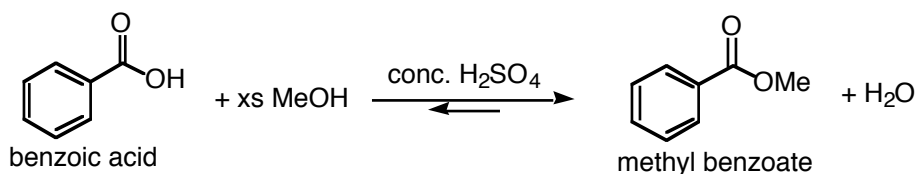


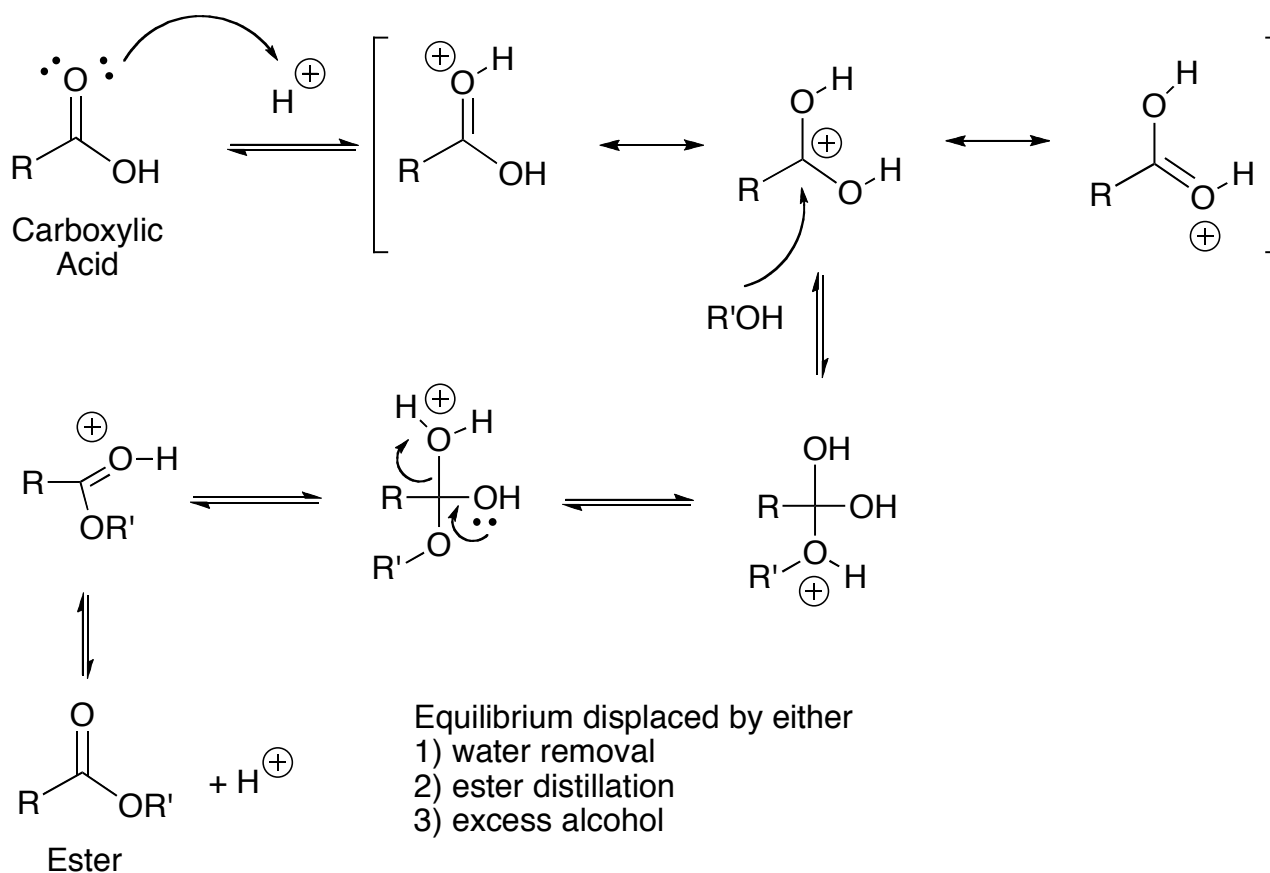
Handout Esterification and Acetalization

1) Fischer Esterification:



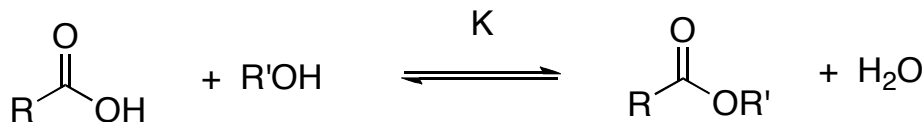
Example: esterification of benzoic acid to methyl benzoate.

MECHANISM (Fischer esterification)



The overall process of esterification is one involving an equilibrium among a variety of compounds, and for the reaction to give a high yield; the equilibrium must be shifted toward the products: the desired ester, and water. This can be accomplished either by removing one or more of the products from the reaction mixture as they are formed or by using a large excess of one of the starting reagents.

The effect of the latter approach is obvious from consideration of the mass law relating starting materials and products (equation). Increasing the amount of either the alcohol or the carboxylic acid will result in an increase in the amount of products formed since the equilibrium constant, *K*, for the reaction-must remain constant at a given temperature, no matter what quantity of either reagent is used. Removing water is also a strategy and drying agents can be used, or azeotropic distillation. However, azeotropic distillation is not possible for all alcohols.



$$K = \frac{[\text{RCOOR}'] [\text{H}_2\text{O}]}{[\text{RCOOH}] [\text{R}'\text{OH}]}$$

Problem Assignment

THIS PROBLEM MUST BE ANSWERED IN YOUR NOTEBOOK AND WILL BE PART OF YOUR GRADE

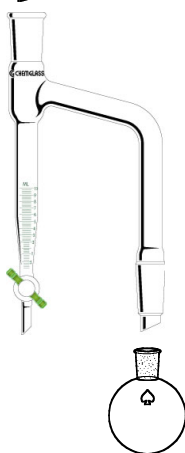
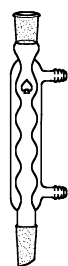
Assuming the equilibrium constant for the esterification of benzoic with methanol is $K = 3$, calculate the theoretical yield of methyl benzoate expected using the following conditions:

6.1 g of benzoic acid and 20 mL of methanol, and 2 mL of concentrated sulfuric acid.

Concentrated sulfuric acid is added as a catalyst in the esterification procedure, even though another acid (benzoic acid) is one of the organic reagents used. Why is the sulfuric acid necessary?

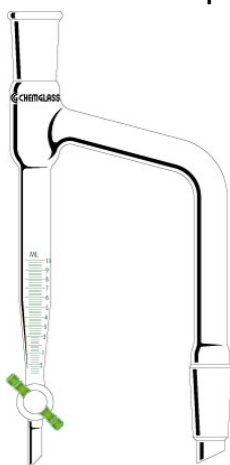
Azeotropes can be distilled using a Dean-Stark trap. If the azeotrope separates into two phases upon cooling, then water can be removed. This is the case with water/toluene and water/benzene (among other).

For example benzoic acid + *n*-BuOH can be esterified (with H_2SO_4) as a catalyst, without using a large excess of alcohol. Think about how the Dean-Stark trap (glassware below) might work.



Distillation of azeotropes

To remove water as it is forming, a drying agent can be used, or a Dean-Stark apparatus if the solvent forms an azeotrope



Distilling receiver - Dean-Stark apparatus

EQUILIBRIA, RATES, ENERGY DIAGRAMS, MECHANISMS

TABLE: Relationship between K_{eq} and ΔG°

ΔG° (kcal/mol)	K_{eq}	More stable state (%)
0	1	50
0.1	1.2	54.5
0.24	1.5	60
0.5	2.4	69.7
0.82	4.0	80
1	5.4	84.4
1.30	9	90
2	29.3	96.7
2.72	99	99
5	4631	99.98
10	2.1×10^7	99.999996

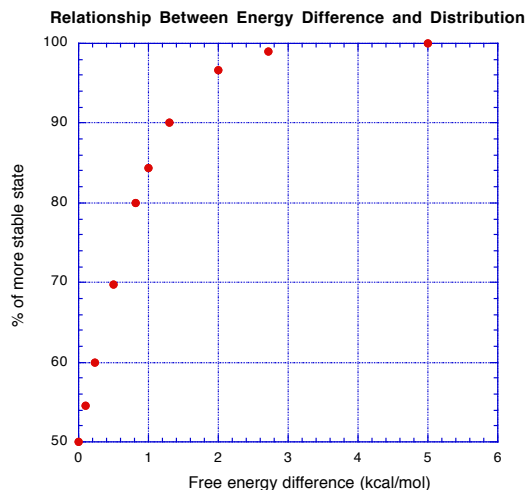
$$\Delta G^\circ = -RT \ln K$$

$$\Delta G^\circ = -2.3RT \log K$$

$$K = e^{-\Delta G^\circ/RT}$$

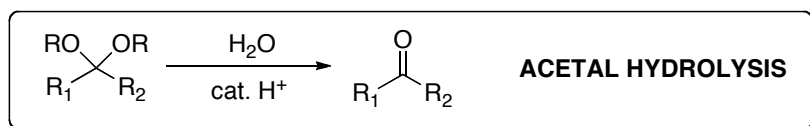
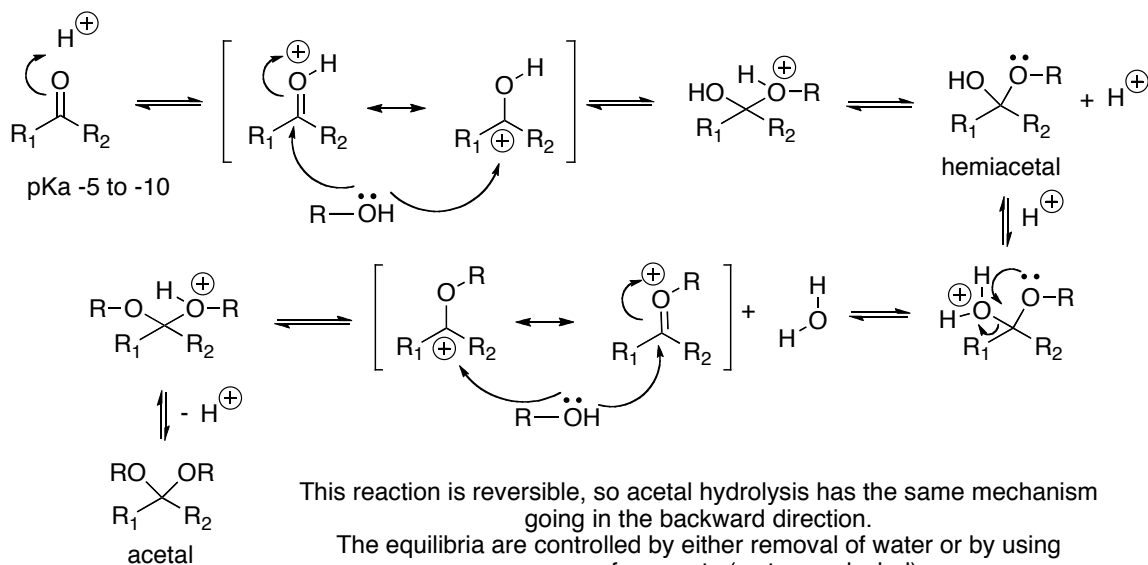
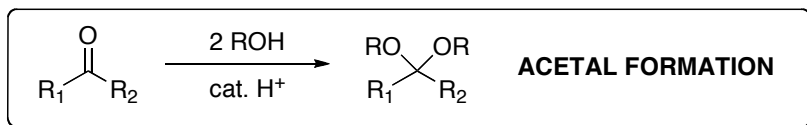
$$K = 10^{-\Delta G^\circ/2.3RT}$$

Note: at 25°C, the value of 2.3RT is about 1.4 kcal/mol

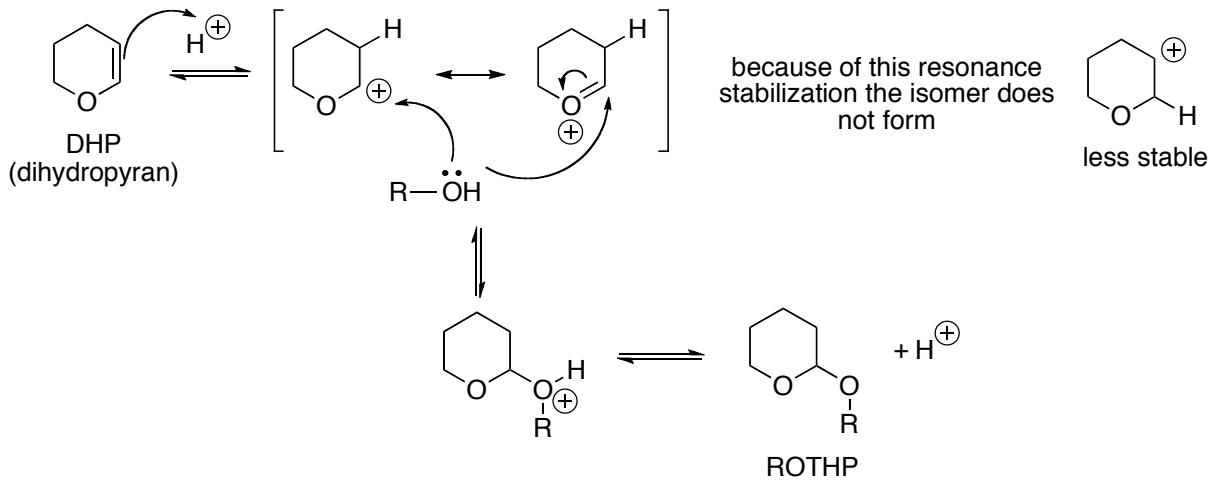


Le Chatelier's Principle: a system at equilibrium responds to a disturbance/stress so as to minimize the disturbance/stress.

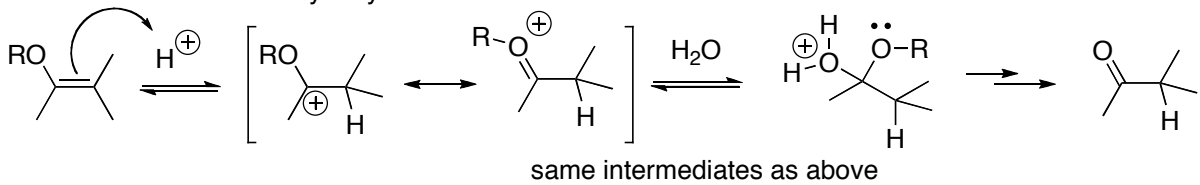
2) Acetalization (acetal formation)



Related reaction: alcohol protection to ROTHP (THP = tetrahydropyranyl)



Related reaction: enol ether hydrolysis



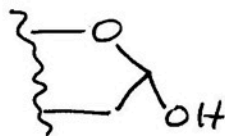
Hemiacetal:

STRUCTURES

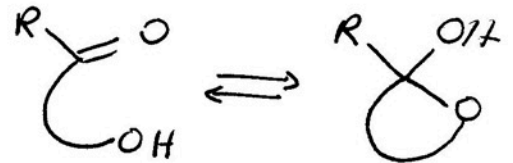
Almost all natural sugars are D (configuration) and in the ring form in solution



β -anomer
(OH above the plane)



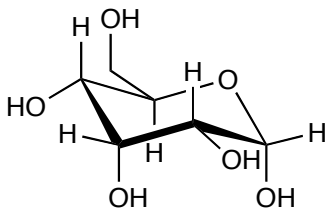
α -anomer
(OH below the plane)



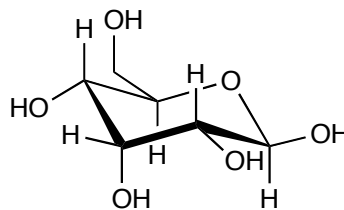
R = H aldose
R \neq H ketose

= D D . 1

HEMIACETALS



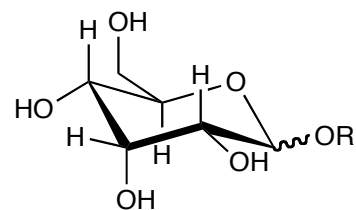
α -pyranose



β -pyranose

carbohydrates: $[C(H_2O)]_n$

ACETALS

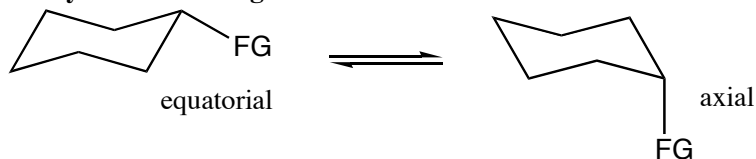


(disaccharide, polysaccharide)
R = sugar

The Anomeric Effect

Conformational analysis of cyclohexanes

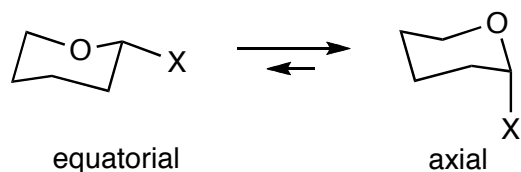
TABLE: Approximate A Values (Free Energy Difference between Equatorial & Axial Substituents on a Cyclohexane Ring)



FG = functional group

Functional Group	Approx. ΔG° kcal/mol	Functional Group	Approx. ΔG° kcal/mol	Functional Group	Approx. ΔG° kcal/mol
HgCl	-0.25	OMe	0.6	CH=CH ₂	1.7
HgBr	0.0	OH (protic sol)	0.9-1.0	CH ₃	1.8
CN	0.15-0.25	OH (aprotic sol)	0.5-0.6	C ₂ H ₅	1.8
F	0.25	NO ₂	1.1	<i>i</i> -Pr	2.1
I	0.46	SPh	1.1-1.2	C ₆ H ₁₁	2.2
Br	0.5-0.6	COOEt	1.1-1.2	Me ₃ Si	2.5
OTs	0.51	COOMe	1.3	Ph	2.8
Cl	0.52	COOH	1.4	<i>t</i> -Bu	4.9
OAc	0.71	NH ₂	1.4		

ANOMERIC EFFECT



when X is electronegative (OH, OR, Cl, etc.) then the axial conformation is more stable

Origin of the anomeric effect: the lone pair on the ring oxygen (HOMO) interacts with the C-X antibonding orbital (σ^*), thus stabilizing the axial conformer.

