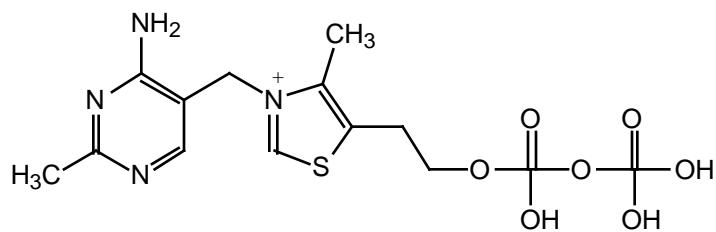


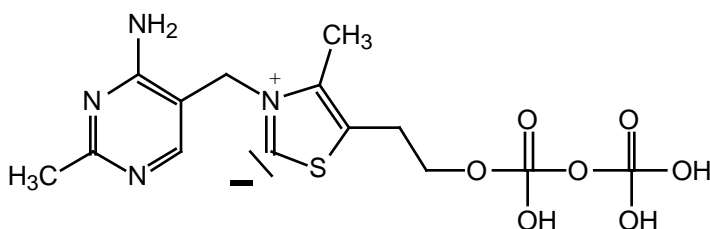
GTQ on Vitamin B₁. (50 points, recognition, transposition, synthesis, disconnection, mechanism)

(a) Vitamin B₁ is thiamine pyrophosphate (TPP). Thiamine is a fancy thiazolium ion with a 2-hydroxyethyl side chain. The vitamin is an ester of the thiamine. Draw the structure of the product that results by deprotonation of vitamin B₁. Draw the structure again but this time abbreviate the side chain containing the heterocycle as R and the side chain that contains the phosphate as R'. (5 points)

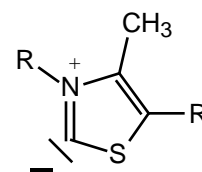


TPP = Vitamin B₁

Deprotonated Vitamin B₁

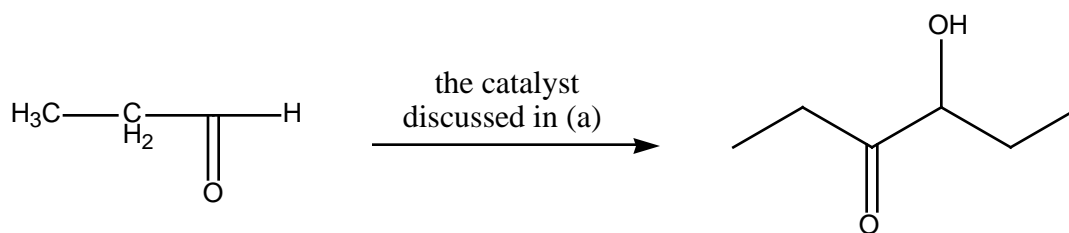


Abbr.:

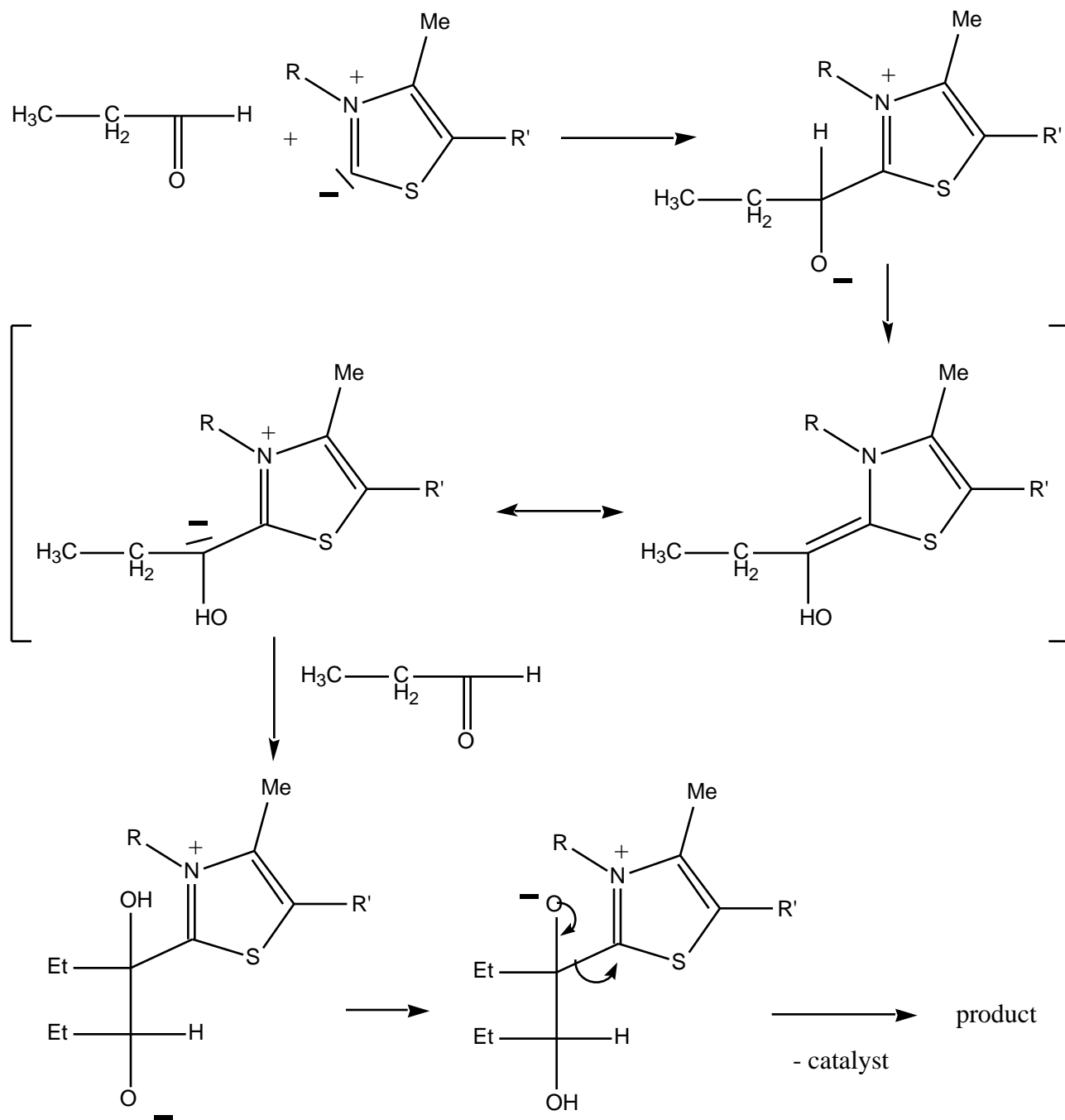


(b) Suppose you treat propanal with deprotonated vitamin B₁. What do you get as the product? Draw the product of the overall reaction and write down a complete mechanism for this reaction. While working on the mechanism realize what happens to the H-atom that came with the aldehyde function. (15 points)

Overall Reaction of Propanal with Deprotonated Vitamin B₁

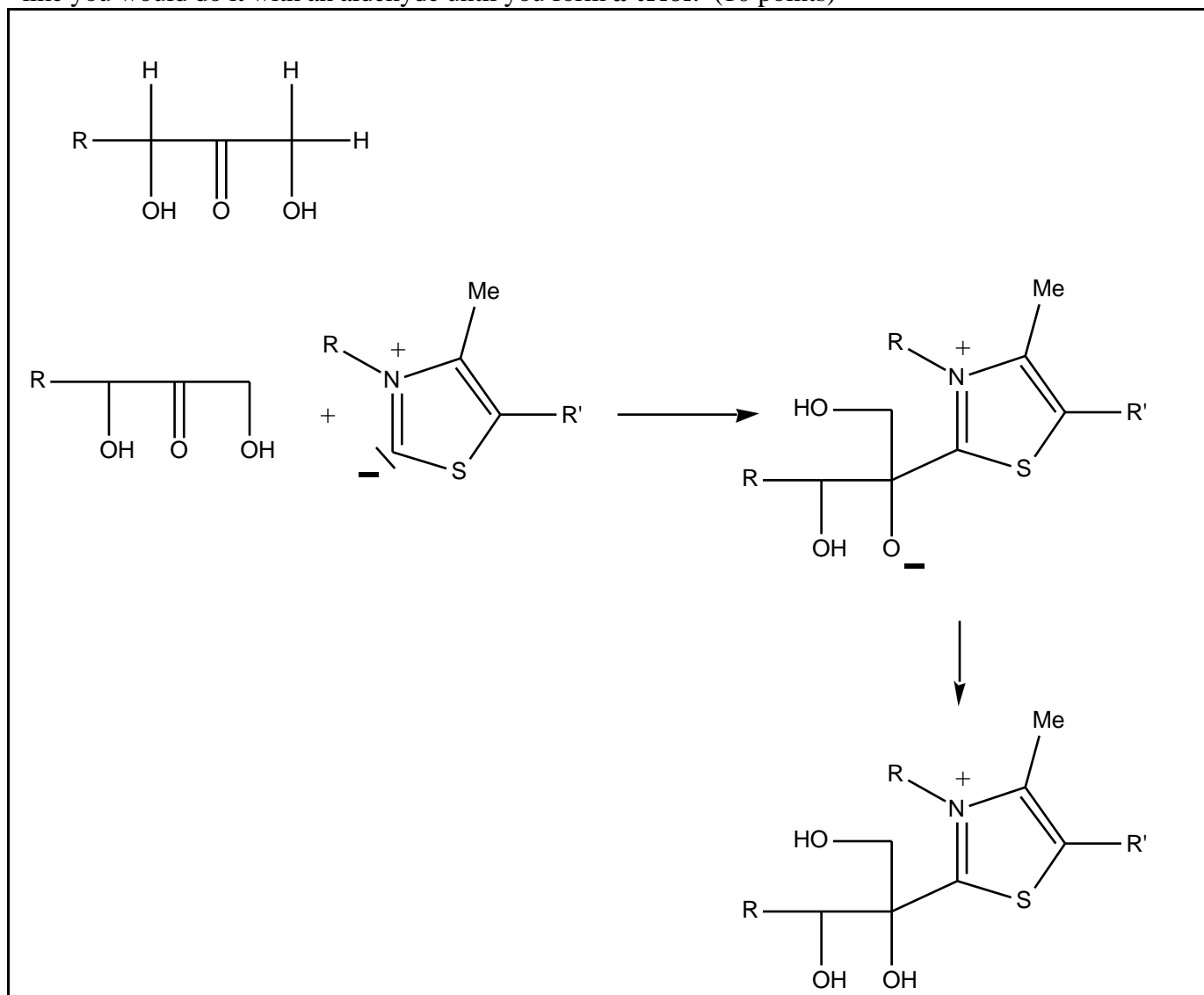


Mechanism for the Reaction of Propanal with Deprotonated Vitamin B₁

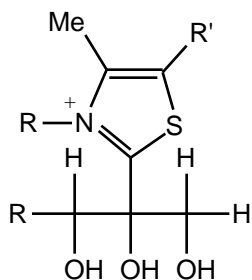


Alpha hydroxycarbonyls occur in sugars and we want to look at a simple sugar with the general formula $R-CHOH-CO-CH_2-OH$. This is an alpha,alpha-dihydroxy ketone and we want to see how this sugar reacts with deprotonated vitamin B₁. There are two important things to realize: (1) We will react this **ketone** with vitamin B₁ while (in lecture) we learned the thiazolium ion catalyzed dimerization for **aldehydes** only. So, we will have to see what will be different for the ketones compared to the aldehydes. (2) You might be very confused (and rightly so!) by the presence of the **hydroxy groups**. You would expect to see the **formation** of an alpha-hydroxy carbonyl in the normal thiazolium ion catalyzed dimerization of aldehydes. There is no rule that prohibits the presence of such hydroxy groups in the carbonyl compound.

(c) Let's look at the reaction of deprotonated vitamin B₁ with the sugar. Do this reaction step by step just like you would do it with an aldehyde until you form **a triol**. (10 points)



(d) This is where the difference lies between this sugar ketone and the reaction of the aldehydes. In the case of the sugar the triol can only stabilize by elimination of either of the groups R-CHOH- or -CH₂-OH as a cation (instead of the proton that leaves in the aldehyde case). Decide which of these groups leaves and write down the product. (5 points)

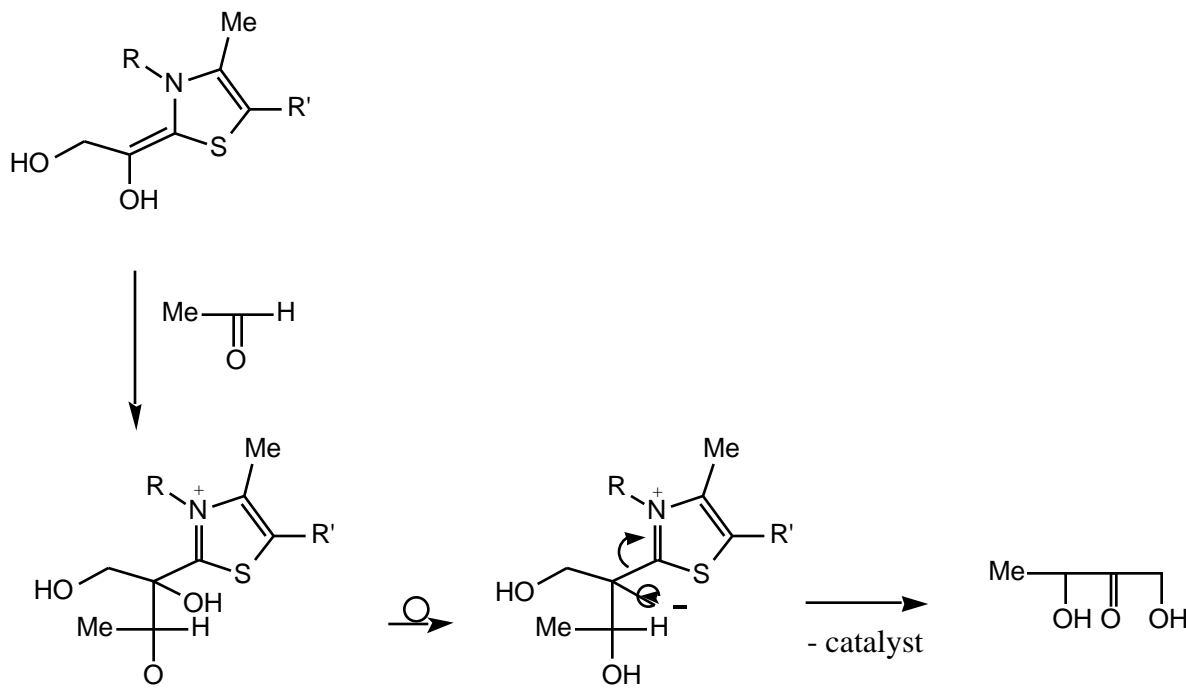


Clear cut: The R-CH-OH group leaves as the cation.

Both possibilities give O-stabilized carbenium ions.

The RCHOH also benefits from the inductive effect of the methyl group.

(e) React the product formed in (d) **with acetaldehyde**. Comment on what the overall reaction sequence (c) - (e) has achieved. (15 points)



OVERALL REACTION: The RCHOH group was replaced by the MeCHOH group.