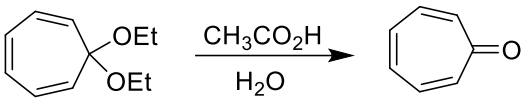
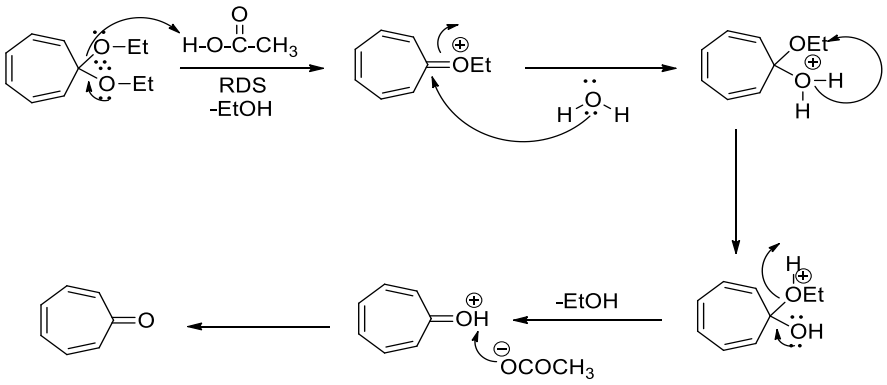
CML 103 (2020) Final (Total Marks: 50)

Part-1

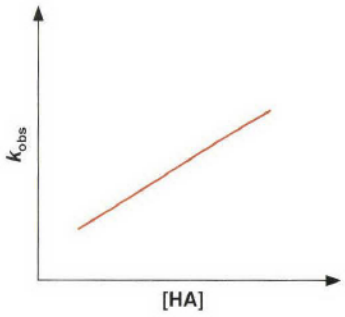
1. Q. The following reaction occurs by a general-acid catalyzed mechanism. Propose a mechanism for this reaction. Draw every step clearly and cite the rate determining step. (0.5*6)
   Propose minimum five experiments you can devise to support your proposed mechanism. (5)

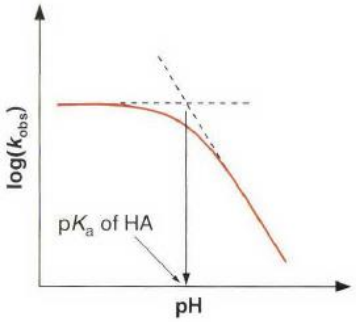


A.



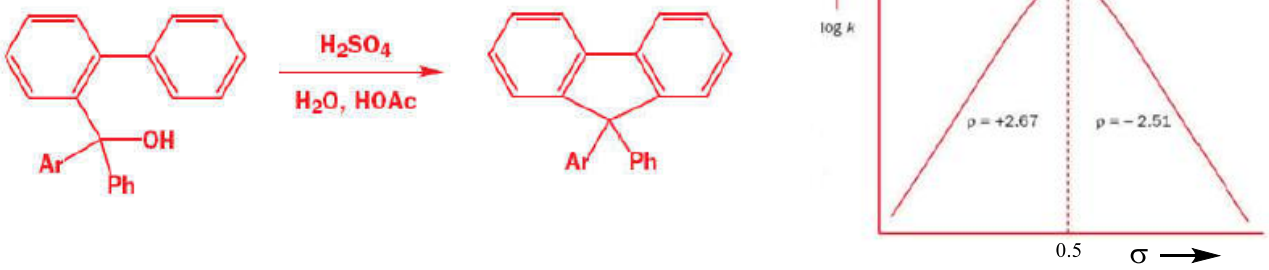
1. $\Delta S^{\#}$ = large – value
2. $k_{O\text{-}H}/k_{O\text{-}D}$ > 2.0; primary KIE or rate in H_2O is faster than in D_2O
3. ρ = (-) vs
4. Rate = k [substrate]^1 [CH_3CO_2H]^1
5.





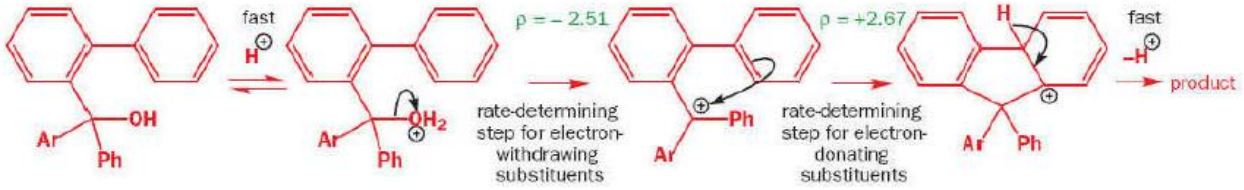
2. Q. Draw the possible mechanism of the following cyclization reaction, and assign the rate determine steps with reasons that follows the non-linear Hammett plot given below. (3+3)

Hammett plot



A. 1 mark showing each 3 steps correctly. (3); 1 mark each for assigning correct rds for ews (electron withdrawing substituents) and eds. (2); 1 marks for mentioning ews and eds in appropriate step or explaining . (1)

B.



3. In the large-scale industrial production of methylamines, methanol and NH_3 are reacted at 350–500 °C and 20 bar in the presence of Al_2O_3. A mixture of mono-, di-, and trimethylamine is obtained with an equilibrium content of ca. 62% trimethylamine. However, trimethylamine is of only minor economic importance. Suggest how the product spectrum could be modified to favor mono- and dimethylamine. (3)

A. The product selectivity towards smaller amines can be obtained by using porous alumina with appropriate sizes. The confined space within pores of alumina can enhance the selectivity towards smaller amines via shape-selective catalysis.

4. Answer each of the following with reference to the corresponding substituent constants considering both inductive and resonance electronic contributions. Illustrate your answer showing resonance structures for substituted benzoic acids, where appropriate.

(a) The σ_{meta} and σ_{para} values for the $–CO_2CH_3$ group are both positive with $\sigma_{para} > \sigma_{meta}$. (2)

A.

a) The σ_{meta} and σ_{para} values for the $-CO_2CH_3$ group are 0.33 and 0.45, respectively. This carbomethoxy group is therefore electron withdrawing by both inductive and resonance effects. The carbonyl carbon (C=O) is bears a slightly positive charge as a result of the more electronegative oxygen atoms it is bonded to, giving rise to an inductive withdrawing effect. We can roughly say that $\sigma_I \sim 0.33$ and $\sigma_R \sim 0.12$.

Moreover, the carbonyl carbon is sp^2 hybridized and can therefore participate in resonance when bonded to an aromatic ring. The extra resonance structure in which the negative charge resides on the carbonyl oxygen contributes to the withdrawing ability of this substituent

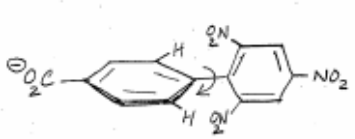
(b) The values of σmeta for the methoxy substituent ($-OCH_3$) is positive, whereas the values for σ_{para} is negative. (2)

A.

b) The σ_{meta} and σ_{para} values for the $-OCH_3$ group are 0.12 and -0.27, respectively. This means that the methoxy group is electron withdrawing by induction and electron donating by resonance. In the meta position, the electronic effect is governed by the fact that the oxygen of the methoxy group bonded to an aromatic carbon is more electronegative and $\sigma_I \sim 0.12$. However, in the para position we have additional resonance effects as a result of the lone pair electrons on oxygen being donated back into the aromatic ring (depicted below). The observed σ_{para} value is the sum of both effects and is net donating. We can therefore estimate that $\sigma_R \sim -0.39$.

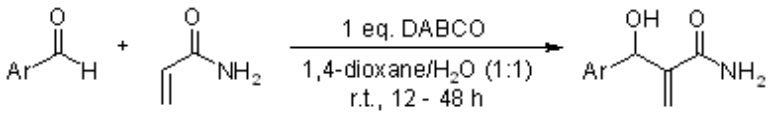
(c) The picryl (2,4,6-trinitrophenyl) substituent, $-C_6H_2(NO_2)_3$ is relatively large with the ortho nitro groups sterically interfering with atoms in the ortho positions on an adjacent aromatic ring. Predict the sign and relative magnitude of σ_{meta} and σ_{para} for the picryl substituent. (3)

c) The picryl substituent is electron withdrawing due to the inductive effect of the three nitro groups pulling electron density from the aromatic ring. There is no appreciable resonance contribution when picryl is in the *para* position as can be seen by the fact that $\sigma_{meta} \sim \sigma_{para}$ (0.42). This lack of resonance contribution can be understood by considering the large steric interactions that result in a significant twist angle between the two aromatic rings. The extent of conjugation drops off steeply with the dihedral angle between adjacent p-orbitals. Hence $\sigma_R \sim 0$ in this case.

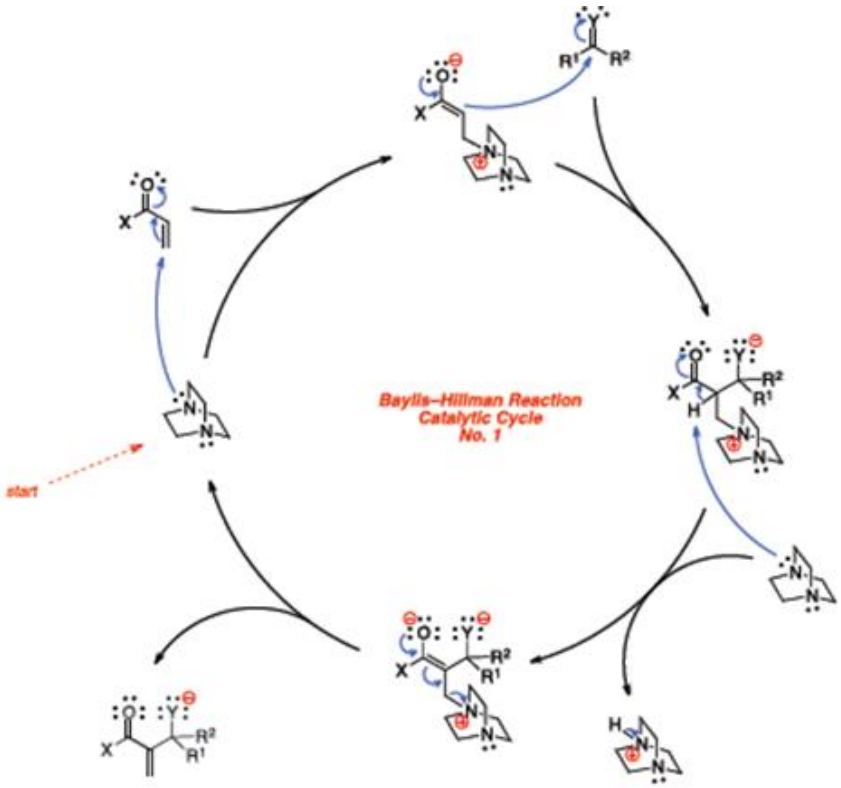


steric hinderance betw. ortho NO_2 groups and H's on adjacent aromatic ring results in twisted structure and loss of p-orbital overlap ($\therefore \sigma_R \sim 0$)

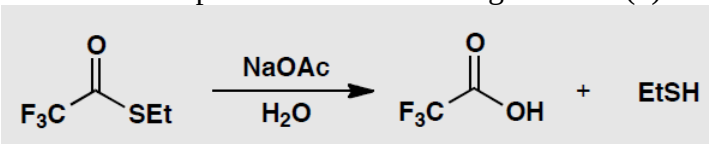
5. Draw the mechanism of the following reaction. Show all the steps clearly. (6)



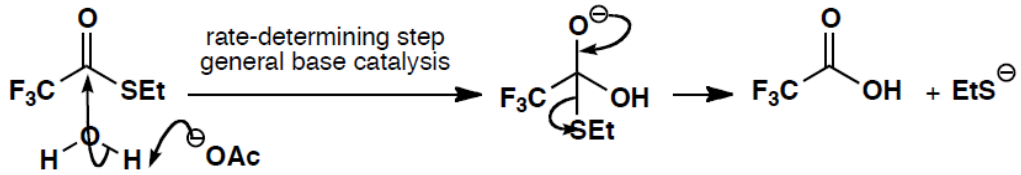
A. 1.5 point for showing each of the 4 steps in the catalytic cycle.



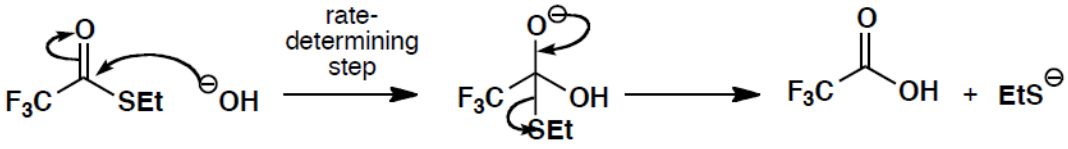
6. Between pH 2 and 7 the rate of hydrolysis of this ester is independent of pH. At pH 5 the rate is proportional to the concentration of acetate ion (AcO^-) in the buffer solution and the reaction goes twice as fast in H_2O as in D_2O. Suggest a mechanism for the pH-independent hydrolysis. (2) Above pH 7, the rate increases with pH. What kind of change is this? (2)



A. a)

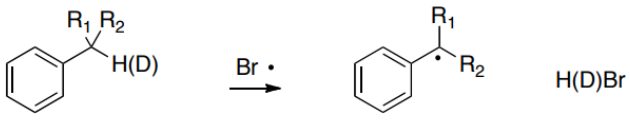


b) Above pH 7, the hydrolysis becomes specific base catalysis.



7. What can you infer about the nature of the transition state based on the KIE data of the following reaction? (3)

Consider the KIE data for the following reaction



R_1	R_2	k_H/k_D
H	H	4.9
CH_3	H	2.7
CH_3	CH_3	1.8

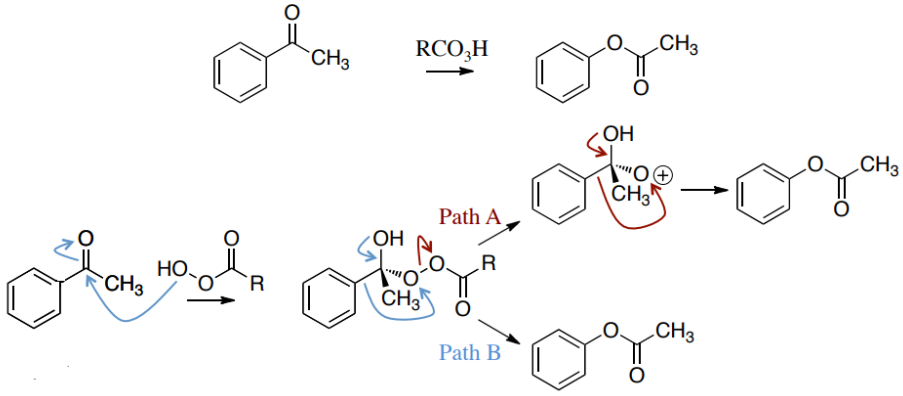
A. 1. Primary KIE as the C-H or C-D bond is broken in RDS. (1)

2. The stability of the transition state changes with more alkyl substituents, the primary KIE indicates the transition state is moving away from symmetrical with more alkyl substituents as seen be the lower values (further away from a predicted maximum value of ~8).

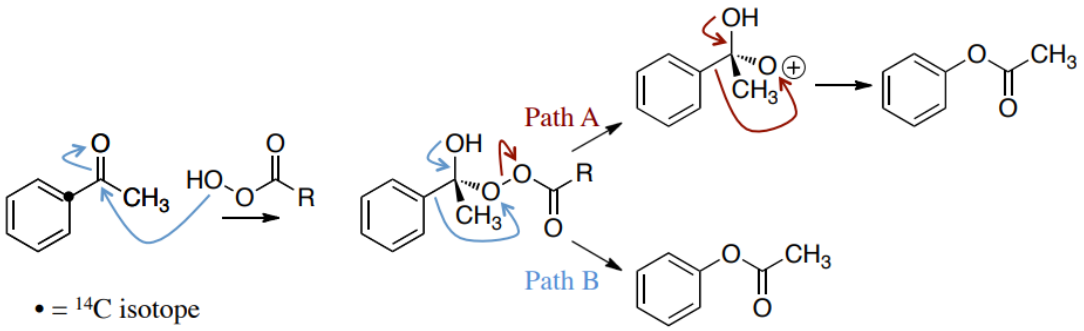
   Or, transition state becoming more bent with more alkyl substituents (2)

8. Propose minimum two experiments you can devise, that can be used to distinguish between A- and B-pathway given below. Explain each experiment how it can distinguish one pathway compare to the other pathway. (6)

Consider a Baeyer-Villiger oxidation



A. 1.



To distinguish possible pathway A or B, a ^{14}C isotope was placed at position indicated and a $k^{12}C/k^{14}C$ KIE of 1.048 was determined

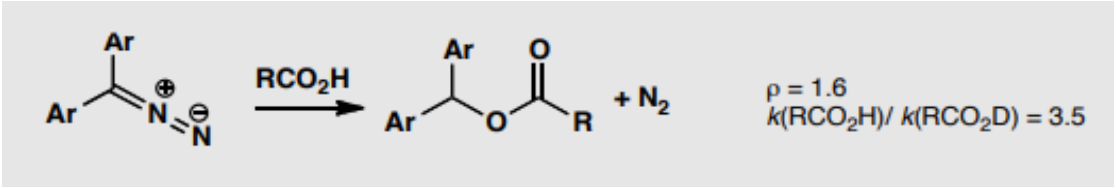
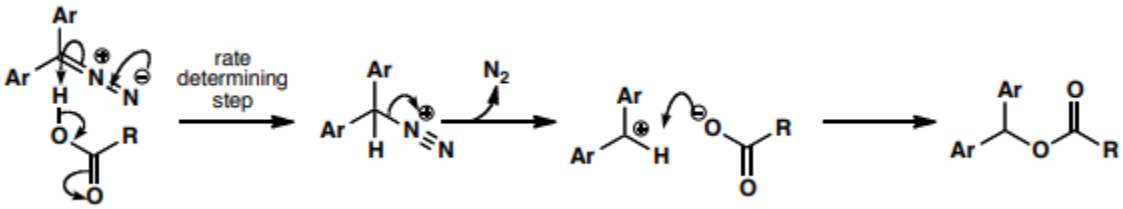
Corresponds to a 1° KIE for $^{12}C/^{14}C$ (maximum would be 1.24), therefore must be path B

287

2. From Hammett plot,
   A pathway: ρ should be close to -1 to -2 as + charge is developing but far from aromatic ring.

   B pathway, ρ would be close to zero as no charge is developing.

9. The reaction of diazo compound with carboxylic acid give gaseous nitrogen and esters as products. Based on the experimental data given below, draw a suitable mechanism and cite the rate determining step. (4)
Also, draw the energy profile diagram of the same reaction pathway. (3)



A. The reaction has a normal kinetic isotope effect (RCO_2H reacts faster than RCO_2D) while the second has an inverse deuterium isotope effect (RCO_2H reacts slower than RCO_2D). This suggests that there is a rate-determining proton transfer in the first reaction but specific acid catalysis in the second (i.e. fast equilibrium proton transfer followed by slow reaction of the protonated species). Protonation occurs at carbon in both reactions, and this can be a slow step.