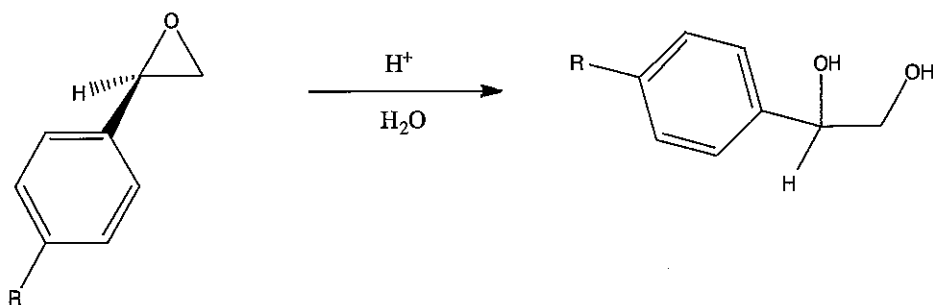


Mechanism Problems

1. The following data was used to investigate the reaction below:



A. The rate of the reaction is measured in a series of buffers at different concentrations but the same pH. The rates of reaction do not change across the series of buffers. What does this suggest about the mechanism?

This suggests that pH ($[H_3O^+]$) controls the rate, not all acids present in solution. This occurs in a pre-equilibrium acid catalysis, which is specific acids catalysis.

B. The effect of changing substituents on rate is as follows.

R =	Rate constant ($M^{-1}s^{-1}$)	σ_p
methoxy	11000	-.78
H	5.8	0
chloro	2.0	.11
methyl	116	-.31

How would you use these data to calculate the rho (ρ) value for this reaction? According to these data, would ρ be positive or negative? Would the reaction rate be increase by electron withdrawing groups or electron donating groups? What do these data suggest about the mechanism?

First, find the rate ratio for each substituent. For example, for methoxy, $\frac{k_{\text{ome}}}{k_H} = \frac{11000}{5.8}$. Then plot these values versus the sigma values. Plotting, this would make ρ negative. The rate is increased by EDG, which suggest that positive character develops in the rate determining TS.

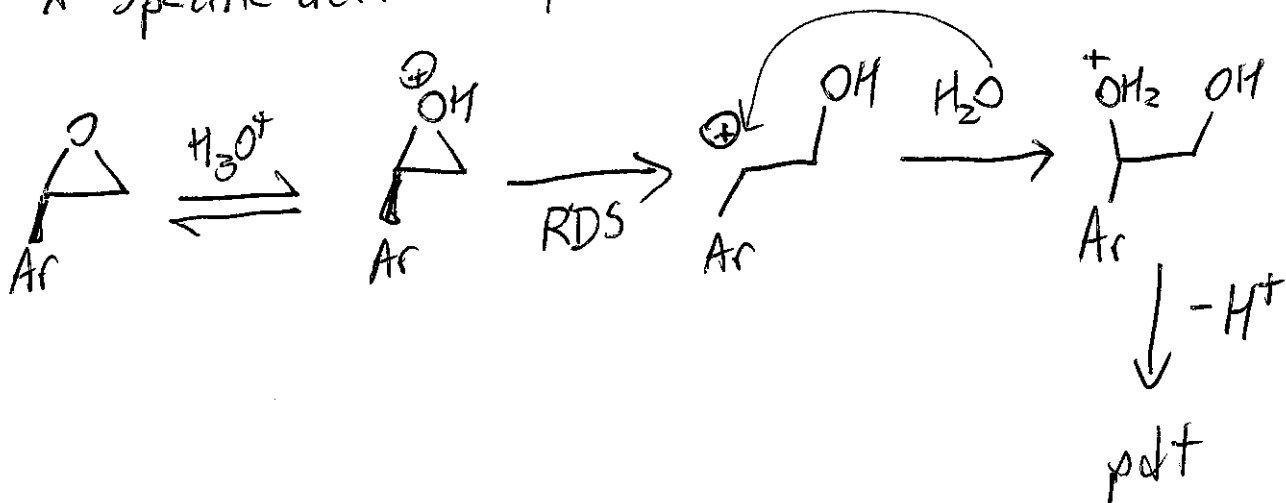
C. If the reaction is run in $^{18}\text{OH}_2$, the isotope label ends up only in the benzylic position (closer to the aryl group.) Starting with the optically active substrate above, the hydrolysis leads to an optically inactive product (a racemic mixture.) Propose a full mechanism for this reaction, and label the rate determining step.

* Since isotope is incorporated only at benzylic position, the E^+ center is the benzylic center. No attack on the less substituted carbon!

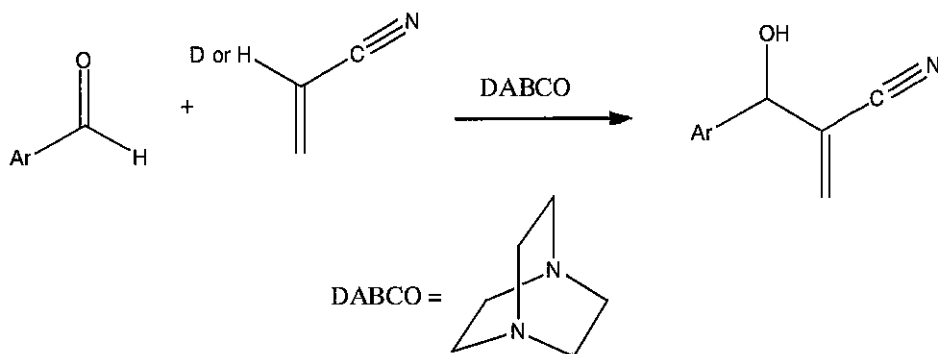
* Racemization is consistent with carbocation formation.

→ This is also consistent with LFER data.

* Specific acid catalysis tells us which step is RDS.



2. Propose a mechanism for the following reaction, and explain how it is consistent with each piece of data.



Data:

A. $\text{rate} = k [\text{DABCO}][\text{aldehyde}][\text{nitrile}]$

All these compounds are involved in the mechanism up to, and including, the Rate Determining step.

B. DABCO works better than other amines as a catalyst for this reaction. The reason for this is that, while DABCO is not the strongest amine base, it is a very good nucleophile.

This sterically unhindered lone pair acts as a nucleophilic catalyst, because it is not incorporated into the final product.

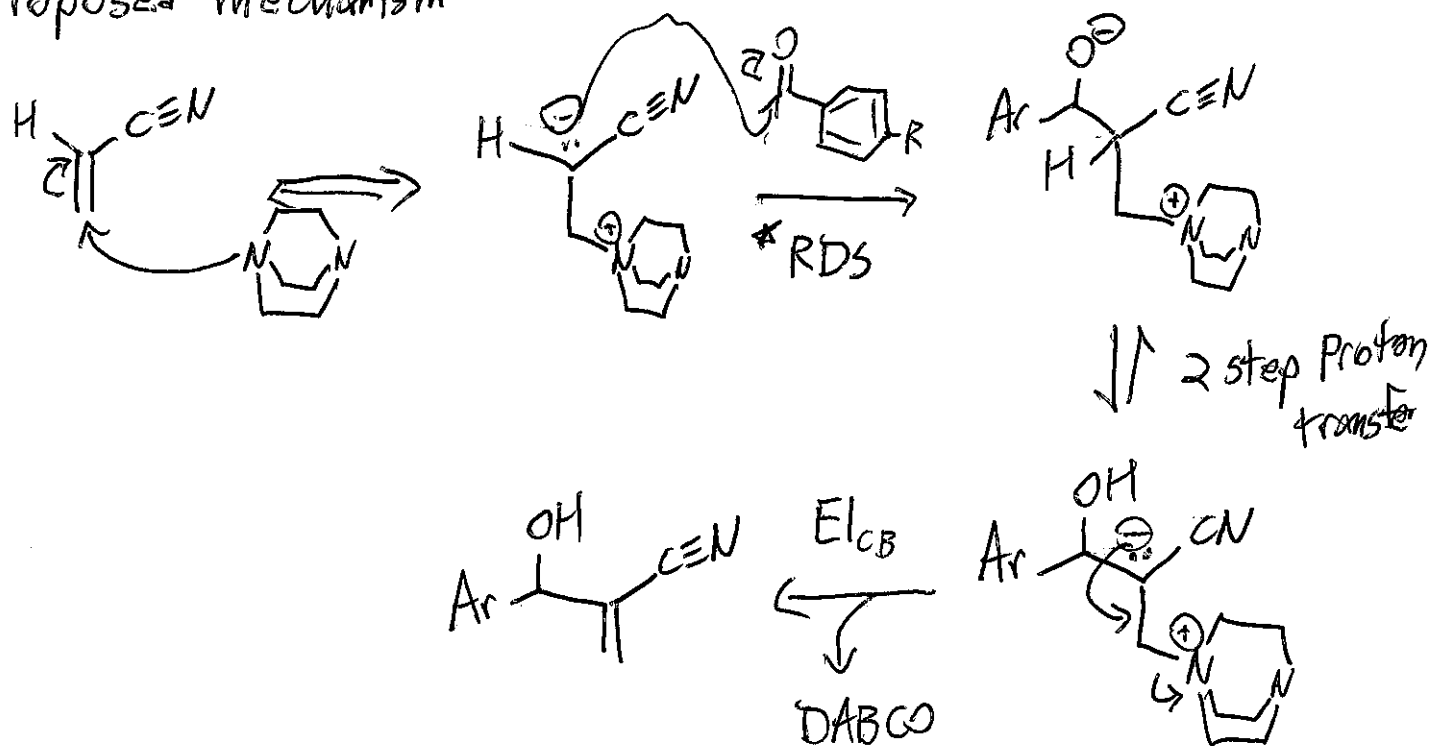
C. The Hammett ρ value for this reaction is +2.5.

An EWG speeds this reaction, meaning that δ^- charge is developing in the RDS.

D. When R = deuterium, the KIE is $k_H/k_D = 1.03 \pm 0.1$.

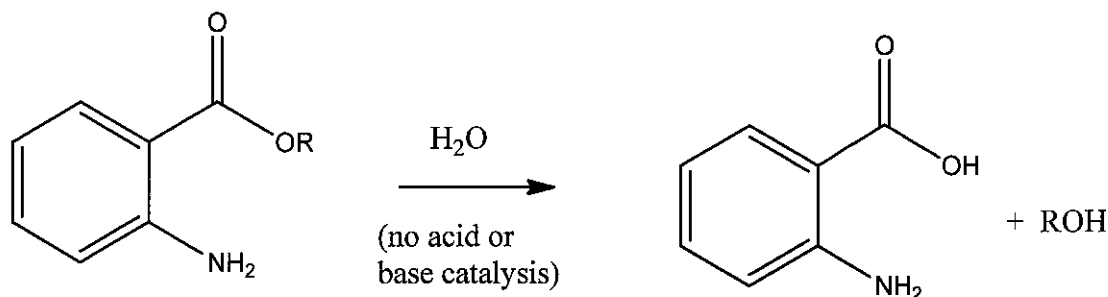
The proton α to the nitrile is not removed in the RDS - not a primary KIE.

Proposed mechanism



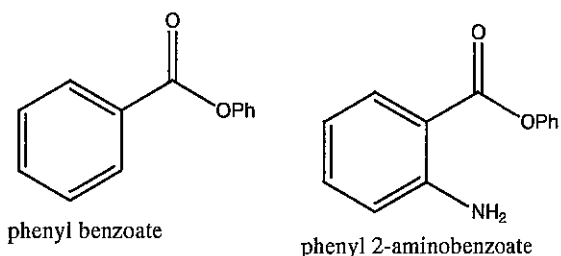
★★ Another acceptable mechanism would involve an $\text{E}_{2\text{c}}$ elimination of DABCO rather than $\text{E}_{1\text{cB}}$.

3. Propose a mechanism for the following reaction, and explain how it is consistent with each piece of data.



Data:

A. The rate of hydrolysis of phenyl benzoate is 10 times slower than phenyl 2-aminobenzoate.



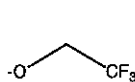
The amine is involved before the RDS. Usually, an EDG would be expected to slow a Nu: Acyl substitution, because δ^- charge is developing

B. When the reaction is run in D_2O , the reaction rate is slowed by a factor of two ($k_H/k_D = 2$)

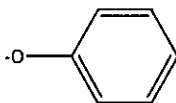
A primary, normal KIE suggests that a $\text{D}-\overset{\uparrow}{\text{O}}-\text{D}$ bond is being broken in the RDS.

C. When R was changed (as in the figure below), the β_{lg} value was determined to be about 0.

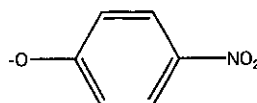
Leaving group:



worst LG
(pKa = 12)



moderate LG
(pKa = 10)



best LG
(pKa = 7)

The nature of the LG does not affect the rate, so the LG step is after the RDS

D. When acid is added to the reaction, the rate of reaction decreases significantly.

Added acid would protonate the amine, so the protonated amine is less reactive. The amine lone pair must catalyze the rxn.

