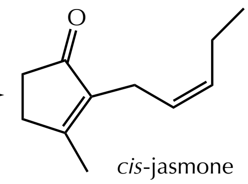
These questions do not appear in the book.

A. As part of the synthesis of *cis*-jasmone, a fragrant component found in jasmine flowers, an intramolecular aldol condensation was carried out as shown. Provide the structure of the starting compound, molecule A, in the box below.

$C_{11}H_{18}O_2$
molecule A

KOH →



cis-jasmone

+ H_2O

In addition to *cis*-jasmone there are three other potential aldol condensation products that could arise from molecule A. They are constitutional isomers of cis-jasmone. In the three boxes below, provide the structures of each of the other potential aldol condensation products. Note: the order in which you draw the structures does not matter.

condensation product B

condensation product C

condensation product D

Of the three structures you drew above (B, C and D), which is the closest in stability to cis-jasmone? Write the letter corresponding to the structure:

Circle each of the statement(s) that is true:

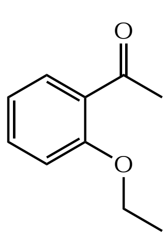
cis-Jasmone is the most stable aldol condensation product that could be formed in the reaction.

cis-Jasmone is the least stable aldol condensation product that could be formed in the reaction.

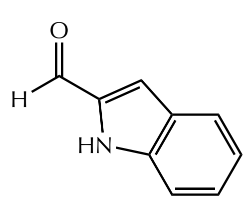
The nucleophile in this reaction is an enol.

Elimination to form the conjugated double bond is the final step in the reaction mechanism.

B. From *J. Med. Chem.* **2015**, *58*, 1244. Provide the structure of the product.



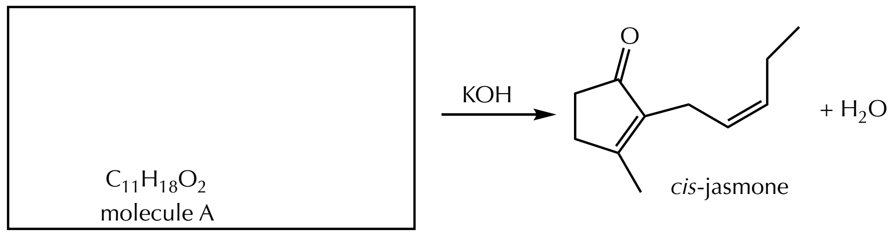
+



NaOH → CH_3CH_2OH

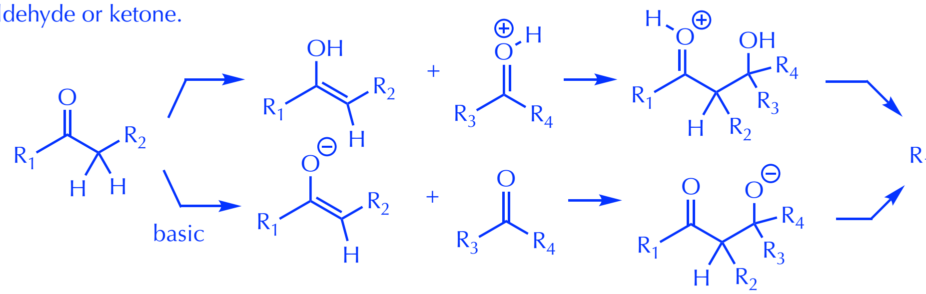
Chemistry 215 • Thinking in Blue • Week 08

A. As part of the synthesis of *cis*-jasmone, a fragrant component found in jasmine flowers, an intramolecular aldol condensation was carried out as shown. Provide the structure of the starting molecule, molecule A, in the box below.



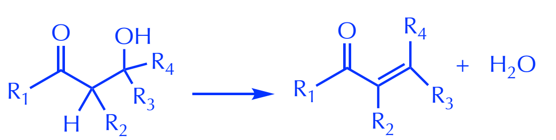
The text of the problem provided the identification, and the equation reinforces this with the molecular formula for molecule A as well as the indication of water forming in the balanced equation. Thus, there are lots of reminders that this is an example of an “intramolecular aldol condensation.” However, if you do not know what aldol condensation means, in general, or what it means to be an intramolecular aldol condensation, in particular, you are unlikely to be able to figure this out from this information.

An aldol reaction is when an enol or enolate nucleophile undergoes an addition reaction to the carbonyl carbon of an aldehyde or ketone.

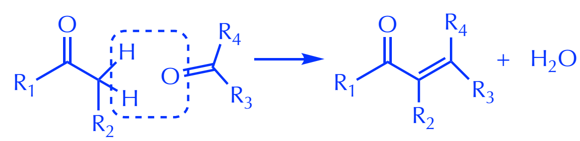


aldol reaction product (stereoisomers)

In the aldol condensation, the aldol reaction product dehydrates (undergoes elimination of water), which can happen under acidic or basic conditions. The elimination reaction is favorable because the proton being lost is acidic and the double bond that forms is conjugated with the carbonyl (that is, these are delocalizable electrons with the corresponding resonance contributors). Structurally, that loss of the elements of water can be visualized when comparing the two original starting materials side by side.

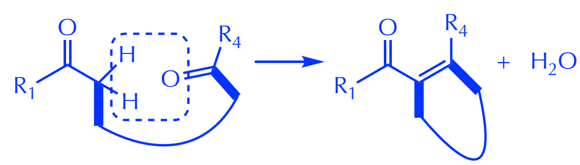


aldol reaction product → aldol condensation product (E & Z)



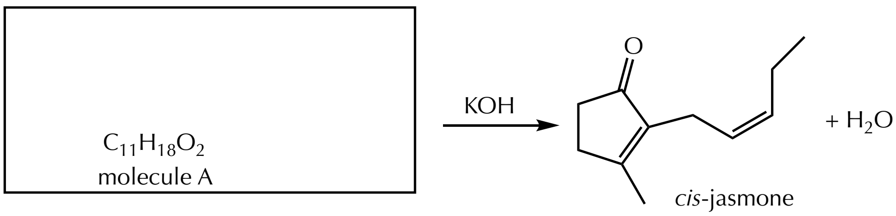
this does not represent an actual reaction process, but it nicely represents a way to think about the overall reaction outcome; having more than one way to think about a reaction is useful

By having multiple representations for these general relationships, it becomes easier to move between different ideas. Seeing how the intermolecular and intramolecular aldol condensation reactions compare, for example, finishes what a person needs to have in mind when reading this question. Notice also that showing the water molecule in the original question is a reinforcing clue, as is having a molecular formula for molecule A that has all of the atoms of the organic product ($C_{11}H_{16}O$) plus the water ($C_{11}H_{18}O_2$).



comparable thinking used to represent the overall change in the intramolecular aldol condensation, with respect to the intermolecular version (directly above)

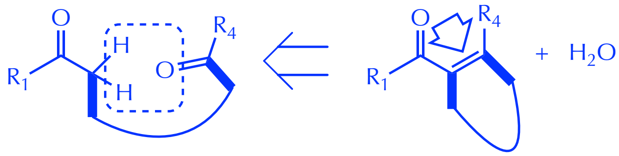
A. As part of the synthesis of *cis*-jasmone, a fragrant component found in jasmine flowers, an intramolecular aldol condensation was carried out as shown. Provide the structure of the starting molecule, molecule A, in the box below.



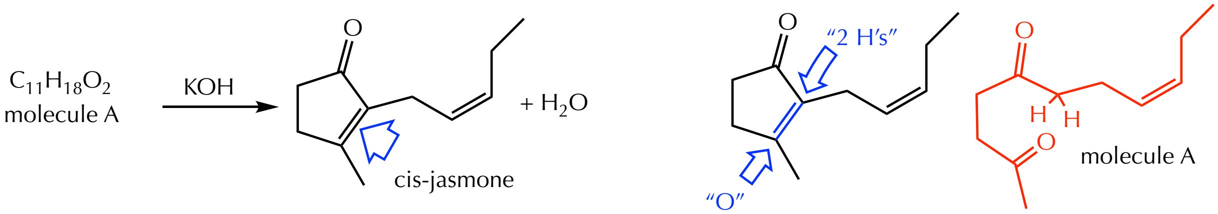
In addition to *cis*-jasmone there are three other potential aldol condensation products that could arise from molecule A. They are constitutional isomers of *cis*-jasmone. In the three boxes below, provide the structures of each of the other potential aldol condensation products. Note: the order in which you draw the structures does not matter.

condensation product B	condensation product C	condensation product D

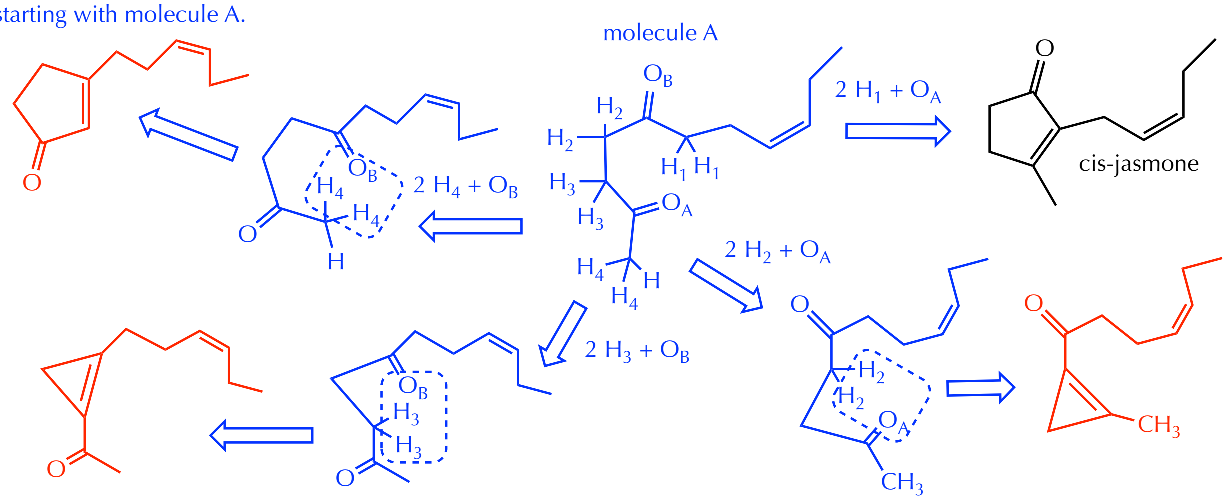
In this question, the product from the intramolecular aldol condensation is given, so this representation of the general relationship is particularly useful because the mechanism is not being requested, only the structure of the starting material. This is the general idea that needs to be applied to this case.

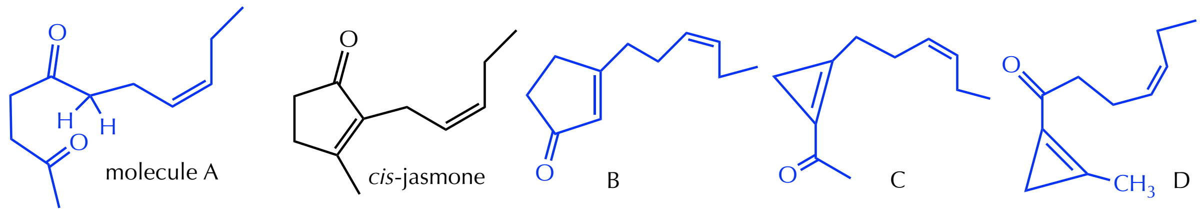


The double bond that is conjugated with the carbonyl is the one that forms in the reaction, and the elements of water need to be reintroduced into the starting material: the two H's on the side of the carbonyl in the product, and the oxygen atom on the other carbon that ends up as a double bond.



Exactly the same analysis can be used to identify the other three aldol condensation products that are possible, starting with molecule A.





Of the three structures you drew above (B, C and D), which is the closest in stability to cis-jasmone? Write the letter corresponding to the structure: B (the other two, with 3-membered rings, would be strained

Circle each of the statement(s) that is true:

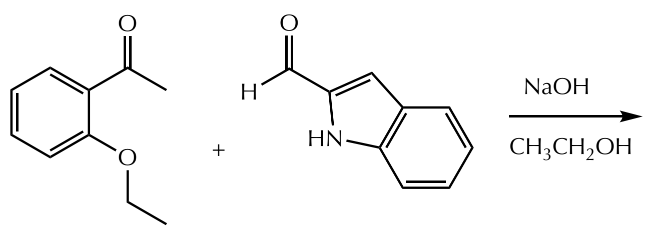
cis-Jasmone is the most stable aldol condensation product that could be formed in the reaction.
TRUE 5-membered better than 3-membered, more substituted double bond more stable

cis-Jasmone is the least stable aldol condensation product that could be formed in the reaction.
FALSE 5-membered better than 3-membered, more substituted double bond more stable

The nucleophile in this reaction is an enol.
FALSE under base conditions, the reaction would involve an enolate

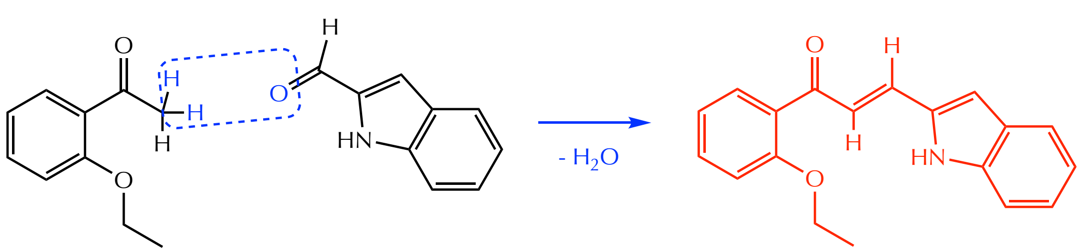
Elimination to form the conjugated double bond is the final step in the reaction mechanism.
TRUE that is a correct description of the mechanism

B. From *J. Med. Chem.* **2015**, *58*, 1244. Provide the structure of the product.



The only real clues about the identification of this question are (1) there is one each of typically more reactive groups in each molecule (ketone on the left, aldehyde on the right) and (2) it is an exam (and an exam page) where aldol condensations were being tested. This latter point is risky, naturally. In addition, there is no explicit indication about whether an aldol reaction versus an aldol condensation is expected, so (3) understanding that the elimination product is the usual result, in the absence of information to the contrary, is the assumption that would need to be made here.

At that point, the analysis requires the same application of the general principle of "aldol condensation" that was used in part A.



the ketone is the only one with acidic carbon-H's for forming an enolate, so this is the only possible enolate nucleophile

and that leaves the aldehyde as the electrophile that is added to by the enolate

the (E) diastereomer is shown; the (Z) is also possible