof. Yaswant D. Vankar
Department of Chemistry
Indian Institute of Technology, Kanpur

Module No # 03
Lecture No # 16
Further Synthetic and Mechanistic Aspects of Tamao-Fleming Oxidations

Hello everyone, I would like to welcome you all lecture of today first we will look at what we did last time in a very brief manner. Towards the end I introduced the Fleming Tamao oxidation and discussed the oxidation of carbon silicon bond to the corresponding carbon OH bond where we discussed the mechanism of the flaming condition based oxidation.

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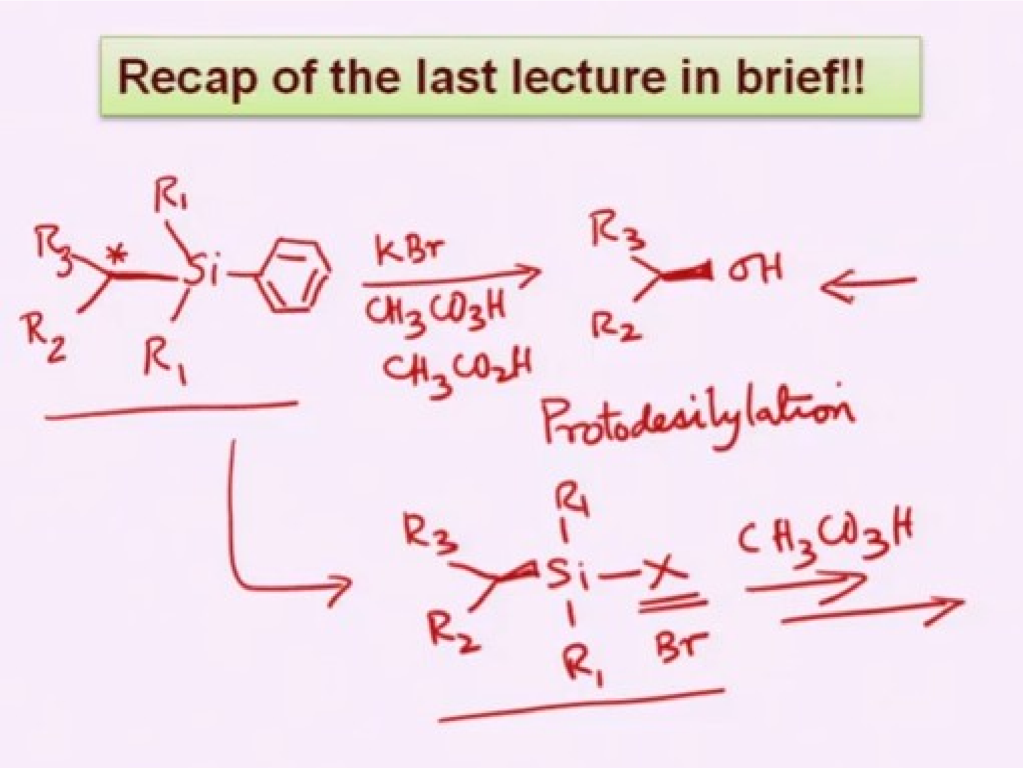

Recap of the last lecture in brief!!

So what we had discussed last time was that if one has a substrate of this type where we have a phenyl ring attached. And there are 2 groups which are attached here and of course you have the substrate on which we have say here we put it R 1. And this is the, if we put it as R 2 here and this as R 3 then we have the asymmetric centre here. And what we discussed was that in the presence of potassium bromide per acetic acid like this and acetic acid as a solvent.

One can convert the substrate to the corresponding alcohol with the retention of the stereochemistry here. What we did was proto desilylation and we proceeded via the corresponding halide which is present on the silicon where you have the phenyl ring was replaced by X which is like a bromine. And then of course we went further so there was this conversion of this silicon substrate to the corresponding the silicon halide substrate and then we did the oxidation with the, per acid here.

So you had CH_3 CO_3H which underwent somewhat like Baeyer Villiger oxidation type of substrate and finally basic workup followed by protonation led to the corresponding alcohol like this here. So we will see now how this 2 step process can also be done in a slightly different way and how modifications have been done to get one step or one pot operation.

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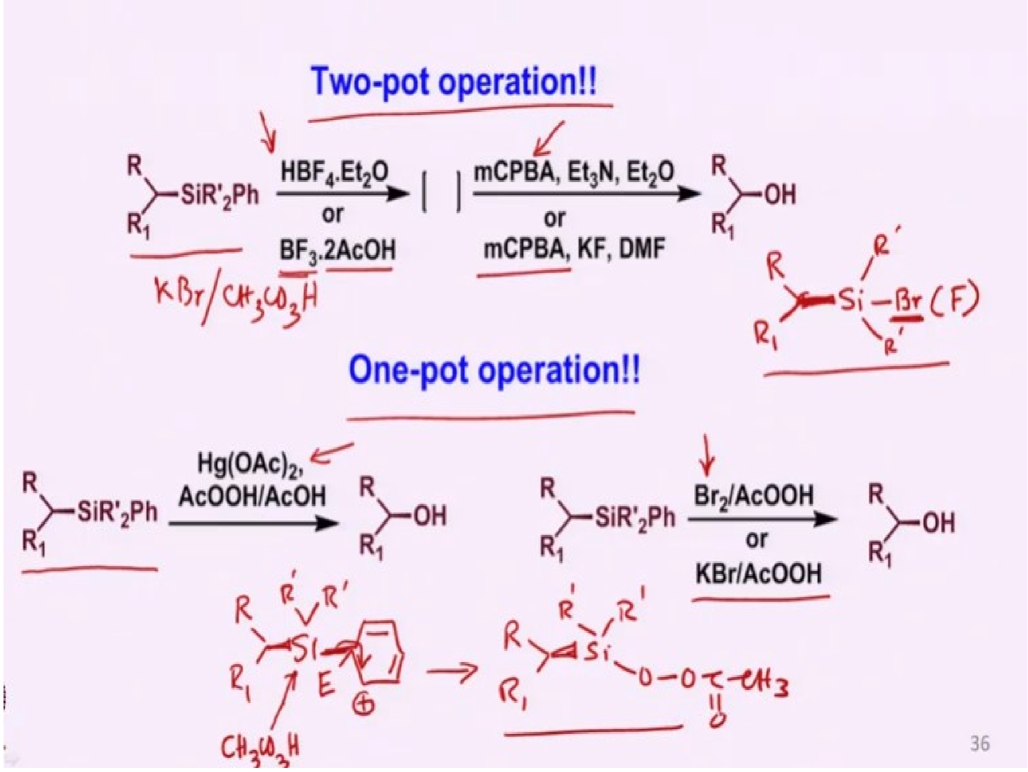

Two-pot operation!!

One-pot operation!!

So these 2 pot operation which I; showed where substrate of this kind was reacted with the potassium bromide and per acetic acid. But one can also use somewhat different reagent systems such as HBF $_4$ Fluoroboric acid of BF $_3$ ethorate and acetic acid of combination and this act as source of proton as well as F- as a nucleophile. So instead of getting what we saw last time instead of getting silicon and bromide what we saw the last time instead of bromide now what you will get is a fluoride.

Because it HBF $_4$ as well as BF $_3$ acetic acid is a source of F^-. So instead of getting this bromide one gets fluoride and then one can use in presence of any per acid such as meta chloroperbenzoic acid one can use triethylamine as a base or potassium fluoride as a base. So one can then convert that silicon fluoride based intermediate to the corresponding alcohol similar to the mechanism that we discussed using Baeyer Villiger type of oxidation.

Now they also invented a one pot operation here in the one pot operation what they have done is that they start with the similar substrate of the silicon type. And now they use say for example mercuric acetate as a reagent in presence of per acetic acid and acetic acid. So one can also use bromine molecular bromine or potassium bromide and per acetic acid. Also but it is a one-step operation that means the intermediate which is form like this which is going to be say somewhat like this.

The electrophile attaches to this particular carbon atom of the aromatic ring and the positive charge is formed here. Now it is very clear that this bond has to break and you regain the aromaticity in the process this silicon is attached by the, per acid we one uses say for example here you have CH $_3$ CO $_3$H. So your, Per acid attacks onto this silicon in the same pot leading to the corresponding which is expected to undergo the rearrangement of which I termed as Baeyer Villiger type of oxidation.

So this is the substrate that one can directly get under these conditions where any electrophile such as mercury plus or Br+ in the acetic acid and parasitic acid medium can directly give this one. So this is an advantage of using a one pot operation rather than isolating. But then there are both the options which are present and can be utilized for both the protocols can be utilized.

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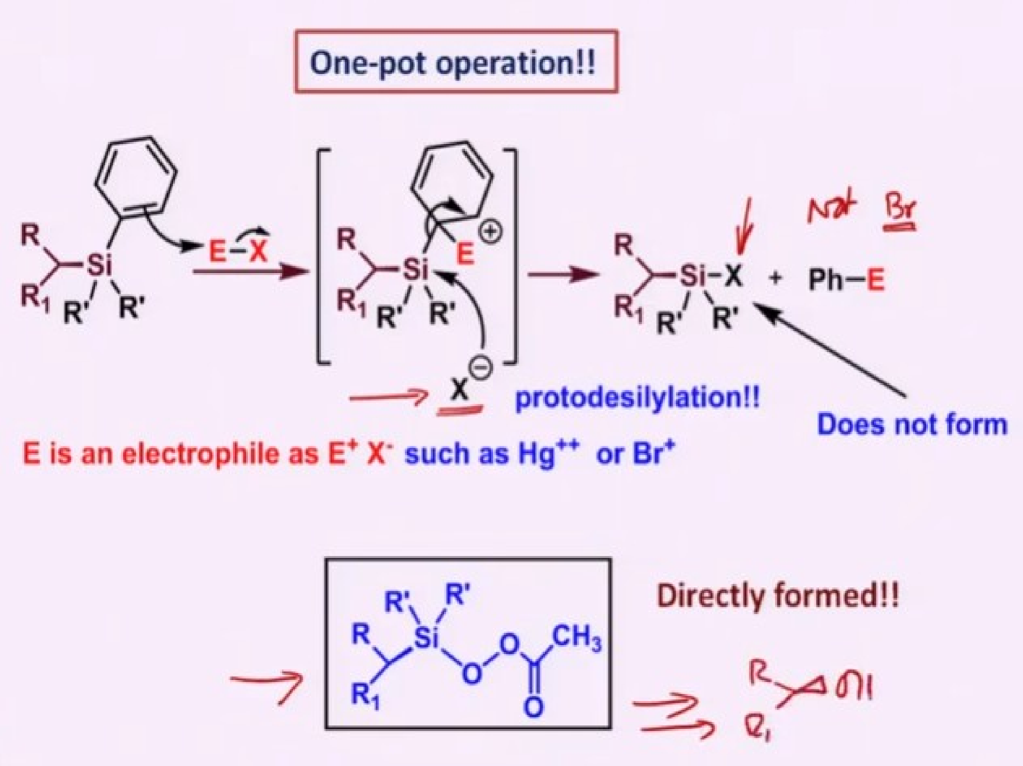

One-pot operation!!

protodesilylation!!

E is an electrophile as $E^+ X^-$ such as Hg^{++} or Br^+

Does not form

Directly formed!!

So as I said the electrophile reacts with the benzene and now nucleophile can directly attack on this one and in this particular X is not a halide not bromide or any other halide not bromide ion or bromine. But it is as I explained earlier that directly the electrophile allows the acid the parasite to react to form this substrate and which undergoes oxidation eventually to form the corresponding alcohol.

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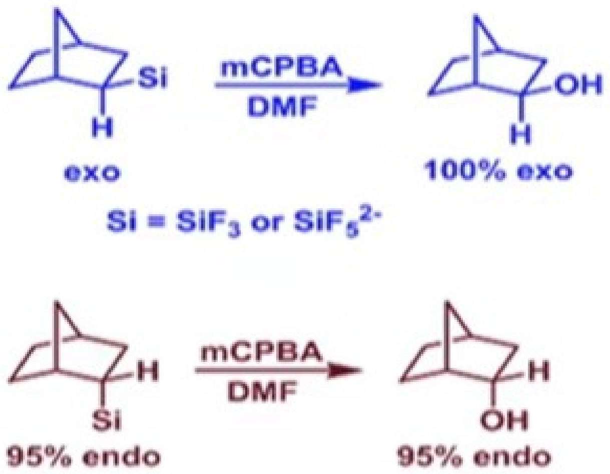
Evidence for retention of stereochemistry

Tamao



Si = SiF_3 or SiF_5^{2-}

Now what is the evidence for retention of stereochemistry in Tamao-Fleming oxidation? The evidence was provided by a set of experiments that the Tamao reported. What he did was he started with a silicon containing moiety like this which is a bicyclic bridged molecule. In which he had the carbon silicon bond in an exo-oriented fashion. Of course there will be substituents as somehow used on silicon like this.

Then he carried out the oxidation under his Tamao oxidation condition then what he obtained was the exo alcohol which was 100% exo. In a similar fashion reason when he started with another molecule in which the silicon now was endo oriented this particular compound had 95% silicon in endo orientation. This particular molecule led to the formation of the endo product again in 95% indicating that there is a 100% retention of the stereochemistry.

These set of experiments clearly indicate that there is retention of stereochemistry in Tamao-Fleming oxidation.

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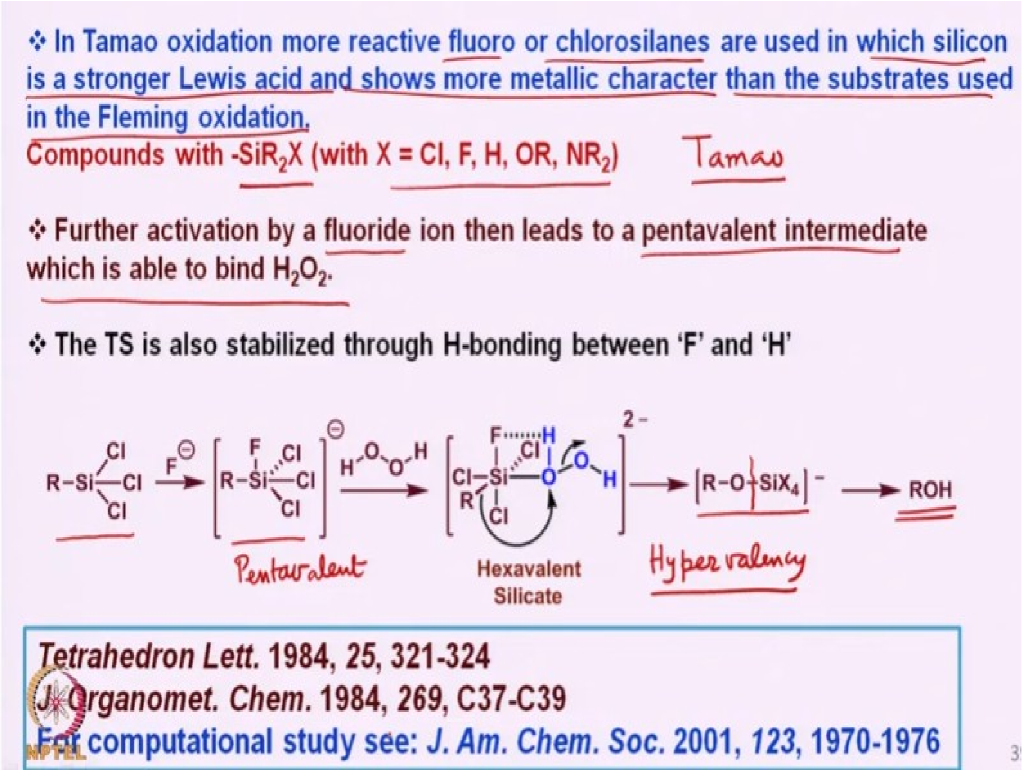

- In Tamao oxidation more reactive fluoro or chlorosilanes are used in which silicon is a stronger Lewis acid and shows more metallic character than the substrates used in the Fleming oxidation.

Compounds with -SiR_2X (with X = Cl, F, H, OR, NR_2) Tamao

- Further activation by a fluoride ion then leads to a pentavalent intermediate which is able to bind H_2O_2.

- The TS is also stabilized through H-bonding between 'F' and 'H'

Tetrahedron Lett. 1984, *25*, 321-324

J. Organomet. Chem. 1984, *269*, C37-C39

For computational study see: *J. Am. Chem. Soc.* 2001, *123*, 1970-1976

Now in the Tamao oxidation the more reactive fluoro or chlorosilanes are used in which silicon is a stronger Lewis acid and shows more metallic character than the substrates used in the Fleming oxidation. So you have a substrate like this which is SiR_2 X where x is chlorine fluorine hydrogen or NR 2. These are the substrates these are the groups which are used on silicon in while carrying out the Tamao type of oxidation which I have not yet discussed in detail but now we will do that.

Now further activation by a fluoride ion then leads to pentavalent intermediate which is able to bind hydrogen peroxide. Now it is something like this if one takes a silicon substrate which is having here shown as 3 chlorines but also can start with only one halogen. Then the fluoride ion is attached is reacted with which forms a pentavalent intermediate this is a pentavalent intermediate.

And then hydrogen peroxide also reacts with it to form the hexavalent silicate ion. It is a an example of hyper valency. So one can start with a tetravalent silicon going to pentavalent and then to hexavalent silicate ions. And then there is a transfer of R group what is supposedly a chiral group if one starts with a chiral substrate to the corresponding oxygen which is attached to the silicon.

And then there is a loss of OH^- and we get an intermediate of this type where oxygen is now attached to the silicon and the R group has been transferred onto the oxygen which is attached to the silicon then of course one has the hydrolysis to form the corresponding OH here. So this is the Tamao oxidation in which we have a slightly, different requirements as far as the starting material is concerned and of course one uses the fluoride ion.

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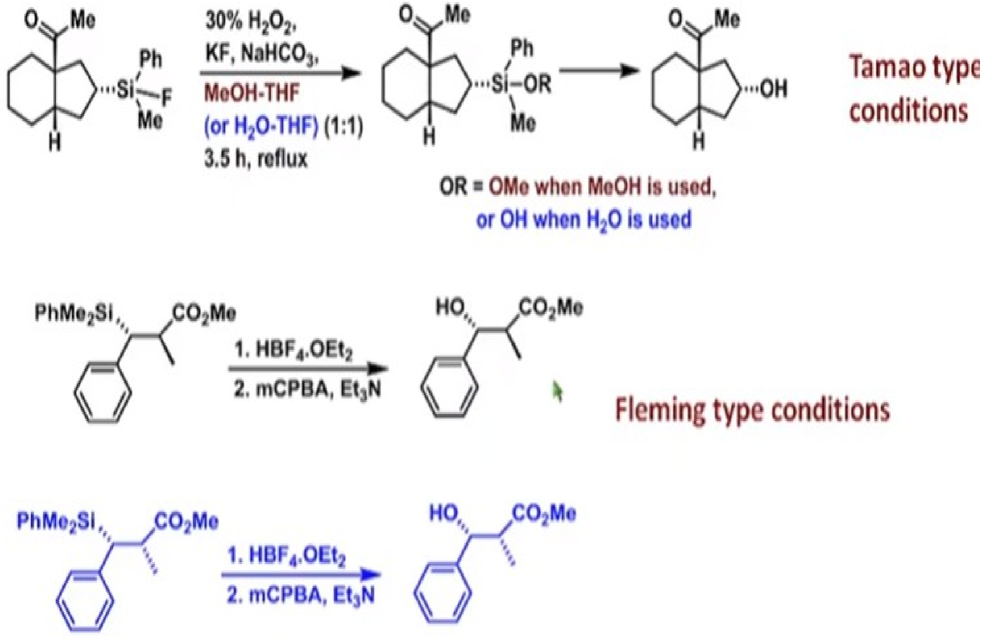

Chem. Rev. 1997, 97, 2063-2192

So if we start with a substrate of this kind here for example where the carbon silicon bond has a well-defined stereochemistry that is alpha orientation here with of course fluoride attached to the silicon and under Tamao conditions which utilizes 30% hydrogen peroxide potassium fluoride. And the basic conditions and using methanol or water as a solvent along with THF then one directly gets the hydroxy compound with the retention of stereochemistry like this.

It has been shown that in case when methanol is used as a solvent along with THF then an intermediate of this kind where OR is nothing but O methyl is obtained as an intermediate. Or when water THF is used as a solvent system then here OH group has been observed to be present. And this particular intermediate them under the same condition leads to the formation of this hydroxy compound.

Indicating that in these Tamao, type of oxidations these types of intermediates are first formed. In the case of Fleming type of conditions which is very different from the amount condition we of course have to have a phenyl group here. And we have now a well-defined stereochemistry at this junction where carbon and silicon bond is formed and of course we have another well-defined stereochemistry at the adjacent carbon atom.

And under acidic conditions when the reaction is carried out there is retention of stereochemistry of the hydroxy group in the final product. In a similar fashion irrespective of the stereochemistry of this particular carbon-Carbon bond here if this is; alpha oriented then of course irrespective of the stereochemistry of this and this. Whatever is the stereochemistry of the carbon silicon bond that is what is, translated into the final product that means there is again retention of stereochemistry.

So looking at these 2 examples it is very clear that the stereochemistry on the carbon atom here does not have any influence on this stereochemistry of the final product. That is in the case of the Tamao-Fleming oxidation there is an retention of stereochemistry in the final product.

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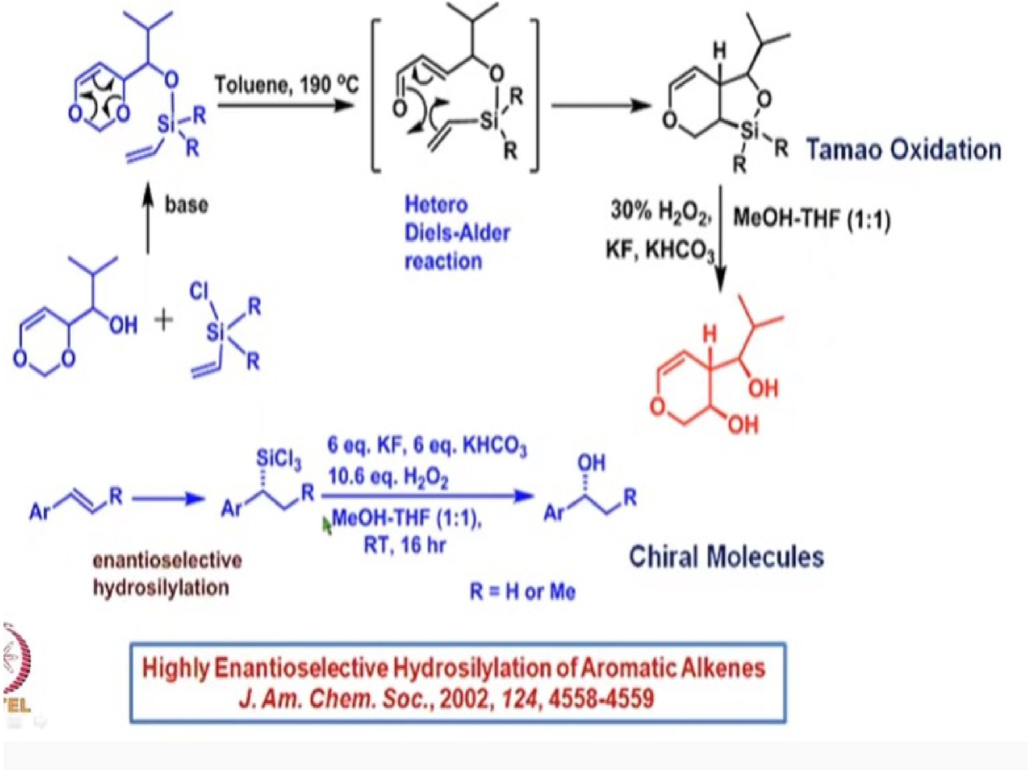

Highly Enantioselective Hydrosilylation of Aromatic Alkenes
J. Am. Chem. Soc., 2002, *124*, 4558-4559

Now there is a very interesting reaction that we would like to look at it where this particular organosilane compound has been converted into a very useful dihydroxyl molecule of this kind which is a useful synthon in organic synthesis. Now this organosilane molecule has been prepared by reacting, this hydroxy compound with the chlorosilane of this basic condition.

And then allowed to undergo a thermolysis at 190 degree whereby this undergoes cleavage as I have shown here to release this alpha beta unsaturated aldehyde. And since there is already an olefin present in the molecule this undergoes a hetero Diels Alders reaction. Because we can consider this particular part as a heterodiene the Diels Alders reaction is a concerted process.

So this particular heterodyne reaction leads to the formation of this particular bicyclic molecule with well-defined zero chemistry at the newly generated asymmetric centre Now if we allow this bicyclic molecule in which there is a carbon silicon bond with well-defined stereochemistry to undergo Tamao based oxidation under these conditions then carbon silicon bond which is beta oriented leads to the formation of a carbon hydroxy bond which is also beta oriented that means with the retention of the stereochemistry.

And this oxygen silicon bond under these conditions undergoes cleavage leading to the formation of the corresponding diol. That means we have converted this very interesting starting material into a very highly useful dihydroxy compound which is very useful synthon in organic synthesis by utilizing 2 reactions namely hetero Diels Alder reaction and the Tamao oxidation.

Now, if we take a substrate of this particular type and if it is chiral molecule that means optically pure molecule. Then here under Tamao oxidation conditions we can convert this into the corresponding alcohol which is optically pure because the stoichiometry is optically pure. And this particular stoichiometry can be prepared from this olefin which is an aromatic alkene by enantio-selective hydroxy silaylation a process that has been described in this particular paper.

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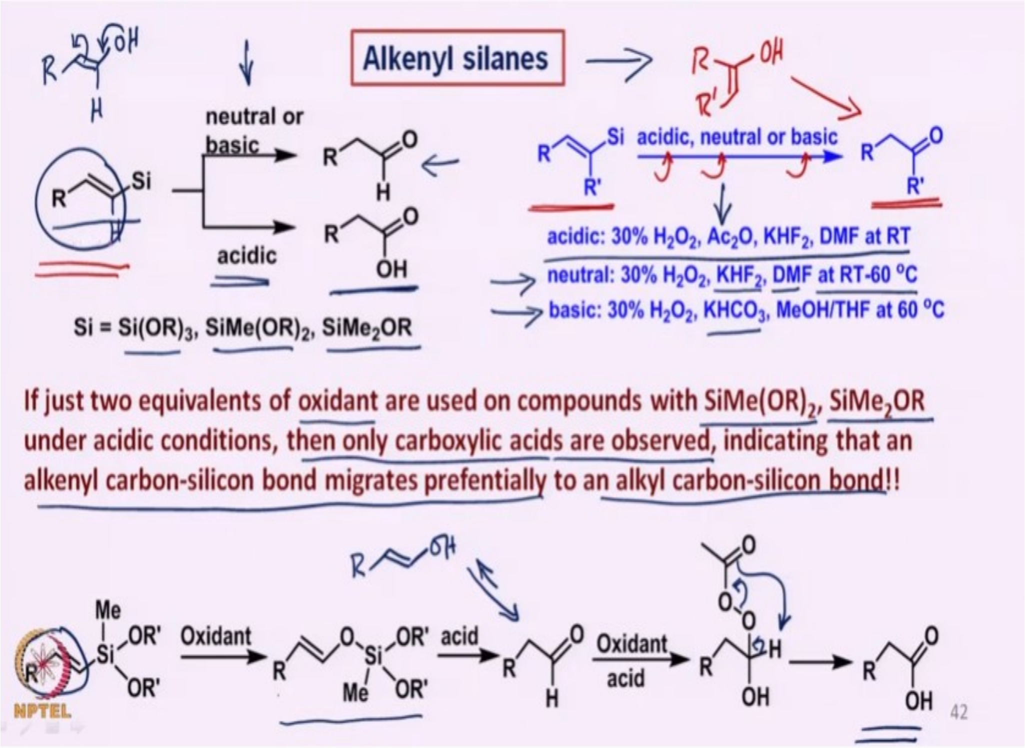

Alkenyl silanes

Si = $Si(OR)_3$, $SiMe(OR)_2$, $SiMe_2OR$

acidic: 30% H_2O_2, Ac_2O, KHF_2, DMF at RT

neutral: 30% H_2O_2, KHF_2, DMF at RT-60 °C

basic: 30% H_2O_2, $KHCO_3$, MeOH/THF at 60 °C

If just two equivalents of oxidant are used on compounds with $SiMe(OR)_2$, $SiMe_2OR$ under acidic conditions, then only carboxylic acids are observed, indicating that an alkenyl carbon-silicon bond migrates prefentially to an alkyl carbon-silicon bond!!

Now we have substrates of these type alkenyl silanes which can under neutral or basic conditions which employ something like this you have a neutral conditions hydrogen peroxide. Then this KHF2 then you have DMF at room temperature to 60 degrees then you have a, basic conditions under which you use potassium bicarbonate and methanol at 60 degree. Under these conditions when a substrate of this type which has 1 hydrogen present here leads to the corresponding aldehyde.

That means under these conditions what is formed is something of this type. So this total alkenyl group is transferred to the oxygen. And then of course you get an OH and which is nothing but an aldehyde because this will come here and this will come here and it will form corresponding aldehyde. But under the acidic conditions if one takes hydrogen peroxide acetic and hydride KHF 2 which is now an acidic condition in these acidic conditions one gets the corresponding acid.

So what is observed is that if the substituents are like this on the silicon then what is founded is if just 2 equivalents of oxidant are used 2 equivalents of oxidant are used, 2 equivalents of oxidant are used on compounds with this type of substitutions on silicon under acidic conditions. Then only carboxylic acids are observed to be formed it indicates that alkenyl carbon silicon bond migrates preferentially

So this is the migration this is the electronic silicon bond that migrates to the oxygen of the oxidizing agent like hydrogen peroxide. Then that forms an intermediate of this kind here the methyl silicon bond is not transferred or does not migrate. When the acid is used here the hydrolysis will give the aldehyde by the same way as the earlier and that forms the corresponding aldehyde.

Which again reacts with the oxidant to form like parasite parasitic acid or hydrogen peroxide is added in this one gets the oxidation to the corresponding acid. So basically it indicates that under acidic conditions you have a slightly different where you have the acetic and hydride that is used that leads to per acid here and this is what the, per acid is? And that undergoes oxidation of this type to form the acid.

So this alkenyl silanes are utilized to get to the corresponding aldehydes or to the acids but of course if one starts with a substrate in which there are 2 substitutions here this was mono substituted and if it is a di-substituted then obviously. You will get the alcohol coming like this where carbon silicon bond is replaced by the carbon silicon bond is replaced by the carbon oxygen bond that leads to the corresponding diketone.

So under these conditions it does not matter what conditions are used whether acidic neutral or basic you can only get the corresponding ketone. On the other hand when the substrate is mono substituted mono substituted in the sense that only one substituent is present as R here there are 2 substituents present of course silicon will be common in both the cases. So in the case when there is a mono substitution one can get the possibility of getting the corresponding acid if the acidic conditions are used.

So we will stop it at this stage today's lecture and we will take up other oxidations in the next class. So what I discussed today was basically these Tamoa-Fleming oxidations mechanisms and their applications in different types of conversions where you can convert an enantio selective Carbon silicon bond or a chiral carbon silicon bond to the corresponding chiral OH bond. And therefore you have a possibility of generating chiral molecules without any problem.

If you; have a possibility of making the chiral carbon silicon substrates. So you can go ahead and the references that I give or the materials that I discussed carefully we will take up the other oxidations next time thank you.