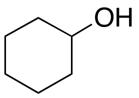
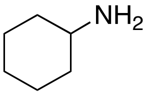
19.4 Physical Properties

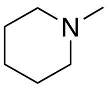
Key: hydrogen bond strength depends on acidity of the hydrogen and basicity of the N or O

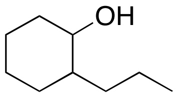
1. **Water Solubility**: All amines hydrogen-bond water → impacts solubility
   a. Because R_3N---HOH bond is stronger (due to amine lone-pair basicity) than ROH---HOH, amines tend to better H-bond water and are more soluble than oxygen analogs
   b. Based on basicity (the acidity of water's hydrogen is common)
2. **Boiling Point:** 1° and 2° amines hydrogen bond themselves, but 3° amines don't
   a. Boiling point for similar mw amines: 1°, 2° amines > 3° amines
   b. amines generally have lower boiling points than analogous oxygen compounds
      - Boiling point for similar mw: $RCO_2H > RCH_2OH > RCH_2NH_2$
   c. for boiling point, the weaker acidity of the N-H hydrogens weakens the hydrogen-bonding strength more than the greater basicity of the Nitrogen lone pair.
3. Amines stink! (ammoniums don't)

1. Boiling Points. Rank the following in terms of boiling point, 1 being highest, 4 being lowest.

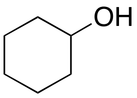


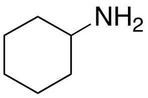


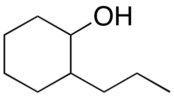


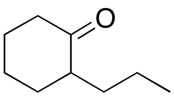


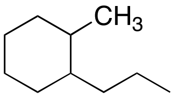
2. Water Solubility. Rank the following in terms of water solubility, 1 being most water soluble, 5 being least water soluble.



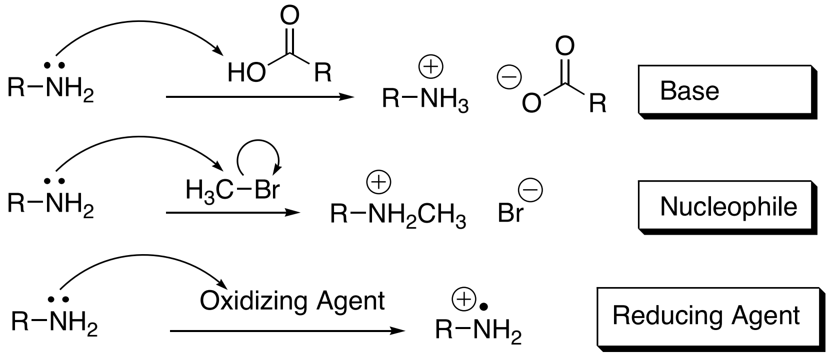








B. Basicity of Amines: Reactivity of the Nitrogen Lone Pair (19.5,6)

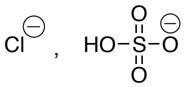
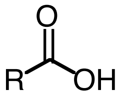
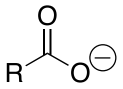
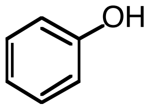
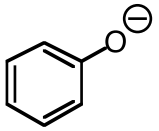
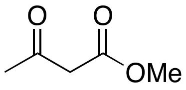
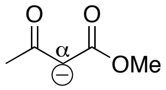
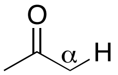
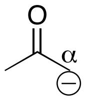


•The nitrogen lone pair dominates amine reactivity

•Trends in base strength, nucleophile strength, and redox strength follow similar patterns, based on lone pair stability/reactivity

Neutral amine bases are stronger than:	Neutral amine bases are weaker than:
1. Neutral oxygens (water, alcohol, ketones…)	1. Anionic hydroxide or alkoxides
2. Carboxylate anions (resonance stabilized)	2. Anionic nitrogen or carbon bases

Acidity/Basicity Table 19.1: Neutral Acids and Anionic Bases

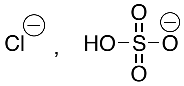
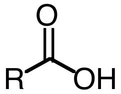
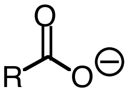
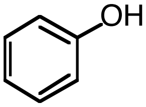
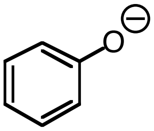
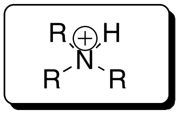
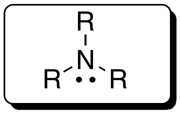
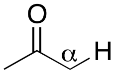
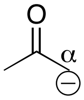
Class	Neutral Acid Structure	Ka	Acid Strength	Anion Base	Base Strength
Strong Acids	H-Cl, H_sSO_4	10^{2}			
Carboxylic Acid		10^{-5}			
Phenol		10^{-10}			
1,3-Dicarbonyl		10^{-12}			
Water	HOH	10^{-16}		$HO^{\ominus}$	
Alcohol	ROH	10^{-17}		$RO^{\ominus}$	
Ketones and Aldehydes		10^{-20}			
Amine (N-H)	$(iPr)_2N\text{-}H$	10^{-33}		$(iPr)_2N^{\ominus}Li^{\oplus}$	
Alkane (C-H)	RCH_3	10^{-50}		$RCH_2^{\ominus}$	

Quick Checklist of Acid/Base Factors

1. **Charge**
2. **Electronegativity**
3. **Resonance/Conjugation**
4. **Hybridization**
5. **Impact of Electron Donors/Withdrawers**
6. **Amines/Ammoniums**

- **When comparing/ranking any two acids or bases, go through the above checklist to see which factors apply and might differentiate the two.**
- **When a neutral acids are involved, it's often best to draw the conjugate anionic bases, and to think from the anion stability side.**

Acidity/Basicity Table 19.2: With both Neutral and Cationic Acids and both Neutral and Anionic Bases

Class	Structure	Ka	Acid Strength	Base	Base Strength	
Strong Acids	H-Cl, H_2SO_4	10^2		 $Cl^{\ominus}$, $HO-S(=O)_2-O^{\ominus}$		**S**mell **A**wful!
Hydronium	H_3O^+, ROH^+ cationic	10^0		H_2O, HOR neutral		**H**umans
Carboxylic Acid		10^{-5}				**C**uz
Phenol		10^{-10}				**P**eople
Ammonium Ion (Charged)	 Charged, but only weakly acidic!	**10^{-12}**		 Neutral, but basic		**A**gainst
Water	HOH	10^{-16}		$HO^{\ominus}$		**W**orking
Alcohol	ROH	10^{-17}		$RO^{\ominus}$		**A**re
Ketones and Aldehydes		10^{-20}				**K**ingdoms
Amine (N-H)	$(iPr)_2N$-H	10^{-33}		$(iPr)_2N^{\ominus}Li^{\oplus}$		**A**nimal
Alkane (C-H)	RCH_3	10^{-50}		$RCH_2^{\ominus}$		**A**ll

Notes to remember

1. Average neutral amine a thousand billion times **more basic than a neutral oxygen** (**electronegativity** factor)
2. An average neutral amine is thousands of times **less basic than** non-resonance stabilized **hydroxide or alkoxide anions** (**charge** factor)
3. But average neutral amine **millions** of times **more basic** than highly resonance-stabilized **carboxylate anion** (**resonance** factor trumps charge factor in this case)
4. **Ammonium cations** are million of times **less acidic than** neutral **carboxylic acids**, but are **more acidic than neutral water/alcohol**!
5. Neutral amine can completely deprotonate carboxylic acids, but not water or alcohols.
6. Therefore hydroxide can deprotonate ammoniums, but carboxylates cannot.

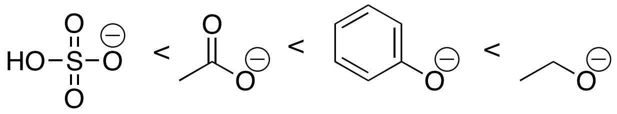
More Detailed Discussion of Acid/Base Patterns/Factors to remember

1. Charge
   - Nonfactor on Table 19.1, since all of the "acids" have the same charge (neutral)
   - In Table 19.1, all of the "bases" have the same charge (anion, single negative charge)
   - **Normally, all else equal, cations are more acidic than neutrals, and anions more basic than neutrals. (See Table 19.2)**

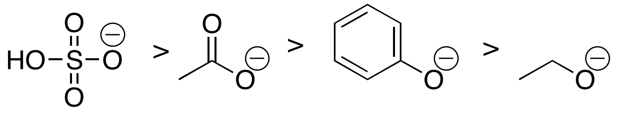
2. Electronegativity:
   - Acidity: H-X (halogen) > H-O > H-N > H-C
   - Basicity: $X^{\ominus} < O^{\ominus} < N^{\ominus} < C^{\ominus}$
   - Anion Stability: $X^{\ominus} > O^{\ominus} > N^{\ominus} > C^{\ominus}$

3. Resonance/Conjugation:
   - Oxygen Series:
     Acidity: sulfurice acid > carboxylic acid > phenol > alcohol

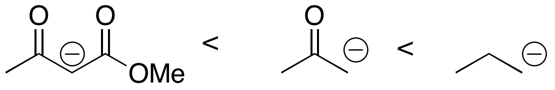
     Anion Basicity:



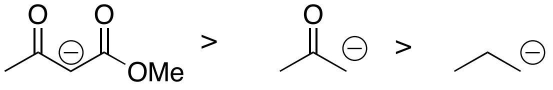
     Anion Stability:



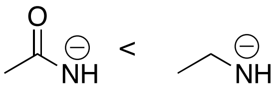
   - Carbon Series:
     - Acidity: 1,3-dicarbonyl > ketone (monocarbonyl) > alkane
     - Anion Basicity:



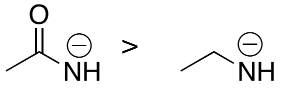
     - Anion Stability:



   - Nitrogen Series:
     - Acidity: amide > amine
     - Anion Basicity:



     - Anion Stability:



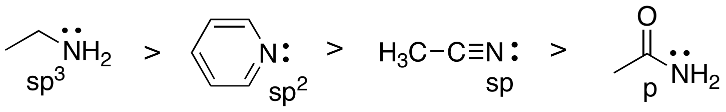
   - Note: Resonance is often useful as a tiebreaker (for example, molecules in which both have O-H bonds and both have equal charge, so that neither the charge factor nor the electronegativity factor could predict acidity/basicity)
   - NOTE: Resonance can sometimes (not always) trump electronegativity or even charge.
     - Example of resonance versus electronegativity: a C-H with carbonyl resonance (ketone/enolate case) is more acidic than an N-H with no resonance help but less acidic than an O-H with no resonance help. A C-H with two

carbonyl resonances (a 1,3-dicarbonyl case) is more acidic than even an O-H that has no resonance help.

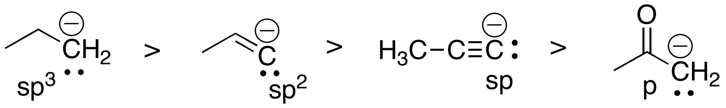
- o Example of resonance versus charge: A carboxylate anion, with serious resonance stabilization, ends up being so stabilized that it is even less basic than a neutral, uncharged amine! A hydrogen sulfate anion from sulfuric acid is less basic than not only neutral amines but also neutral oxygen (water, etc.)

4. Hybridization:
   - For lone-pair basicity, (all else being equal), $sp^3 > sp^2 > sp > p$

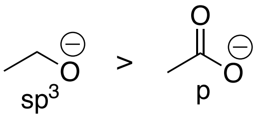
Neutral Nitrogen Series



Carbanion Series



Oxygen Anion Series



- This means that for acidity, alkynes > alkenes > alkanes

5. Electron donating/electron withdrawing substituents:
   - Electron withdrawing substituents will stabilize negatively charged anions, but will destabilize positively charged cations.
     - o This means a withdrawer will increase the acidity of a neutral acid because it will stabilize the resulting anion.
     - o This means a withdrawer will decrease the basicity of a neutral base because it will destabilize the resulting cation
   - Electron donating substituents will stabilize positively charged cations, but will destabilize negatively charged anions.
     - o This means a donor will increase the basicity of a neutral base because it will stabilize the resulting cation. The resulting cation will be less acidic.

Basicity: $H-NH_2 < R-NH_2$ (ammonia, alkyl amine) Cation Acidity: $H-NH_3^{\oplus} > R-NH_3^{\oplus}$ Cation Stability: $H-NH_3^{\oplus} < R-NH_3^{\oplus}$

ammonia alkyl amine

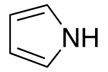
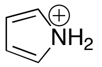
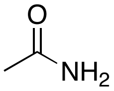
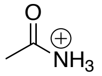
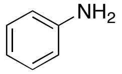
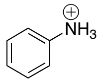
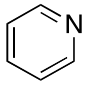
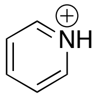
     - o This means a donor will decrease the acidity of a neutral acid because it will destabilize the resulting anion, and will increase the basicity of the anion

Acidity: $H-O-H > R-O-H$ Anion Basicity: $H-O^{\ominus} > R-O^{\ominus}$ Anion Stability: $H-O^{\ominus} > R-O^{\ominus}$

water alcohol

6. Ammonium Cations as Acids and Neutral Amines as Bases
   - Neutral amines are more basic than any neutral oxygen (electronegativity factor)
   - Neutral amines are less basic than most anionic oxygens, including alkoxides, hydroxides (charge factor)
   - However, neutral amines are more basic than highly resonance-stabilized carboxylate anions (in this case, resonance factor trumps the charge factor).

Table 9.3 Relative Basicity of Different Classes of Neutral Nitrogen Compounds.

Entry	Structure of Amine Base	Base Strenth	Lone Pair Hybrid		Impact On Base Strength	Structure of Ammonium Acid	K_a	Acid Strenth
1			P	Aromatic, Conjugated	Decrease		10^{1}	
2			P	Conjugated, Electron-Withdrawing Carbonyl	Decrease		10^{0}	
3			P	Conjugated	Decrease		10^{-4}	
4			sp^2				10^{-5}	
5	**NH_3**		**sp^3**	**Reference**		$^{\oplus}NH_4$	**$10^{-9.3}$**	
6	$EtNH_2$		sp^3	Alkyl Donor	Increase	$Et\overset{\oplus}{N}H_3$	$10^{-10.6}$	
7	Et_2NH		sp^3	Alkyl Donor	Increase	$Et_2\overset{\oplus}{N}H_2$	$10^{-10.8}$	
8	Et_3N		sp^3	Alkyl Donor	Increase	$Et_3\overset{\oplus}{N}H$	$10^{-11.0}$	

General Amine Basicity Patterns.

a. Relative basicity correlates Lone pair hybridization: sp^3 (entries 5-8) > sp^2 (entry 4) > p (entries 1-3) (hybridization factor)

b. Within the sp^3 amines, increasing alkyl substitution increases basicity (entries 5-8): 3º > 2º > 1º > NH_3 (electron donating group factor)

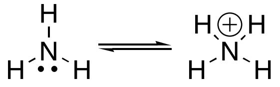
Note: patterns (a) and (b) essentially cover everything.

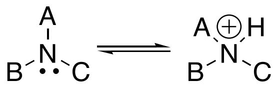
c. Amides are much less basic than amines, or even other nitrogens with p-lone pairs (less than amines reflects hybridization and conjugation; amides are less basic than other p-hybrid conjugated lone pairs because or the electron-withdrawing group factor).

d. Conjugated nitrogens are in general less basic than isolated nitrogens (both hybridization and conjugation factors)

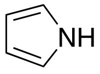
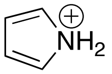
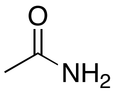
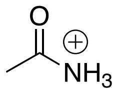
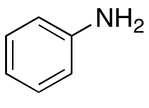
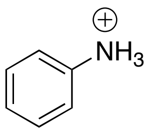
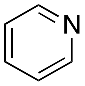
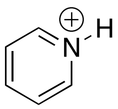
- Note: The **acidity of conjugate ammonium cations (conjugate acids relative to the amines) is directly and inversely related to the basicity of the neutral amines**.
- Key: remember patterns (a) and (b) above. That should help you solve relative basicity problems. If given ammoniums, draw the related conjugate neutral amines, rank them as bases, and realize that the strongest amine base relates to the weakest ammonium acid.
- You should be able to handle any ranking problems involving either amines as bases or their conjugate ammoniums as acids. This should include relative to non-nitrogen acids and bases.

Explanation for Basicity Pattern: Acidity/Basicity is an equilibrium measurement, and thus reflects both product stability and starting material stability.





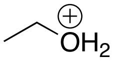
- Anything that **stabilizes the cation increases the basicity** of the nitrogen
- Anything that **destabilizes the cation** **decreases the basicity** of the nitrogen
- Anything that **stabilizes the amine** **decreases the basicity** of the nitrogen (especially if that stabilizing factor is sacrificed upon protonation)
- Anything that **destabilizes the amine** increases it's basicity
- When lone pair is p, that always reflects stabilizing conjugation and reduced basicity. This is the origin of both the p-hybridization factor and the resonance/conjugation factor.

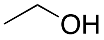
Entry	Base	Conjugate Cation	Substituent And it's Impact	Why: Which Side Is Stabilizied or Destabilized?
5	NH_3	NH_4^+	Reference	
6-8	Et_3N	Et_3NH^+	Alkyl Groups Increase Basicity	**Cation** side stabilized by alkyl groups (electron donors, cation stabilizers)
1			Being part of Aromatic ring Reduces Basicity	**Neutral** side is stabilized by aromaticity. (Aromaticity is lost following protonation.)
2			Acyl/Amide Conjugated To Carbonyl	**Neutral** side is stabilized by conjugation to the carbonyl. That conjugation is lost following protonation. Second, the **cation side is destabilized** by the strongly electron withdrawing carbonyl group.
3			Conjugated To Aromatic	**Neutral** side is stabilized by conjugation. (That conjugation is lost following protonation.)
5			Aromatic. Part of Aromatic Ring	**Amine** side is stabilized by the sp^2 hybridization of the lone pair. An sp^2 lone pair is shorter than an sp^3 orbital. The shorter sp^2 orbital means the electrons are nearer and held more tightly by the nitrogen nucleus, and are thus more stable.

Choose the More Acidic for Each of the Following Pairs: Single Variable Problems

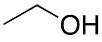
1. NH_3 $^{\oplus}NH_4$

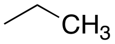
2.





3.





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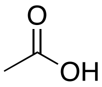

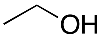

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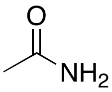

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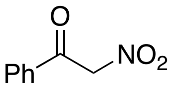
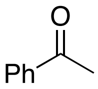
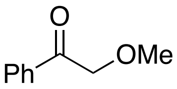






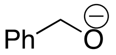
Choose the More **Basic** for Each of the Following Pairs (Single Variable)

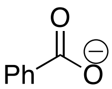
7. NH_3 $NaNH_2$

8. NaOH H_2O

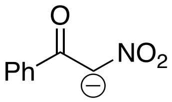
9. NH_3 H_2O

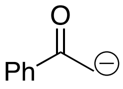
10.

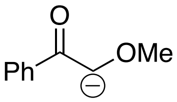




11.





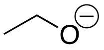


12.

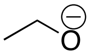
NH_3 O_2N-NH_2

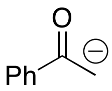
Choose the More **Basic** for Each of the Following (Multiple Variables, apples and oranges…)

13. NH_3



14.





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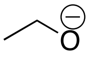
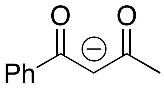




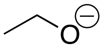
Choose the More Basic for Each of the Following Pairs

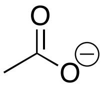
16. NH_3 $NaNH_2$

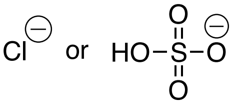
17. NH_3 $NaOH$

18. NH_3 H_2O

19. NH_3 CH_3OH

20. NH_3 

21. NH_3 

22. NH_3 

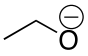
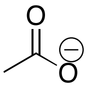
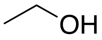
$Cl^{\ominus}$ or $HO{-}SO_2{-}O^{\ominus}$

23. NH_3 CH_3MgBr

24. NH_3 CH_3NH_2

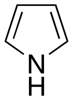
25. For the following sets of bases, rank them, 1 being the most basic.

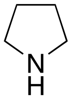
a. CH_3MgBr CH_3NHNa CH_3NH_2 CH_3OH

b.   CH_3NH_2 

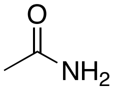
26. Amine Basicity. For the following pairs or sets of bases, rank them, 1 being the most basic.

a.





b.

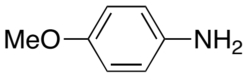


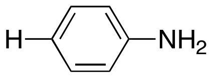
c. benzamide [$PhC(O)NH_2$] aniline ($PhNH_2$) pyridine triethylamine

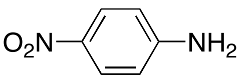
d. triethylamine ethylamine ammonia

e. dimethylamine methylamine aniline ($PhNH_2$)

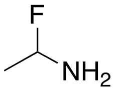
f.

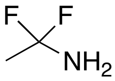






g.





h. triethylamine NaOH

i. methanol methylamine methane

j. CH_3MgBr CH_3NHNa CH_3ONa CH_3NH_2 CH_3CO_2Na CH_3OH

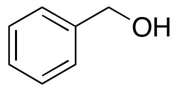
27. Rank the acidity of the following compounds, 1 being most acidic.

a. H_3O^+ $NH_4^+Cl^-$ water acetic acid (CH_3CO_2H) NH_3

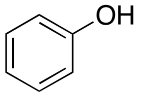
b. H_3O^+ acetic acid (CH_3CO_2H) $Me_3NH^+Cl^-$ ethanol

c. $NH_4^+Cl^-$ $Me_3NH^+Cl^-$ $PhNH_3^+Cl^-$

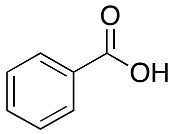
28. Suppose all of the molecules **A-D** are dissolved in diethyl ether.



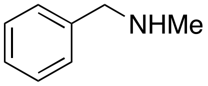
A



B



C



D

a. Which one or ones will extract (dissolve) into aqueous sodium hydroxide? (And why?)

b. Which, if any, will extract into aqueous hydrochloric acid? (And why?)

c. Which, if any, will extract into neutral water? (Why or why not?)

d. Explain how you could use an extraction scheme to separate **D** from **A.**