

## Mechanistic Organic Chemistry Homework

The following problems would be good practice to test your knowledge on these topics. You can look up the answers by finding the references at the back of this handout.

Kinetics: 7, 10

LRER: 4, 5, 6

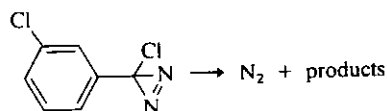
Kinetic Isotope Effects: 9, 12, 22

Overall problems: 3, 11, 14

2. (a) Calculate the enthalpy and entropy of activation ( $\Delta H^\ddagger$  and  $\Delta S^\ddagger$ ) at 40°C for the acetolysis of *m*-chlorobenzyl *p*-toluenesulfonate from the data given:

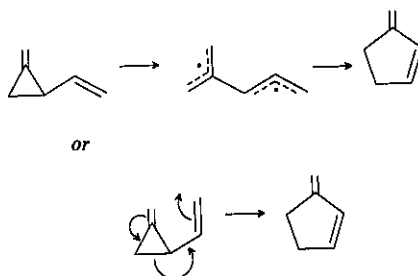
Temp. (°C)	$k \times 10^5$ (s <sup>-1</sup> )
25.0	0.0136
40.0	0.085
50.1	0.272
58.8	0.726

- (b) Calculate the activation parameters  $\Delta E_a$ ,  $\Delta H^\ddagger$ , and  $\Delta S^\ddagger$  at 100°C from the data given for the reaction shown below:



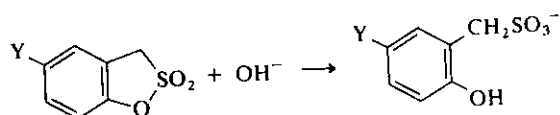
Temp. (°C)	$k \times 10^4$ (s <sup>-1</sup> )
60.0	0.30
70.0	0.97
75.0	1.79
80.0	3.09
90.0	8.92
95.0	15.90

3. 2-Vinylmethylenecyclopropane rearranges in the gas phase to 3-methylenecyclopentene. Two possible reaction mechanisms are:



- (a) Sketch a reaction energy diagram for each process.  
 (b) How might an isotopic labeling experiment distinguish between these mechanisms?
4. In Table 4.3 the phenyl group is assigned both a  $\sigma^+$  and a  $\sigma^-$  value. Furthermore, the signs of  $\sigma^+$  and  $\sigma^-$  are different. Discuss the reasons that the phenyl group has both a  $\sigma^+$  and a  $\sigma^-$  value and explain why they are of a different sign.
5. Match the  $\rho$  values with the appropriate reactions. Explain your reasoning.  
 Reaction constants: +2.45, +0.75, -2.39, -7.29  
 Reactions:  
 (a) nitration of substituted benzenes

- (b) ionization of substituted benzenethiols  
 (c) ionization of substituted benzenephosphonic acids  
 (d) reaction of substituted *N,N*-dimethylanilines with methyl iodide.
6. (a) Determine the value of  $\rho$  for the reaction shown from the data given:

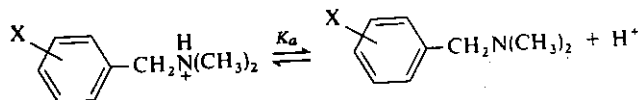


Y	$k(M^{-1} s^{-1})$
H	37.4
CH <sub>3</sub> O	21.3
CH <sub>3</sub>	24.0
Br	95.1
NO <sub>2</sub>	1430

- (b) The pseudo-first-order rate constants for the acid-catalyzed hydration of substituted styrenes in 3.5 M HClO<sub>4</sub> at 25° are given. Plot the data against  $\sigma$  and  $\sigma^+$  and determine  $\rho$  and  $\rho^+$ . Interpret the significance of the results.

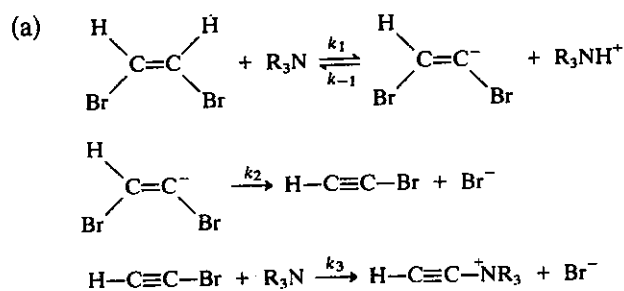
Substituent	$k \times 10^8 (sec^{-1})$
<i>p</i> -CH <sub>3</sub> O	488,00
<i>p</i> -CH <sub>3</sub>	16,400
H	811
<i>p</i> -Cl	318
<i>p</i> -NO <sub>2</sub>	1.44

- (c) The basicity of a series of substituted benzyldimethylamines has been measured. Determine whether these basicity data are correlated by the Hammett equation. What is the value of  $\rho$ ? What interpretation do you put on its sign?

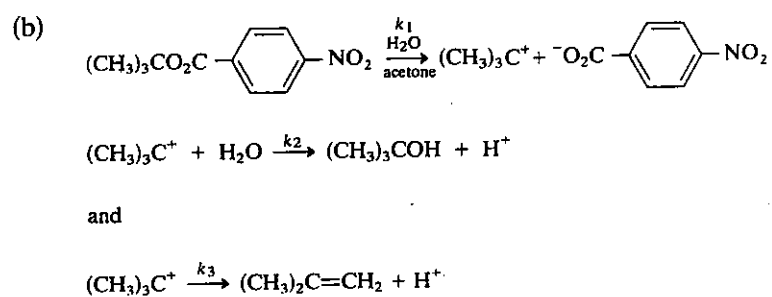


X	$pK_a$
<i>p</i> -CH <sub>3</sub> O	9.32
<i>p</i> -CH <sub>3</sub>	9.22
<i>p</i> -F	8.94
H	9.03
<i>m</i> -NO <sub>2</sub>	8.19
<i>p</i> -NO <sub>2</sub>	8.14
<i>p</i> -Cl	8.83
<i>m</i> -Cl	8.67

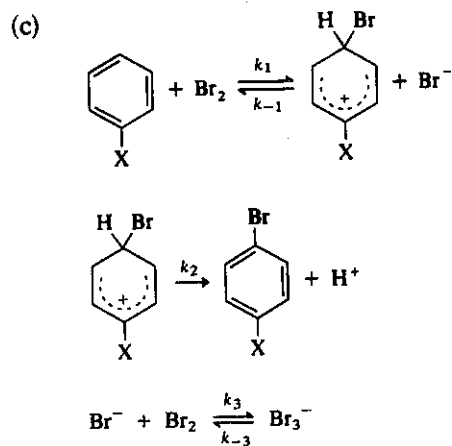
7. Write the rate law that would describe the rate of product formation for each of the following systems:



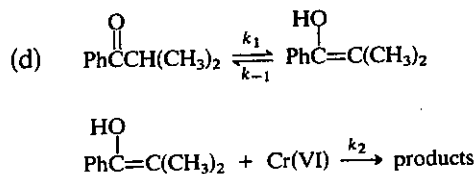
if the second step is rate-controlling and the first step is a preequilibrium.



if the competing product-forming steps are faster than the first step.

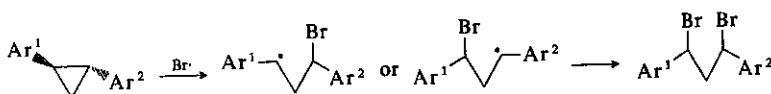


assuming that the  $\sigma$  complex is a steady-state intermediate. The final step is a rapid equilibrium that converts some of the initial  $\text{Br}_2$  to unreactive  $\text{Br}_3^-$ . What is the rate expression if the intermediate goes to product much faster than it reverts to starting material and if the equilibrium constant for tribromide ion formation is large?



where no assumption is made as to the relative magnitude of  $k_1$ ,  $k_{-1}$ , and  $k_2$ .

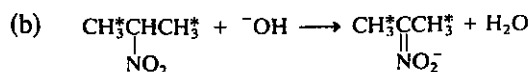
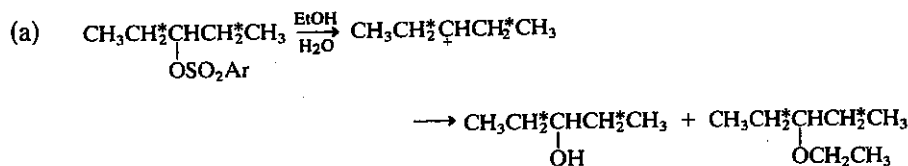
8. The rates of brominolysis of a series of 1,2-diarylcyclopropanes under conditions where the rate is determined by Br· attack and leads to 1,3-dibromo-1,3-diarylpropanes are given below.

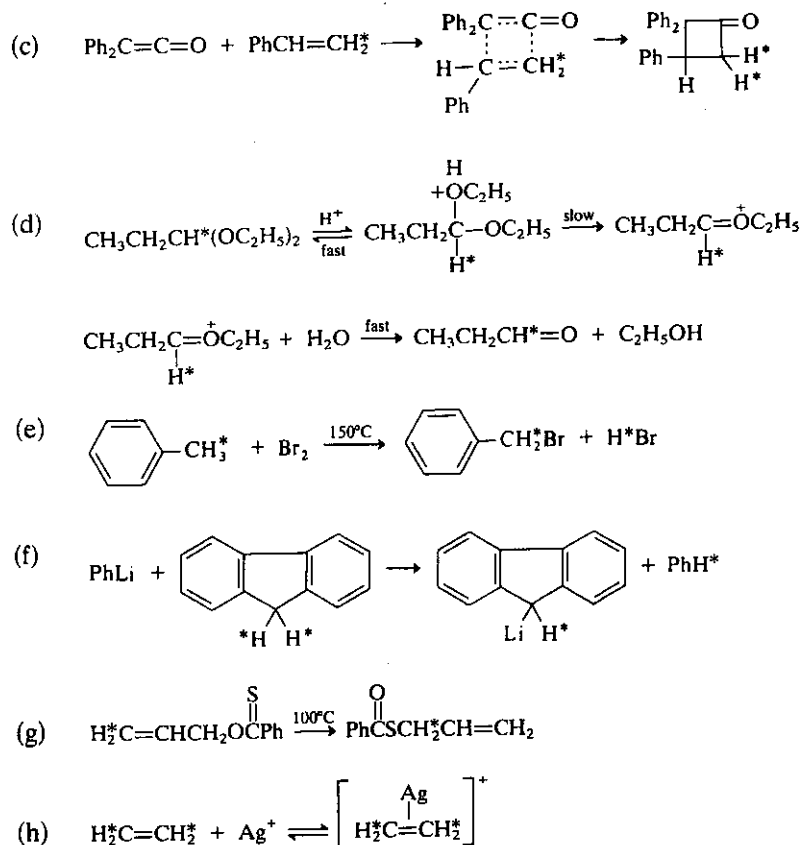


Set up an equation which you would expect to correlate the observed rate of reaction with both the  $\text{Ar}^1$  and the  $\text{Ar}^2$  substituent. Check the performance of your equation by comparing the correlation with the data given below. Discuss the results of the correlation.

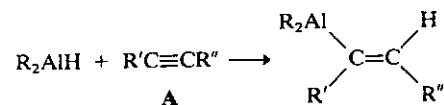
$\text{Ar}^1$	$\text{Ar}^2$	Relative rate	$\text{Ar}^1$	$\text{Ar}^2$	Relative rate
<i>p</i> -MeO	<i>p</i> -MeO	$1.6 \times 10^4$	<i>p</i> -Cl	<i>p</i> -Ph	48
<i>p</i> -Ph	<i>p</i> -MeO	$4.4 \times 10^3$	<i>p</i> -CN	<i>p</i> -Ph	45
H	<i>p</i> -MeO	$2.5 \times 10^3$	<i>p</i> -Br	<i>p</i> -Cl	18
<i>p</i> -Cl	<i>p</i> -MeO	$2.3 \times 10^3$	<i>p</i> -Br	<i>p</i> -Br	15
<i>m</i> -Br	<i>p</i> -MeO	$2.1 \times 10^3$	<i>m</i> -Br	H	10
<i>p</i> -CN	<i>p</i> -MeO	$1.6 \times 10^3$	<i>m</i> -Br	<i>p</i> -Cl	4.8
<i>p</i> -NO <sub>2</sub>	<i>p</i> -MeO	$1.3 \times 10^3$	<i>p</i> -CN	H	1.8
H	<i>p</i> -Ph	$6.8 \times 10^2$	<i>p</i> -NO <sub>2</sub>	H	0.88
<i>p</i> -Cl	<i>p</i> -Ph	$4.3 \times 10^2$	<i>p</i> -Cl	<i>p</i> -CN	0.55
<i>m</i> -Br	<i>p</i> -Ph	$1.8 \times 10^2$	<i>p</i> -Cl	<i>p</i> -NO <sub>2</sub>	0.37
H	H	$1.4 \times 10^2$	<i>p</i> -CN	<i>p</i> -CN	0.046

9. Predict whether normal or inverse isotope effects will be observed for each reaction below. Explain. Indicate any reactions in which you would expect  $k_{\text{H}}/k_{\text{D}} > 2$ . The isotopically substituted hydrogens are marked with asterisks.





10. Reactions of dialkylaluminum hydrides with acetylenes give addition products:

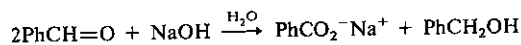


The rate expression for the reaction is

$$-\frac{d[\text{A}]}{dt} = k[\text{A}][(\text{R}_2\text{AlH})_3]^{1/3}$$

Propose a mechanism that could account for the overall four-thirds order kinetics and the appearance of the dialkylaluminum hydride concentration to the one-third power.

11. The Cannizzaro reaction is a disproportionation which takes place in strongly basic solution and converts benzaldehyde to benzyl alcohol and sodium benzoate.



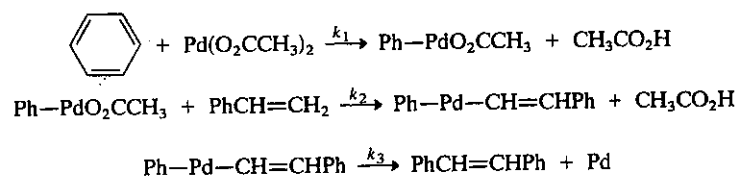
Several mechanisms have been postulated, all of which propose a *hydride ion* transfer as a key step. On the basis of the following results, postulate one or

more mechanisms which are consistent with all the data provided. Indicate the significance of each observation with respect to the mechanism(s) you postulate.

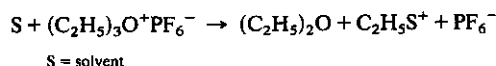
- (1) When the reaction is carried out in  $D_2O$ , the benzyl alcohol contains no deuterium in the methylene group.
- (2) When the reaction is carried out in  $H_2^{18}O$ , both the benzyl alcohol and sodium benzoate contain  $^{18}O$ .
- (3) The reaction rate is given by the expression

$$\text{rate} = k_{\text{obs}}[\text{PhCH=O}]^2[\text{OH}^-]$$

- (4) The rates of substituted benzaldehydes are correlated by the Hammett equation with  $\rho = +3.76$ .
  - (5) The solvent isotope effect  $k_{D_2O}/k_{H_2O}$  is 1.90.
12. A mechanism for olefin arylation by palladium(II) is given below. The isotope effect  $k_H/k_D$  was found to be 5 when benzene- $d_6$  was used. When styrene- $\beta,\beta-d_2$  was used, no isotope effect was observed. Which step is rate-determining?



13. A scale for solvent ionizing power,  $Y^+$ , applicable in solvolysis reactions of cationic substrates, has been developed. For example,



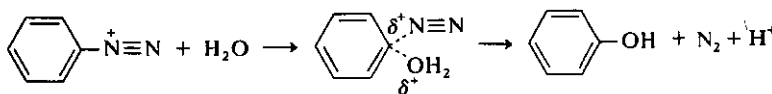
The numerical values of  $Y^+$  are found to be related to  $Y$ , the measure of solvent ionizing power for neutral substrates, by the equation

$$Y^+ = -0.09 Y$$

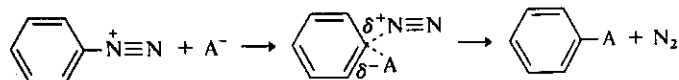
Explain, in qualitative terms, (a) why  $Y^+$  is negative with respect to  $Y$  and (b) why  $Y^+$  is smaller in magnitude than  $Y$  (as is indicated by the coefficient of 0.09).

14. Two mechanisms are among those that have been postulated for decomposition of aryl diazonium salts in aqueous solution containing nucleophilic anions,  $A^-$ :

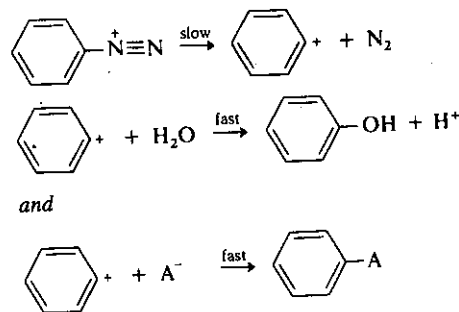
*Mechanism A*



and

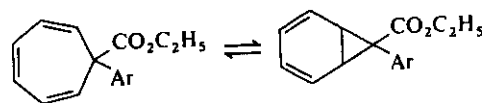


## Mechanism B



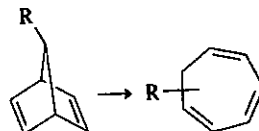
Indicate how each of the following techniques might be applied to distinguishing between these mechanisms:

- kinetic studies
  - rate and product composition as a function of  $[\text{A}^-]$
  - solvent isotope effect studies
  - isotope effect resulting from substitution of D for H at *ortho* positions
  - substituent effect studies
15. Cycloheptatrienes are in many cases in rapid equilibrium with an isomeric bicyclo[4.1.0] heptadiene. The thermodynamics of the valence isomerism has been studied in a number of instances and some of the data are given below. Calculate the equilibrium constant for each case at 25°C. Calculate the temperature at which  $K = 1$  for each system. Are the signs of the enthalpy and entropy as you would expect them to be? Can you discern any pattern of substituent effects from the data?



Ar	$\Delta H^\circ$ (kcal/mol)	$\Delta S^\circ$ (eu)
Phenyl	-5.4	-16.8
<i>p</i> -Nitrophenyl	-3.5	-11.0
<i>p</i> -Methoxyphenyl	-2.3	-7.4

16. Bicyclo[2.2.1]heptadiene rearranges at elevated temperatures to cycloheptatriene and toluene. The reaction is facilitated by substituents at C-7 such as phenyl and alkoxy, in which case cycloheptatrienes are the dominant products.



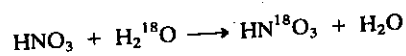


For R = *t*-butoxy, the rate data are given for several temperatures in decane. The reaction is about 50% faster in ethoxyethanol than in decane. Calculate the

Temp. (°C)	$k$ (s <sup>-1</sup> )
139.8	$7.28 \times 10^{-6}$
154.8	$3.37 \times 10^{-5}$
170.3	$1.43 \times 10^{-4}$

activation parameters at 150°C. Although precisely comparable data are not available,  $E_a$  for the gas phase isomerization of norbornadiene is ~50 kcal/mol. Draw a sketch showing the degree of transition state stabilization or destabilization caused by the alkoxy substituent. Is there any basis for regarding the bond cleavage in the rate-determining step to be heterolytic or homolytic? How do you propose that the effect of the substituent group R operates? Can you propose an experiment that might support your proposal?

17. A study of the aromatic nitration reaction in aqueous nitric acid revealed that when no aromatic substrate was present, an incorporation of <sup>18</sup>O from labeled water into nitric acid occurred. The rate of this exchange process was identical with the rate of nitration of several reactive aromatic hydrocarbons. Discuss how this result is consistent with mechanism B on page 188, but not with mechanisms A or C.



18. Comparison of several series of solvolysis reactions which proceed via carbocation intermediates reveals that an  $\alpha$ -cyano group retards the reactions by a factor of about  $10^3$ . A  $\beta$ -cyano group is even more strongly rate-retarding, with the factor being as high as  $10^7$ . Why are both  $\alpha$ - and  $\beta$ -cyano groups rate-retarding? What might cause the  $\beta$ -cyano group to be more rate-retarding than the  $\alpha$ -cyano group?
19. Comparison of the gas phase acidity of benzoic acids with  $\text{p}K_a$  values of the same compounds in aqueous solution provides some interesting relationships.
- (1) The trend in acidity as a function of substituent is the same but the magnitude of the substituent effects is much larger in the gas phase. (The  $\Delta\Delta G^\circ$  for any given substituent is about ten times larger in the gas phase.)
  - (2) Whereas acetic acid and benzoic acid are of comparable acidity in water, benzoic acid is much more acidic in the gas phase.
  - (3) While the substituent effect in the gas phase is assumed to be nearly entirely an enthalpy effect, it can be shown that in solution the substituent effect is largely the result of changes in  $\Delta S$ .

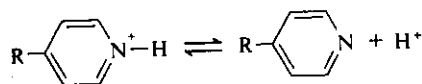
Discuss how the change from gas phase to water solution can cause each of these effects.

20. It has been suggested that the chemical shift of aromatic ring carbons might provide a good indication of the intrinsic electron-releasing or electron-attracting capacity of substituents in circumstances where there is no perturbation by an approaching reagent. Such a perturbation is always present in substituent effects determined on the basis of reactivity. The measured chemical shifts from benzene for the carbon *para* to the substituent are given below. Plot these against  $\sigma$ ,  $\sigma^+$ , and what conclusions do you draw from these plots? If you have access to an appropriate program and computer, determine the "percent resonance" associated with the chemical shift, as determined by the Swain-Lupton equation.

R	$\Delta\delta^a$	R	$\Delta\delta^a$
NH <sub>2</sub>	-9.86	CN	3.80
OCH <sub>3</sub>	-7.75	CCH <sub>3</sub>	4.18
F	-4.49	CO <sub>2</sub> CH <sub>3</sub>	4.12
Cl	-2.05	SO <sub>2</sub> CH <sub>3</sub>	4.64
Br	-1.62	NO <sub>2</sub>	5.53
CH <sub>3</sub>	-2.89	CH=O	5.51
CF <sub>3</sub>	3.19		

a.  $\Delta\delta$  is the change in chemical shift in CCl<sub>4</sub> from benzene in ppm; a negative sign indicates increased shielding.

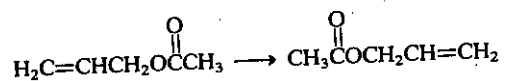
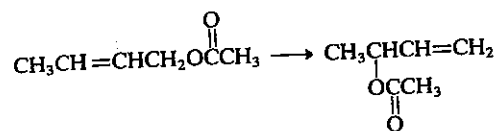
21. The ionization of a series of 4-substituted pyridines has been studied, and both equilibrium acidities ( $pK_a$ ) and enthalpies of ionization have been recorded at 25°C:



R	$pK_a$	$\Delta H^\circ$ (kcal/mol)
H	5.21	4.8
NH <sub>2</sub>	9.12	11.3
OCH <sub>3</sub>	6.58	6.8
CH <sub>3</sub>	6.03	6.1
Cl	3.83	3.6
Br	3.75	3.5
CN	1.86	1.3

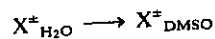
Calculate  $\Delta S^\circ$  for ionization of each compound. Comment on the contribution of  $\Delta H^\circ$  and  $\Delta S^\circ$  terms to the free energy of ionization. Test the data for linear free-energy correlations. Are the linear free-energy correlations dominated by entropy or enthalpy terms?

22. Allyl esters undergo rearrangement reactions at 300°C and above. Two examples are shown, one of which is "degenerate," since the product and reactant are identical:



At least three distinct mechanisms can be written for these reactions. Write down some possible mechanisms, and suggest isotopic labeling studies that could distinguish among the possibilities you have proposed.

23. Estimates of the heat of solvation of various species in DMSO as compared to water have been made, and can be expressed as enthalpies of transfer. Some data are given below. Discuss their significance.



X	$\Delta H_{\text{transfer}}$ (kcal/mol)
K <sup>+</sup>	-8.8
Na <sup>+</sup>	-7.1
Cl <sup>-</sup>	+4.9

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# Answers! See these References!

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