

PS #1 – The Aldol Condensation

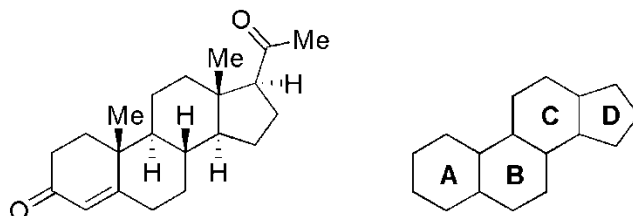
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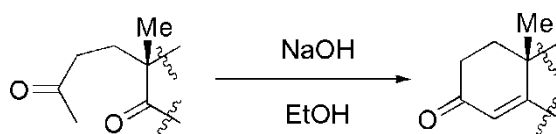
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Progesterone belongs to a class of hormones called progestogens, and is the major naturally occurring human progestogen. You might recognize the fused ring structure common to all steroids. In one synthesis of progesterone (W.S. Johnson, 1971) the A ring was formed in the final step by an intramolecular aldol condensation. Aldol condensation reactions can occur under acidic or basic conditions and are often followed by elimination to form the enone.

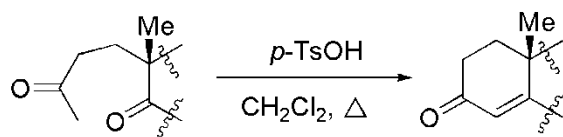
Progesterone:



Part A) Work together and determine the mechanism for the base catalyzed aldol condensation. Give the complete and gory detailed mechanism, *including all proton transfer steps, intermediates, and byproducts*. You may abbreviate the structure of progesterone.



Part B) Now provide the mechanism for the acid catalyzed aldol condensation. Follow the same guidelines as in part A.



Part C) Examine the pK_a values provided below. What is the physical meaning of these numbers? Discuss the conditions necessary to protonate the enolate ion to form the enol. What is the protonation state of the enolate in part A? Part B? When is the ketone protonated? Check back to part A and B and see if the conclusions you have drawn here are consistent with the mechanisms you provided.

