

PROBLEM SET I: ADDITIONS AND ELIMINATIONS

ANSWER KEY

1. How would you distinguish between specific acid catalysis and general acid catalysis in the case of carbonyl hydration? Explain in 30 words or less (5 points).

The rate of specific acid catalyzed reactions depends only on the pH, while the rate of general acid catalyzed reactions depends on the sum of concentrations of all acids in solution. The two can be distinguished by running the reaction at constant pH but with two different concentrations of buffer: if specific acid catalyzed, reaction will show no change in rate.

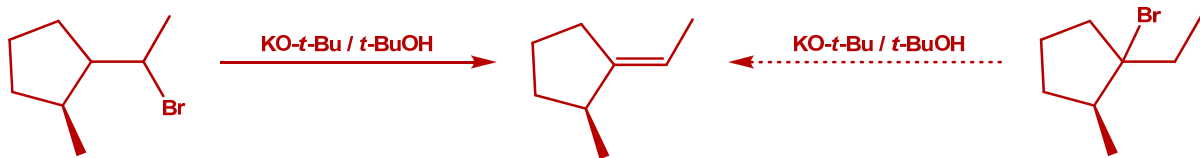
2. The hydrates of aldehydes and ketones are considerably more acidic than normal alcohols ($pK \approx 16-19$). How would you account for this fact? Some reported values are shown below. Explain the order of relative acidity, in 30 words or less (5 points).

<u>Hydrate of...</u>	<u>pK</u>
formaldehyde	13.4
trichloroacetaldehyde	10.0
2,2,2-trifluoro-1-phenylethanone	10.0
2,2,2-trifluoro-1-(4-nitrophenyl)ethanone	9.2

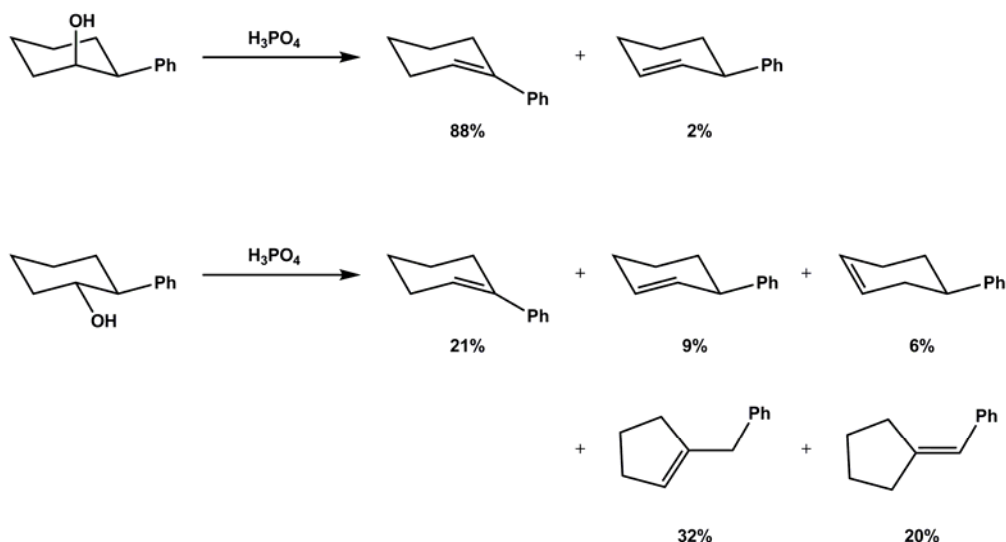
Geminal diols have an additional $-OH$ group which acts as an inductively electron-withdrawing group. This explains why formaldehyde hydrate is a stronger acid than methanol. Minor stabilization of the conjugate base of geminal diols might also come from hydrogen bonding between $-O^-$ and the remaining $-OH$ group. The order of relative acidities is consistent with analogous reasoning for normal alcohols, wherein stronger electron withdrawing groups ($H < CCl_3 < CF_3 < CF_3 + o\text{-nitrophenyl}$) increase the diol's acidity.

3. What alkyl bromide would give (*S,E*)-1-ethylidene-2-methylcyclopentane as the predominant product upon treatment with $KO-t\text{-Bu} / t\text{-BuOH}$? Be careful about drawing the correct stereochemistry (5 points).

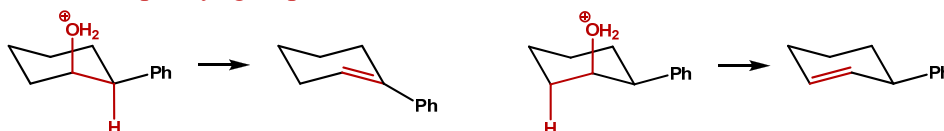
According to the Zaitsev' rule, the desired alkene product will be formed through the elimination of HBr from (2*S*)-1-(1-bromoethyl)-2-methylcyclopentane (shown on the left). The alternative, shown on the right, would tend to give the more substituted alkene product, with the double bond being a part of the five-membered ring:



4. The acid-catalyzed dehydration of 2-phenylcyclohexanol gives very different product ratios depending upon whether the reactant is cis or trans. Write a mechanism for these dehydration reactions that explains the product ratios (10 points).



Cis-isomer undergoes E2 elimination through the anti-periplanar conformation of the starting material. Two different protons can be eliminated, giving rise to two different alkenes. The one on the left is the major product because conjugation with the phenyl group stabilizes its double bond:



Trans-isomer cannot achieve the anti-periplanar arrangement required for the E2-elimination, and instead, a cation is formed and the reaction proceeds according to E1 mechanism. The original cation can deprotonate directly, or undergo one of three possible rearrangements (hydride shifts: blue and red arrows, alkyl shift: green arrow). Additional rearrangements are possible for the secondary benzylic cation (purple cation). Any one of these cations can deprotonate to give the different products observed:

