Advanced Organic Chemistry

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Chapter 2

The Acid-Base Theories

2.1 Brønsted-Lowry Acid-Base Theory

Definition

- **Acid** — any chemical species (molecule or ion) that is able to lose, or "donate" a hydrogen ion (proton).
- **Base** — a species with the ability to gain or “accept” a proton (a base must have a pair of electrons available to share with the proton; this is usually present as *an unshared pair,* but sometimes is *in a π orbital*).

Acid-base reactions: the transfer of a proton from an acid to a base. Protons do not exist free in solution but must be attached to an electron pair.

$$\underset{\text{acid}_1}{\text{A}-\textbf{H}} + \underset{\text{base}_2}{\ddot{\text{B}}\text{H}} \rightleftharpoons \underset{\text{base}_1}{\ddot{\text{A}}} + \underset{\text{acid}_2}{\text{B}-\textbf{H}}$$

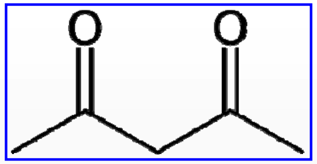
- **Acid-base reactions occur because acids are not equally strong.**

$$HCl + CH_3COO^{\ominus} \overset{K}{\rightleftharpoons} CH_3COOH + Cl^{\ominus}$$

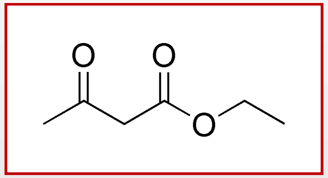
- **Water is amphoteric and can act as an acid or as a base.**

$$CH_3CO_2H + H_2O \rightleftharpoons CH_3CO_2^- + H_3O^+$$

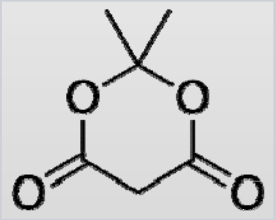
$$H_2O + NH_3 \rightleftharpoons OH^- + NH_4^+$$



acetylacetone



ethyl acetoacetate,



Meldrum's acid: 2,2-Dimethyl-1,3-dioxane-4,6-dione

Acid types:

i. **Mineral acids**: H_2SO_4, HCl, HNO_3, $B(OH)_3$, etc.

ii. **Organic acids**: RCO_2H (HCO_2H, CH_3CO_2H, $PhCO_2H$, PhOH, etc.

iii. **Amines**: NH_3, RNH_2, R_2NH…

iv. **Carbon acids**: Any molecule containing a C-H can lose a proton forming the carbanion.

pK_a value

I. The acid dissociation constant (pK_a) is a quantitative measure of the strength of the acid.

II. The pKa values are much harder to measure for very strong and very weak acids. The values in boldface are exact values; the others are approximate, especially above 18 and below –2.

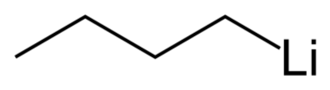
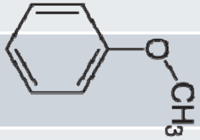
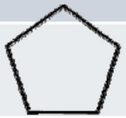
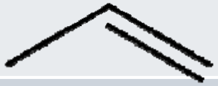
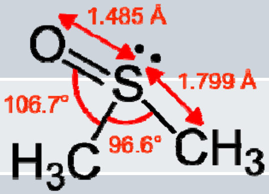
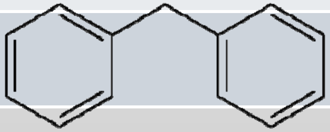
III. Very accurate values can be obtained only for acids weaker than hydronium ion and stronger than water.

IV. The order of acid strength applies when a given acid and base react without a solvent or, when possible, in water. In other solvents the order may be greatly different.

Table 1. pK_a values for some type of acids

Acids	Base	pKa (relative H_2O)	Acids	Base	pKa (relative H_2O)
FSO_3H	FSO_3^-	––	RCO_2H	RCO_2^-	4–5
RSO_3H	RSO_3^-	–12	H_2CO_3	HCO_3^-	**6.35**
$HClO_4$	ClO_4^-	–10	H_2S	HS^-	**7.00**
HCl	Cl^-	–7	NH_4^+	NH_3	**9.24**
H_3O^+	H_2O	**–1.74**	ArOH	ArO^-	8–11
HNO_3	NO_3^-	–1.4	HCO_3^-	CO_3^-	**10.33**
HSO_4^-	SO_4^{2-}	**1.99**	H_2O	OH^-	**15.74**
HF	F^-	3.17	R_2CHOH	R_2CHO^-	16.5
			R_3COH	R_3CO^-	17

Table 2. Carbon acid acidities in pK_a in DMSO.

Name	Formula	Structural formula	pKa
Methane	**CH_4**		**~ 56**
n-Butyllithium	C_4H_9Li		~ 50
Ethane	C_2H_6		~ 50
Anisole	C_7H_8O		~ 49
Cyclopentane	C_5H_{10}		~ 45
Propene	C_3H_6		~ 44
Benzene	C_6H_6		~ 43
Toluene	$C_6H_5CH_3$		~ 43
Dimethyl sulfoxide	$(CH_3)_2SO$		35.5
Diphenylmethane	$C_{13}H_{12}$		32.3

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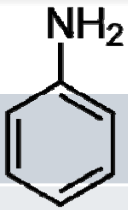
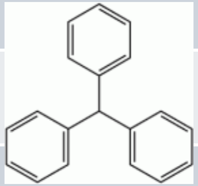
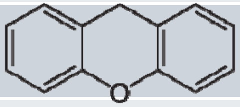
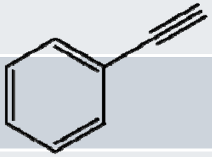
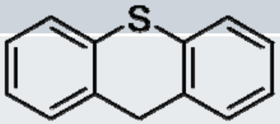
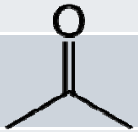
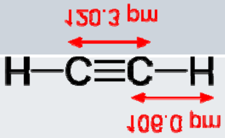
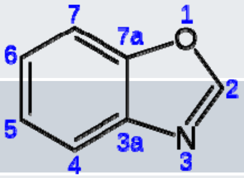
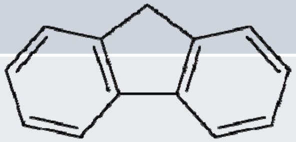
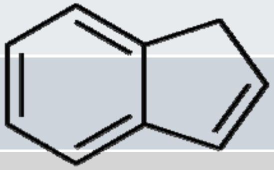
Aniline	**$C_6H_5NH_2$**		**30.6**
Triphenylmethane	$C_{19}H_{16}$		30.6
Xanthene	$C_{13}H_{10}O$		30
Ethanol	**C_2H_5OH**	**$CH_3–CH_2–OH$**	**29.8**
Phenylacetylene	C_8H_6		28.8
Thioxanthene	$C_{13}H_{10}S$		28.6
Acetone	C_3H_6O		26.5
Acetylene	C_2H_2		25
Benzoxazole	C_7H_5NO		24.4
Fluorene	$C_{13}H_{10}$		22.6
Indene	C_9H_8		20.1

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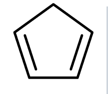
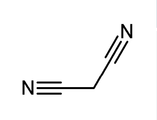
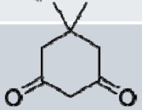
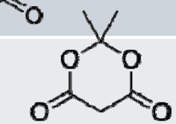
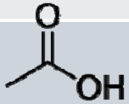
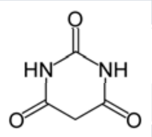
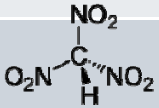
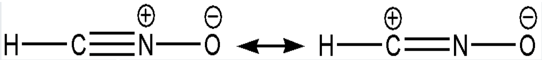
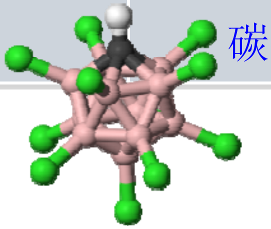
Cyclopentadiene	C_5H_6		18
Malononitrile	$C_3H_2N_2$		11.2
Hydrogen cyanide	HCN	H–C≡N	9.2
Acetylacetone	$C_5H_8O_2$		8.95
Dimedone	$C_8H_{12}O_2$		5.23
Meldrum's acid	$C_6H_8O_4$		4.97
Acetic acid	**CH_3COOH**		**4.76**
Barbituric acid	$C_4H_2O_3(NH)_2$		4.01
Trinitromethane	$HC(NO_2)_3$		0.17
Fulminic acid	HCNO		-1.07
Carborane superacid	$HCHB_{11}Cl_{11}$	 碳硼烷超强酸	-9

pK_{HB}

The **base dissociation constant** or K_b is a measure of basicity. pK_b is the negative log of K_b and related to the pK_a by the simple relationship $pK_a + pK_b = 14$. The larger the pK_{HB}, the more basic is that compound.

TABLE 3. The pK_{HB} values for some types of bases

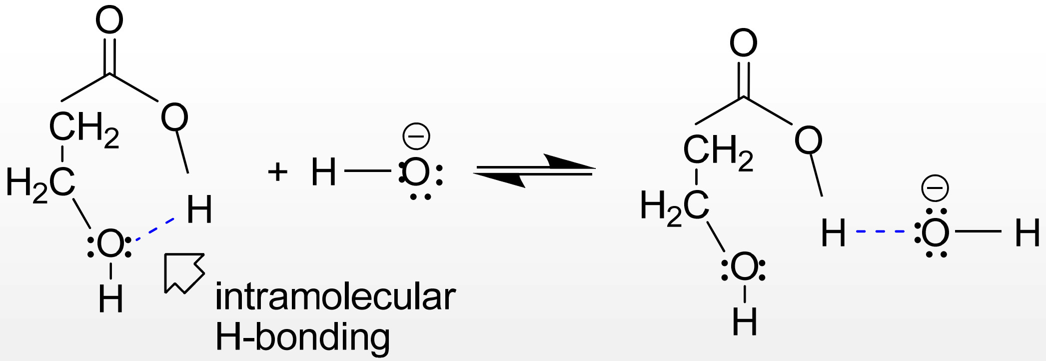
Base	Approximate pK_{HB}
PhCONMe$_2$	2.23
HCONMe$_2$ (DMF)	2.10
PhCONHMe	2.03
18-Crown-6	1.98
Et$_2$NCN	1.63
THF	1.28
CH$_3$COCH$_3$	1.18
CH$_3$COOEt	1.07
1,4-Dioxane	1.03
Et$_2$O	1.01
Bu$_2$O	0.75
MeNO$_2$	0.27
Furan	–0.4

William B. Jensen.
The Origin of the Term Base.
J. Chem. Edu. **83**,1130(2006)

The mechanism of proton transfer reaction

1. $AH + :B \rightleftharpoons AH\cdots :B$
2. $AH\cdots :B \rightleftharpoons A:\cdots HB$
3. $A:\cdots HB \rightleftharpoons A: + HB$

diffusion
controlled



Proton transfers to or from a carbon atom in most cases are much slower than those strictly between oxygen or nitrogen atoms.

◆ H-bonding is very weak or altogether absent for carbon.

◆ Many carbon acids, upon losing the proton, form carbanions that are stabilized by resonance. Structural reorganization (movement of atoms to different positions within the molecule) may accompany this.

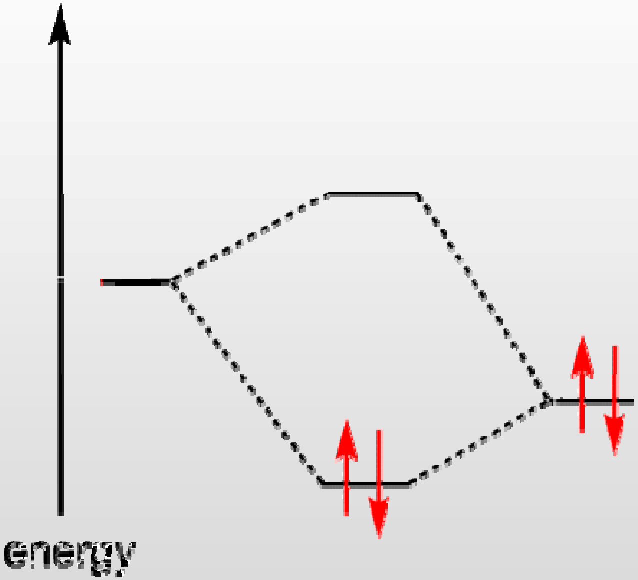
◆ There may be considerable reorganization of solvents around the ion as compared to the neutral molecule.

2.2 Lewis acids and bases. HSAB theory

DEFINITION

- Lewis acid: any species with a vacant orbital.
- Lewis base: a compound with an available pair of electrons, either unshared or in a π orbital.

The modern definition of a Lewis acid is an atomic or molecular species that has an empty atomic or molecular orbital of low energy (LUMO) that can accommodate a pair of electrons, as illustrated in the molecular orbital diagram at the right. A Lewis base is an atomic or molecular species that has a lone pair of electrons in the HOMO



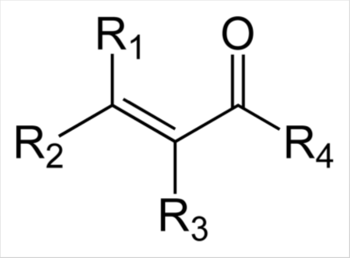
MO diagram depicting the formation of a dative covalent bond between two atoms.

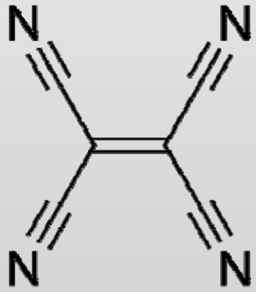
Lewis acids

Lewis acids are diverse. Simplest are those that react directly with the Lewis base. But more common are those that undergo a reaction prior to forming the adduct.

Examples of Lewis acids based on the general definition of electron pair acceptor include:

- **the proton (H^+)** and acidic compounds **onium ions**, such as NH_4^+ and H_3O^+
- **metal cations**, such as Li^+ and Mg^{2+}, often as their aquo or ether complexes,
- **trigonal planar species**, such as BF_3 and carbocations H_3C^+, pentahalides of phosphorus, arsenic, and antimony,
- **electron poor π-systems**, such as enones and tetracyanoethylene (TCNE)





- **Simple Lewis acids**

$BF_3 + F^- \rightarrow BF_4^-$

$BF_3 + OMe_2 \rightarrow BF_3OMe_2$

Both BF_4^- and BF_3OMe_2 are Lewis base adducts of boron trifluoride.

In many cases, the adducts violate the octet rule:

$I_2 + I^- \rightarrow I_3^-$

In some cases, the Lewis acids are capable of binding two Lewis bases:

$SiF_4 + 2\ F^- \rightarrow SiF_6^{2-}$

- **Complex Lewis acids**

Most compounds considered to be Lewis acids require an activation step prior to formation of the adduct with the Lewis base:

$B_2H_6 + 2\ H^- \rightarrow 2\ BH_4^-$ (intermediate $B_2H_7^-$)

Many metal complexes serve as Lewis acids, but usually only after dissociating a more weakly bound Lewis base, often water.

$$[Mg(H_2O)_6]^{2+} + 6\ NH_3 \rightarrow [Mg(NH_3)_6]^{2+} + 6\ H_2O$$

- **H^+ as Lewis acid**

The proton (H^+) is one of the strongest but is also one of the most complicated Lewis acids. It is convention to ignore the fact that a proton is heavily solvated (bound to solvent). With this simplification in mind, acid-base reactions can be viewed as the formation of adducts:

$$H^+ + NH_3 \rightarrow NH_4^+$$
$$H^+ + OH^- \rightarrow H_2O$$

Lewis bases

Some of the main classes of Lewis bases:

- **$NH_{3-x}R_x$** where R = alkyl or aryl. Also, pyridine and its derivatives
- **$PR_{3-x}A_x$** where R = alkyl, A = aryl.
- **Compounds of O, S, Se and Te in oxidation state 2**, including water, ethers, ketones

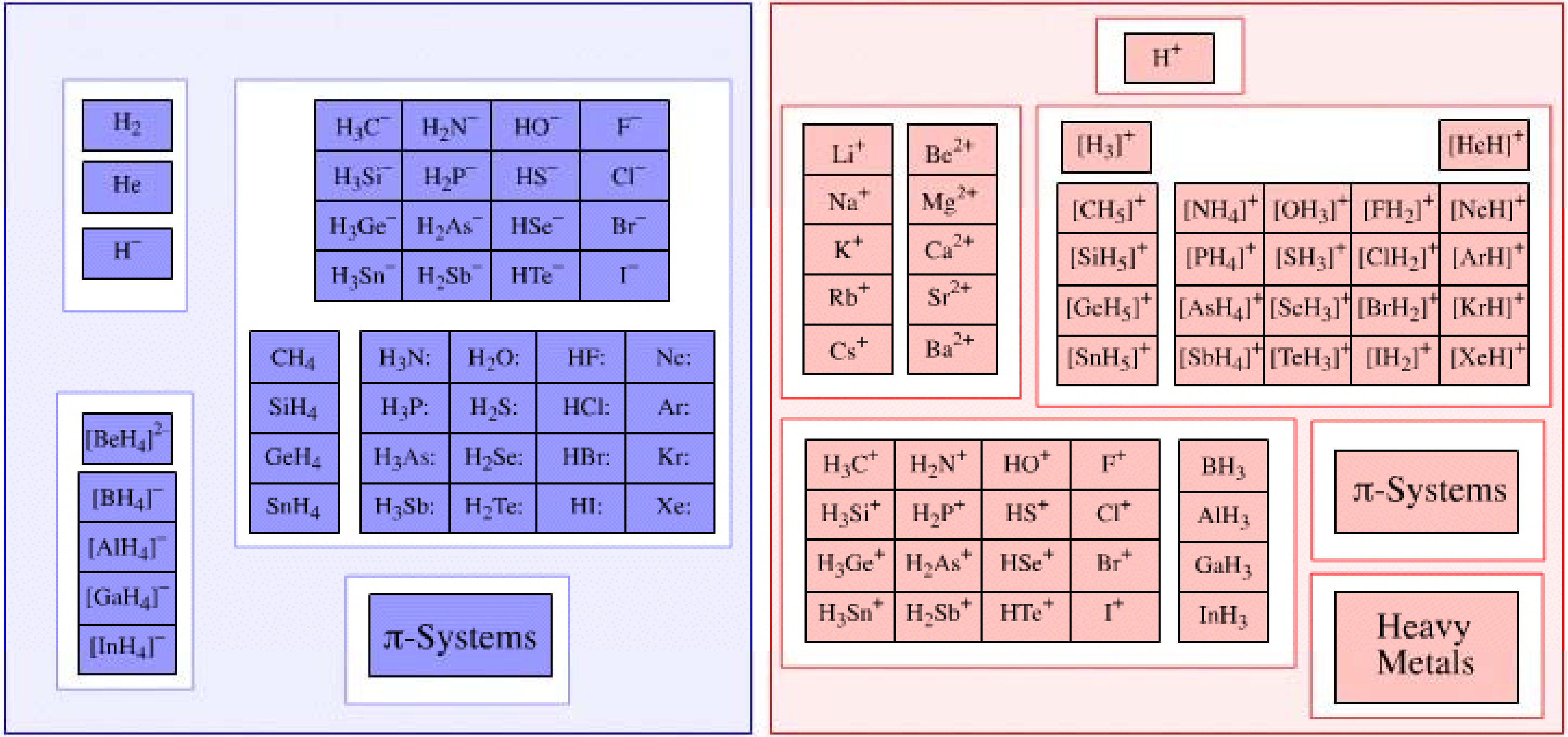
- Examples of Lewis bases based on the general definition of electron pair donor include:

- simple anions, such as **H^-** and **F^-**.
- other lone-pair-containing species, such as **H_2O**, **NH_3**, **HO^-**, and **CH_3^-**
- complex anions, such as sulfate
- electron rich π-system Lewis bases, such as **ethyne, ethene,** and **benzene**

Table 3. The strength of Lewis bases

Heats of binding of various bases to BF_3		
Lewis base	donor atom	Enthalpy of Complexation (kJ/mol)
Et_3N	N	135
quinclidine	N	150
pyridine	N	128
acetonitrile	N	60
Et_2O	O	78.8
THF	O	90.4
acetone	O	76.0
EtOAc	O	75.5
DMA	O	112
DMSO	O	105
tetrahydrothiophene	S	51.6
PMe_3	P	97.3

Diagram of Lewis acids and bases



H_2

He

H^-

H_3C^-	H_2N^-	HO^-	F^-
H_3Si^-	H_2P^-	HS^-	Cl^-
H_3Ge^-	H_2As^-	HSe^-	Br^-
H_3Sn^-	H_2Sb^-	HTe^-	I^-

CH_4	H_3N:	H_2O:	HF:	Ne:
SiH_4	H_3P:	H_2S:	HCl:	Ar:
GeH_4	H_3As:	H_2Se:	HBr:	Kr:
SnH_4	H_3Sb:	H_2Te:	HI:	Xe:

$[BeH_4]^{2-}$

$[BH_4]^-$

$[AlH_4]^-$

$[GaH_4]^-$

$[InH_4]^-$

π-Systems

H^+

Li^+	Be^{2+}
Na^+	Mg^{2+}
K^+	Ca^{2+}
Rb^+	Sr^{2+}
Cs^+	Ba^{2+}

$[H_3]^+$

$[HeH]^+$

$[CH_5]^+$	$[NH_4]^+$	$[OH_3]^+$	$[FH_2]^+$	$[NeH]^+$
$[SiH_5]^+$	$[PH_4]^+$	$[SH_3]^+$	$[ClH_2]^+$	$[ArH]^+$
$[GeH_5]^+$	$[AsH_4]^+$	$[SeH_3]^+$	$[BrH_2]^+$	$[KrH]^+$
$[SnH_5]^+$	$[SbH_4]^+$	$[TeH_3]^+$	$[IH_2]^+$	$[XeH]^+$

H_3C^+	H_2N^+	HO^+	F^+	BH_3
H_3Si^+	H_2P^+	HS^+	Cl^+	AlH_3
H_3Ge^+	H_2As^+	HSe^+	Br^+	GaH_3
H_3Sn^+	H_2Sb^+	HTe^+	I^+	InH_3

π-Systems

Heavy Metals

Lewis acid-base reaction:

A + B: → A—B

- $H^+ + :NH_3 \rightarrow NH_4^+$
- $B_2H_6 + 2H^- \rightarrow 2BH_4^-$
- $BF_3 + F^- \rightarrow BF_4^-$
- $Al_2Cl_6 + 2Cl^- \rightarrow 2AlCl_4^-$
- $AlF_3 + 3F^- \rightarrow AlF_6^{3-}$
- $PCl_5 + Cl^- \rightarrow PCl_6^-$
- Solvation of metal ions:

$[Mg(H_2O)_6]^{2+}$, $[Al(H_2O)_6]^{3+}$, etc.

where the solvent is a Lewis base.

♦ A Lewis acid in action in the Friedel-Crafts alkylation reaction: $RCl + AlCl_3 \rightarrow R^+ + AlCl_4^-$

Ate complex: when a Lewis acid combines with a base to give a negative ion in which the central atom has a higher-than-normal valence, the resulting salt is called an *ate complex.*

$Me_3B + LiMe \rightarrow Me_4B^-Li^+$

$Ph_5Sb + LiPh \rightarrow Ph_6Sb^-Li^+$

Onium salt: similarly, when a Lewis base expands its valence.

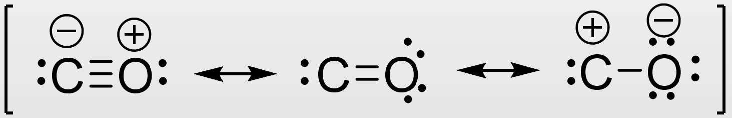
$Me_3N + MeI \rightarrow Me_4N^+I^-$

Ammonium, NH_4^+ (protonated ammonia) ;
Oxonium, H_3O^+, (protonated water);
Iodonium, Ph_2I^+

Comparison with Brønsted-Lowry theory

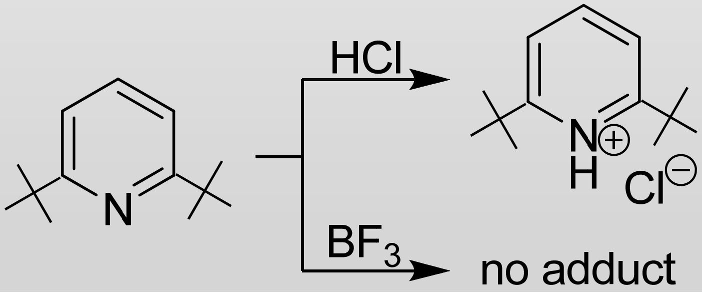
- A Lewis base is usually a Brønsted-Lowry base as it can donate a pair of electrons to a proton; the proton is a Lewis acid as it can accept a pair of electrons. The conjugate base of a Brønsted-Lowry acid is also a Lewis base as loss of a proton from the acid leaves those electrons which were used for the A—H bond as a lone pair on the conjugate base. However, a Lewis base can be very difficult to protonate, yet still react with a Lewis acid.

For example, carbon monoxide is a very weak Brønsted-Lowry base but it forms a strong adduct with BF_3.



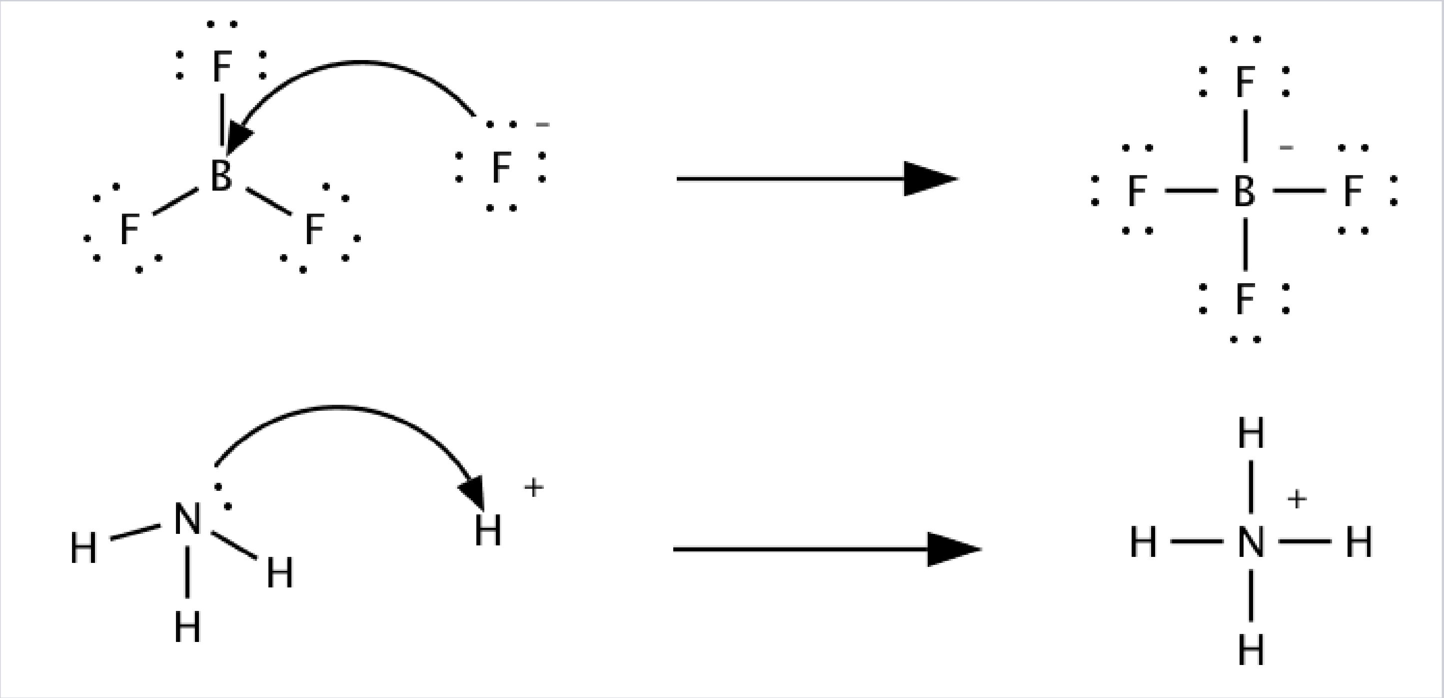
$$CO + BF_3 \longrightarrow BF_3{\cdot}CO$$

CO is Lewis-base but not a Brønsted-base as it can not be protonated.



A Brønsted-base, but not Lewis base for BF_3.

All Brønsted acids are also Lewis acids, but not all Lewis acids are Brønsted acids. 所有的**Brønsted**酸属于**Lewis**酸，但不是所有的**Lewis**酸都属于**Brønsted**酸.



The second reaction can be described using either theory. A proton is transferred from an unspecified Brønsted acid to ammonia, a Brønsted base; alternatively, ammonia acts as a Lewis base and transfers a lone pair of electrons to form a bond with a hydrogen ion.

PresentationPoint

Brønsted acidity of some Lewis acids

- Some Lewis acids also act as Brønsted–Lowry acids

For example:

$$Al^{3+} + 6H_2O \rightarrow Al(H_2O)_6^{3+}$$

The aqua ion formed is a weak Brønsted–Lowry acid.

$$Al(H_2O)_6^{3+} + H_2O \rightarrow Al(H_2O)_5OH^{2+} + H_3O^+ \text{ .....} K_a = 1.7 \times 10^{-5}$$

However, $Mg^{2+} + 6H_2O \rightarrow Mg(H_2O)_6^{2+}$

the Brønsted–Lowry acidity of the aqua ion is negligible ($K_a \sim 10^{-12}$).

- **Boric acid** also exemplifies the usefulness of the Brønsted–Lowry concept for an acid which does not dissociate, but does effectively donate a proton to the base, water:

$$B(OH)_3 + 2H_2O \rightarrow B(OH)_4^- + H_3O^+$$

Here boric acid acts as a Lewis acid and accepts an electron pair from the oxygen of one water molecule, which in turn donates a proton to a second water molecule and therefore acts as a Brønsted acid.

HSAB concept

Hard acids and **hard bases** tend to have:

- Small atomic/ionic radius
- High oxidation state
- Low polarizability
- High electronegativity
- Energy low-lying HOMO (bases) or energy high-lying LUMO (acids).

Example: H^+, alkali ions; OH^-, F^-, etc.

The affinity of hard acids and hard bases for each other is mainly ionic in nature.

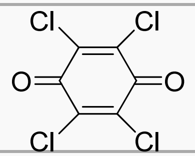
Soft acids and **soft bases** tend to have:

- Large atomic/ionic radius
- Low or zero oxidation state
- High polarizability
- Low electronegativity
- Energy high-lying HOMO (bases) and energy low-lying LUMO (acids).

Example: CH_3Hg^+, Pt^{2+}; H^-, R_3P, I^-, etc.

The affinity of soft acids and bases for each other is mainly covalent in nature.

Table 4. Hard and soft acids and bases

Acids				Bases			
hard		soft		hard		soft	
Hydronium	H^+	Mercury	CH_3Hg^+, Hg^{2+}, Hg_2^{2+}	Hydroxide	OH^-	Hydride	H^-
Alkali metals	Li^+, Na^+, K^+	Platinum	Pt^{2+}	Alkoxide	RO^-	Thiolate	RS^-
Titanium	Ti^{4+}	Palladium	Pd^{2+}	Halogens	F^-, Cl^-	Halogens	I^-
Chromium	Cr^{3+},Cr^{6+}	Silver	Ag^+	Ammonia	NH_3	Phosphine	PR_3
Boron trifluoride	BF_3	borane	BH_3	Carboxylate	CH_3COO^-	Thiocyanate	SCN^-
carboction	R_3C^+	P-chloranil		Carbonate	CO_3^{2-}	carbon monoxide	CO
		bulk Metals	M^0	Hydrazine	N_2H_4	Benzene	C_6H_6
		Gold	Au^+				

Borderline acids:

trimethylborane **$B(CH_3)_3$**, sulfur dioxide **SO_2**, and ferrous **Fe^{2+}**, cobalt **Co^{2+}**, lead **Pb^{2+}** cations.

Borderline bases:

aniline, pyridine, nitrogen **N_2**, and the azide **N_3^-**, bromine **Br^-**, nitrate **NO_3^-** and sulfate **SO_4^{2-}** anions.

Chemical hardness (η)

Pearson and Robert Parr (1983): The chemical hardness is half the difference between the ionization potential (I) and the electron affinity (A).

$$\boxed{\eta = \frac{I - A}{2}}$$

NOTE: The above equation cannot be applied to anions, because electron affinity cannot be measured for them, the assumption is made that η for an anion X^- is same as that for the radical $X\cdot$.

Table 5. Chemical hardness in electron volt

Cations		Molecules		Anions [a]	
H^+	infinite	HF	11.0	F^-	7.0
Al^{3+}	45.8	CH_4	10.3	H^-	6.8
Li^+	35.1	BF_3	9.7	OH^-	5.7
Mg^{2+}	32.6	H_2O	9.5	NH_2^-	5.3
Na^+	21.1	NH_3	8.2	CN^-	5.1
Ca^{2+}	19.5	HCN	8.0	CH_3^-	4.9
K^+	13.6	Me_2O	8.0	Cl^-	4.7
Zn^{2+}	10.9	CO	7.9	$CH_3CH_2^-$	4.4
Cr^{3+}	9.1	C_2H_2	7.0	Br^-	4.2
Cu^{2+}	8.3	Me_3N	6.3	$C_6H_5^-$	4.1
Pt^{2+}	8.0	H_2S	6.2	SH^-	4.1
Hg^{2+}	7.7	C_2H_4	6.2	$(CH_3)_2CH^-$	4.0
Fe^{2+}	7.2	Me_2S	6.0	I^-	3.7
Pd^{2+}	6.8	Me_3P	5.9	$(CH_3)_3C^-$	3.6
Cu^+	6.3	CH_3COCH_3	5.6		
		C_6H_6	5.3		
		HI	5.3		
		C_5H_5N	5.0		
		C_6H_5OH	4.8		
		Cl_2	4.6		
		$C_6H_5NH_2$	4.4		
		Br_2	4.0		
		I_2	3.4		

a. the same as for the corresponding radical.

b. The softness, σ, is the reciprocal of η.

i. Softness/hardness of bases

Softness:

$I^- > Br^- > Cl^- > F^-$

$R_3Sb > R_3As > R_3P > R_3N$

$CH_3^- > NH_2^- > OH^- > F^-$

Hardness:

$RO^- > HO^- > RS^-$

$H_2O > HO^- > O^{2-}$

$C_6H_5O^- > C_6H_5NH_2 > C_6H_5S^-$

$HC{\equiv}C^- > CH_2{=}CH^- > CH_3CH_2^-$

ii. Hardness of acids

$C_6H_5^+ > Me_3C^+ > Me_2CH^+ >$

$CH_3CH_2^+ > CH_3^+$

半径，电负性，杂化状态

The HSAB principle

(i) Hard acids prefer to bond hard bases, and soft acids prefer to bond to soft bases.

NOTE: The rule has nothing to do with acid or base strength but merely says that the product A–B will have extra stability if both A and B are hard or if both are soft.

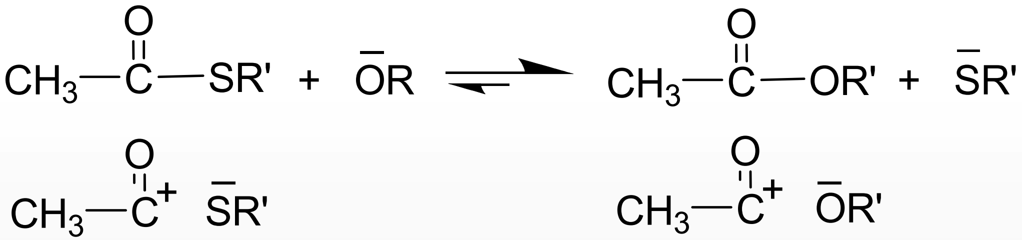
(ii) A soft Lewis acid and a soft Lewis base tend to form a covalent bond, while a hard acid and a hard base tend to form ionic bonds.

- **Solubility**: Hard solvents (HF, H_2O, and the protic solvents) tend to solvate strong solute bases (F^-, the oxygen anions). Dipolar aprotic solvents (Me_2SO, CH_3COCH_3) are soft solvents with a preference for solvatating large anions and soft bases.
- **Coordination chemistry**: Numerous experiments have been done to determine the relative ordering of ligands and transition metal ions in terms of their hardness and softness.

Pearson, Ralph G. *J. Chem. Educ.* **1968** (45): 581–586; 643–648

Application of the HSAB principle in organic chemistry

(1) Nucleophilic substitution and elimination

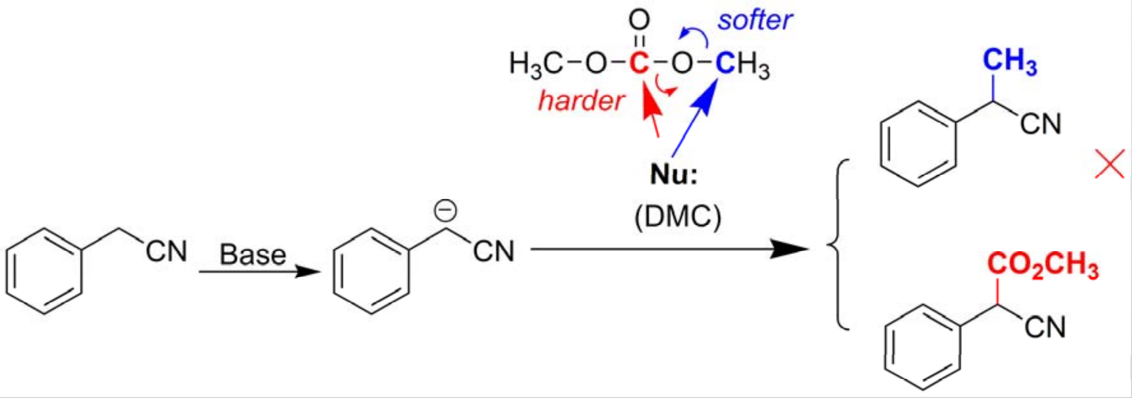


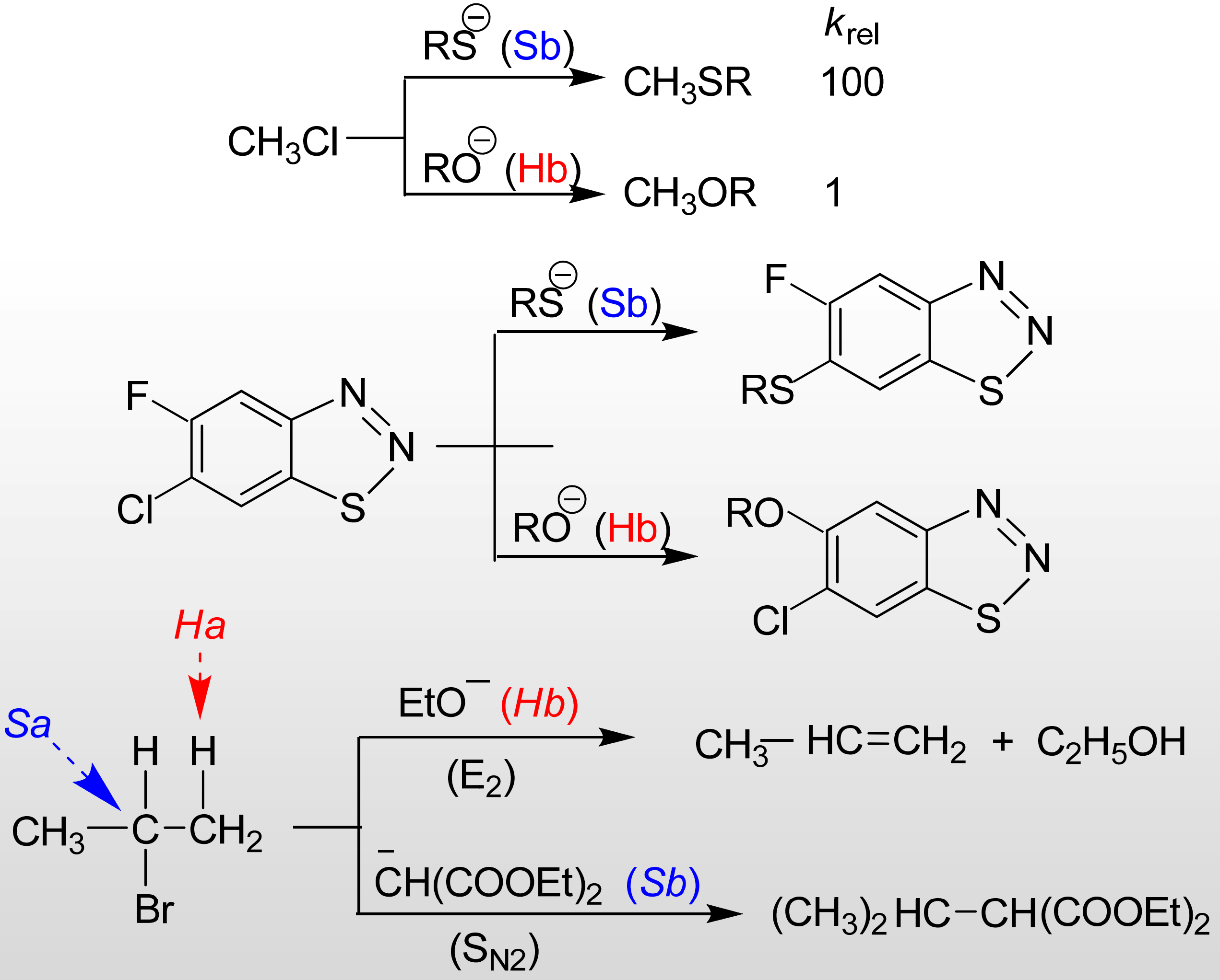
$$CH_3-\overset{O}{\overset{\|}{C}}-SR' + \bar{O}R \rightleftharpoons CH_3-\overset{O}{\overset{\|}{C}}-OR' + \bar{S}R'$$

$$CH_3-\overset{O}{\overset{\|}{C}}{}^{+}\quad \bar{S}R' \qquad\qquad CH_3-\overset{O}{\overset{\|}{C}}{}^{+}\quad \bar{O}R'$$

hard acid-soft base hard acid-hard base

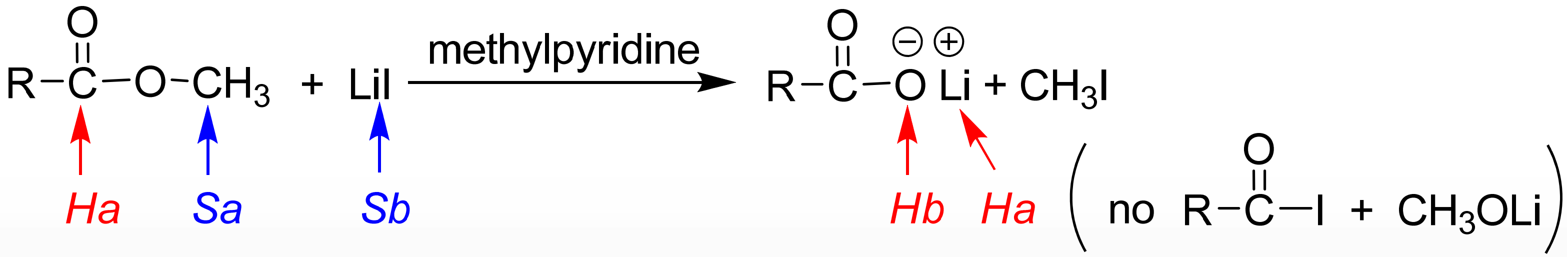
The HSAB principle predicts that the equilibrium should lie to the right, because the hard acid CH_3CO^+ should have a greater affinity for the hard base RO^- than for the soft base RS^-. Indeed, thiol esters are easily cleaved by RO^- or hydrolyzed by dilute base (OH^- is also a hard base).



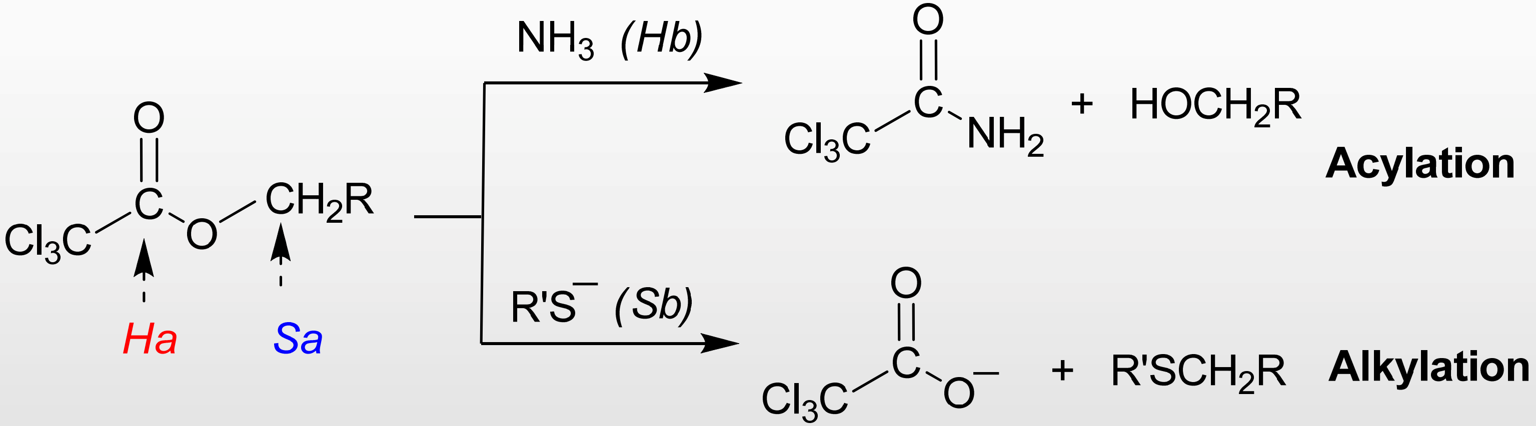


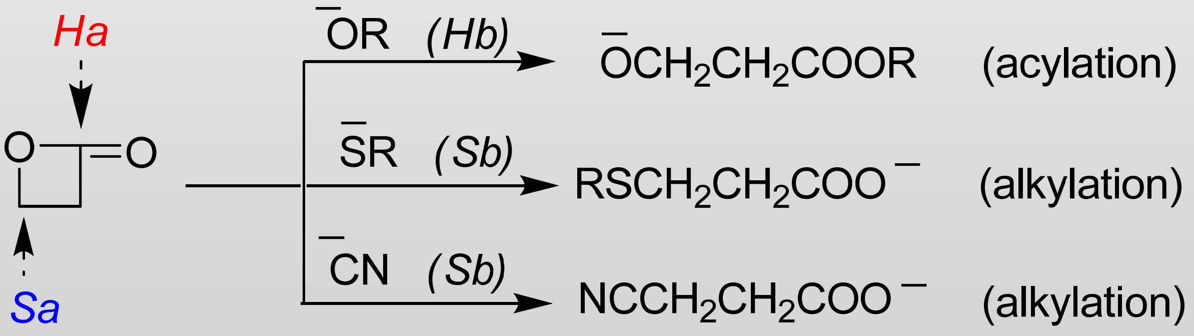
Generally, a soft base tends to substitution, a hard base tends to elimination.

(2) Alkylation / Acylation



$$R{-}\overset{\overset{O}{\|}}{C}{-}O{-}CH_3 + LiI \xrightarrow{\text{methylpyridine}} R{-}\overset{\overset{O}{\|}}{C}{-}\overset{\ominus}{O}\,\overset{\oplus}{Li} + CH_3I \quad \left(\text{no } R{-}\overset{\overset{O}{\|}}{C}{-}I + CH_3OLi\right)$$

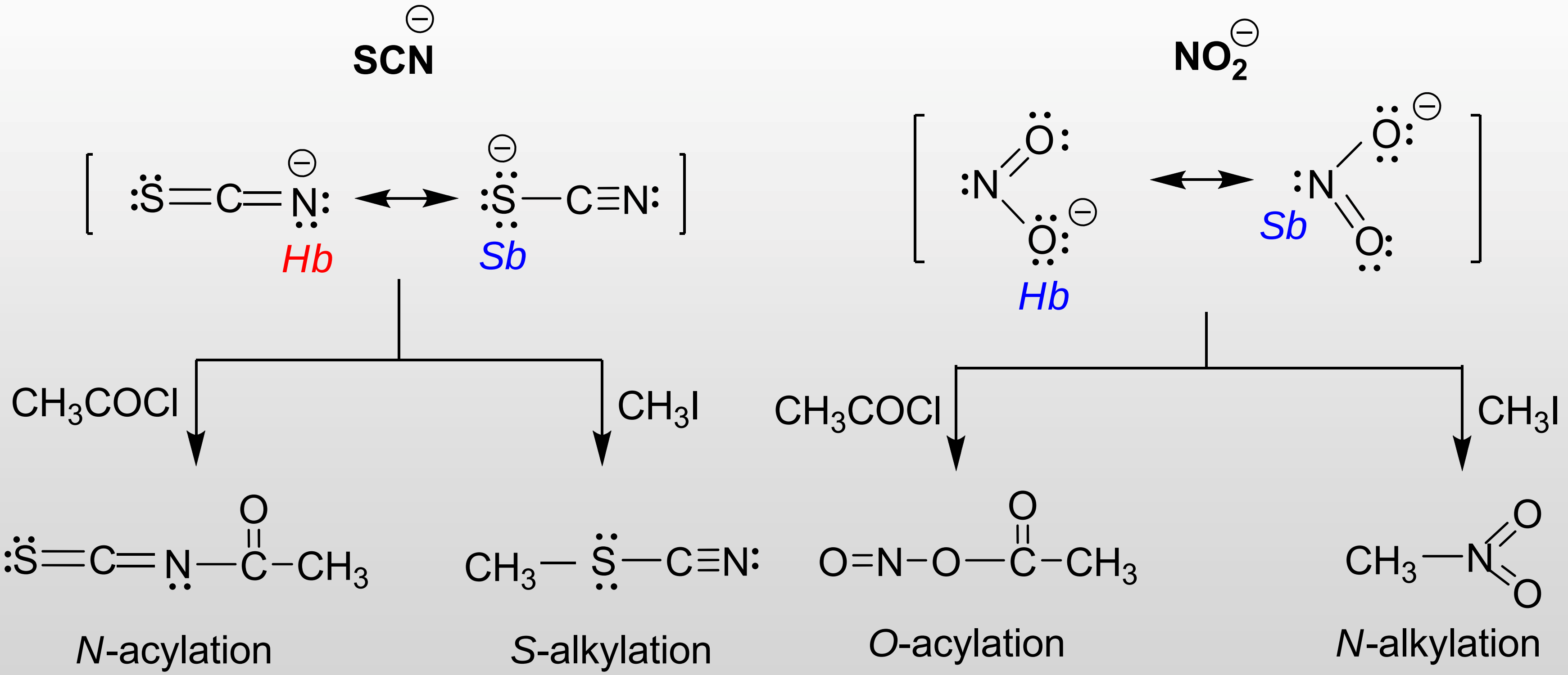




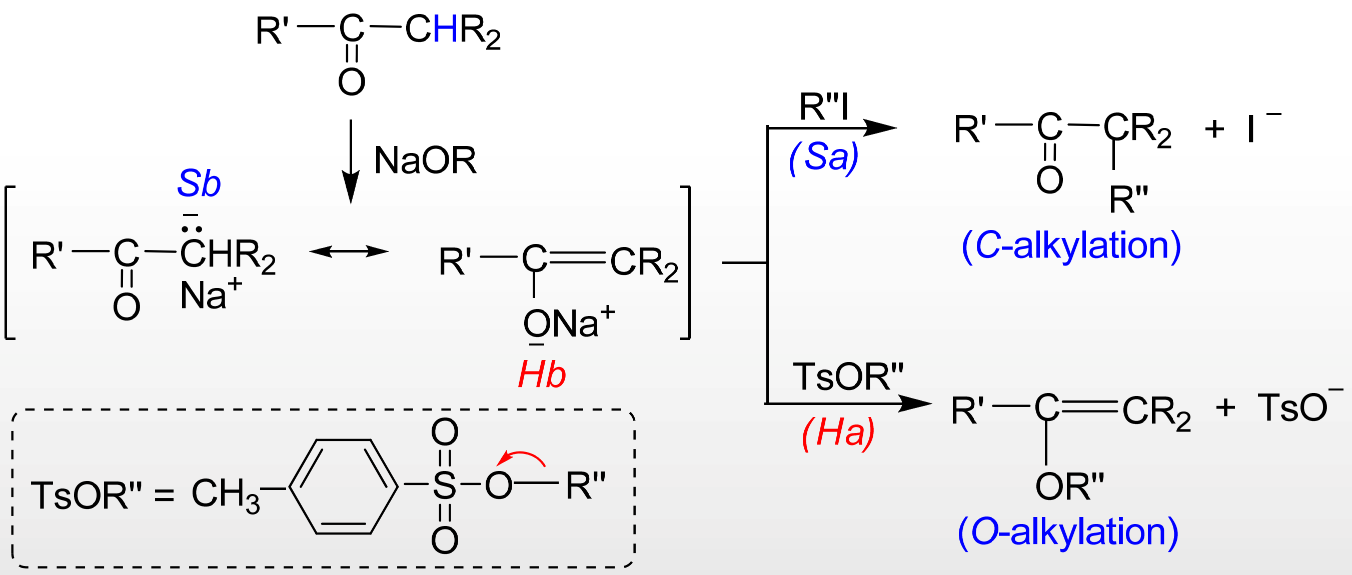
Ambident nucleophile

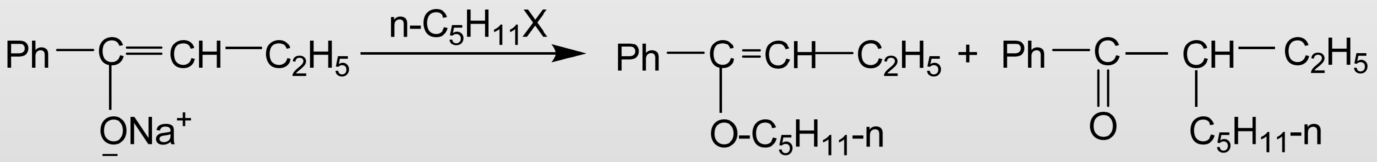
*An **ambident nucleophile** is one that can attack from two or more places, resulting in two or more products.*

i. SCN^- and NO_2^-



ii. Enolate ion: O/C alkylation ratio often depends on the hardness or softness of alkylating agents.



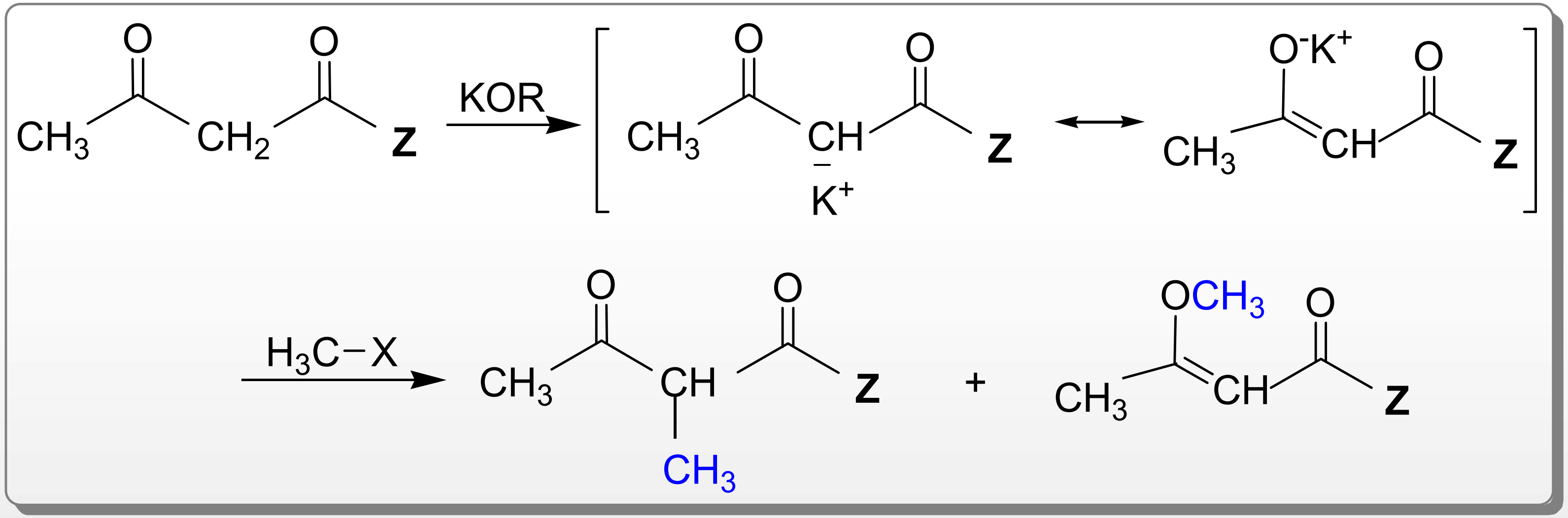


$$Ph-\underset{O^-Na^+}{C}=CH-C_2H_5 \xrightarrow{n\text{-}C_5H_{11}X} Ph-\underset{O\text{-}C_5H_{11}\text{-}n}{C}=CH-C_2H_5 + Ph-\underset{\underset{O}{\|}}{C}-\underset{C_5H_{11}\text{-}n}{CH}-C_2H_5$$

Softness ↓

$n\text{-}C_5H_{11}X$	*O*-alkylation	*C*-alkylation
X= Cl	1.2	1.0
Br	0.64	1.0
I	0.23	1.0

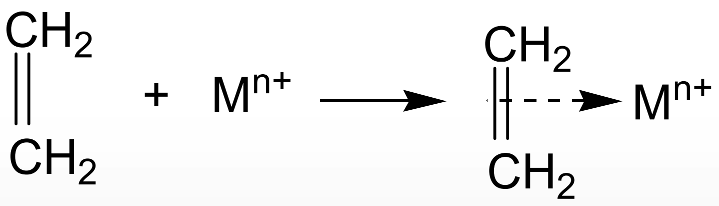
iii. β-biketone and β-ketoesters



Z	X	*C*-alkylation / %	*O*-alkylation / %
CH_3	I	**70**	0
CH_3	OSO_2CH_3	26	31
OEt	OSO_2CH_3	30	**36**

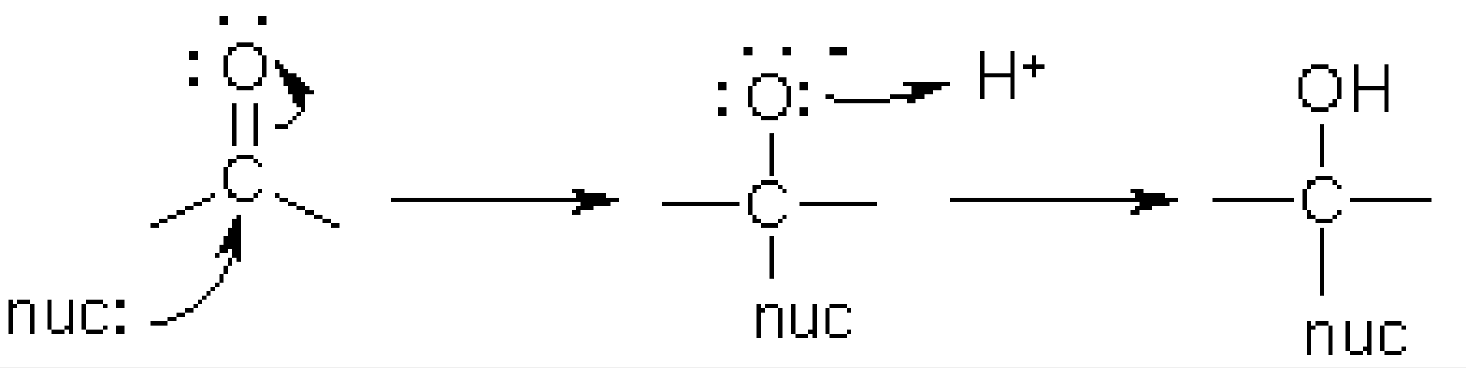
The results show that *O*/*C* alkylation depends on the softness or hardness of leaving groups in the alkylating agents.

(3) Addition reaction

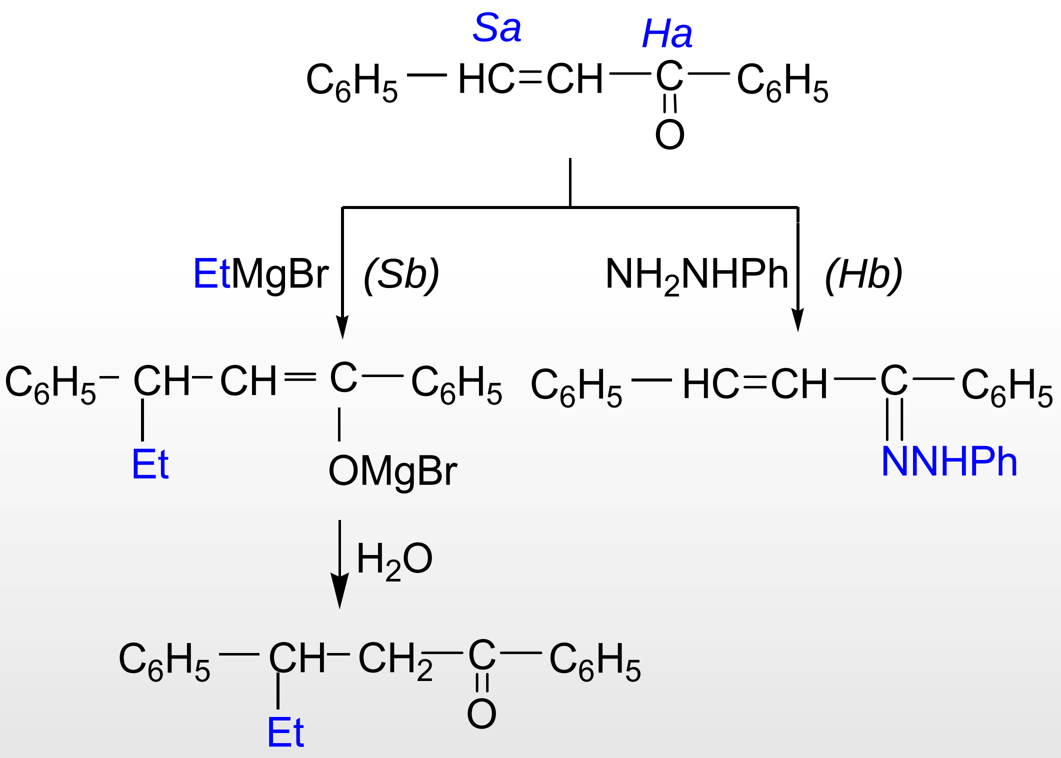


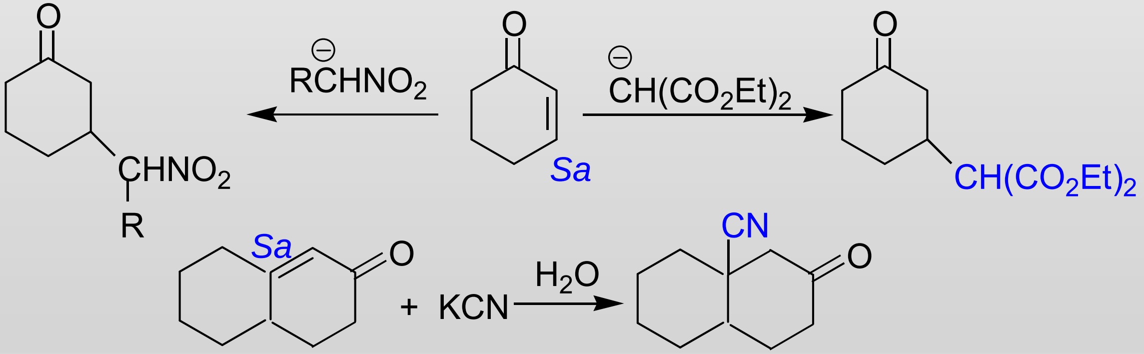
(Ag^+, Cu^+, Pd^{2+}, Hg^{2+})

Alkenes or aromatic compounds are soft bases, and should prefer to complex with soft acids.



Carbonyl compounds are hard acids, should prefer to react with the hard carbonyl agents.


Sa
Ha
C6H5 — HC=CH — C(=O) — C6H5
EtMgBr (Sb)
NH2NHPh (Hb)
C6H5 − CH(Et) − CH = C(OMgBr) — C6H5
C6H5 — HC=CH — C(=NNHPh) — C6H5
H2O
C6H5 — CH(Et) − CH2 — C(=O) — C6H5

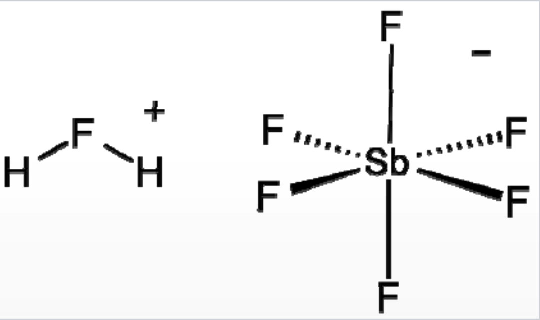

⊖
RCHNO2
CHNO2
R
Sa
⊖
CH(CO2Et)2
CH(CO2Et)2
Sa
O
+ KCN
H2O
CN
O

2.3 Superacid and Superbase

- A **superacid** is an acid with an acidity greater than that of 100% pure sulfuric acid.

CF_3SO_3H, FSO_3H (~ 1000 times than H_2SO_4).

- The strongest superacids are prepared by the combination of two components, a strong Lewis acid and a strong Brønsted acid.



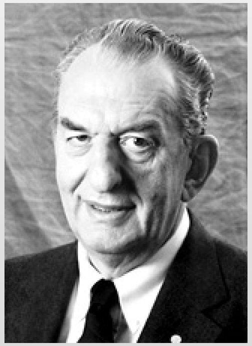
♦ **Fluoroantimonic acid** ($HF\text{-}SbF_5$) is 10^{16} times stronger than 100% sulfuric acid.

♦ Olah's **magic acid:** $FSO_3H\text{–}SbF_5$

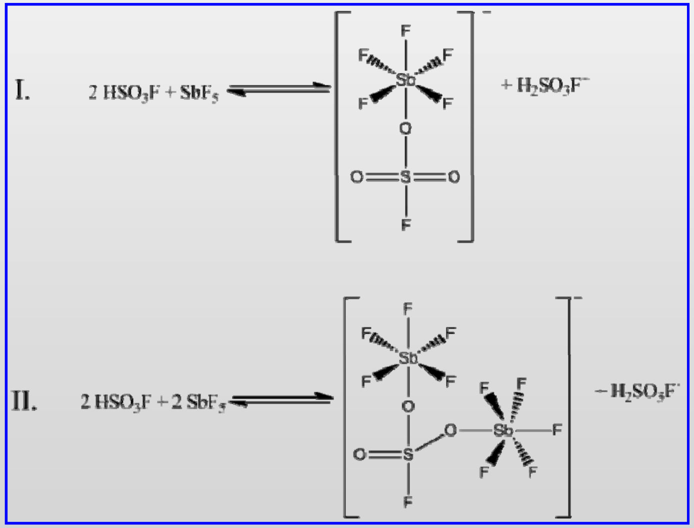
$$CH_4 + H^+ \rightarrow CH_5^+$$

$$CH_5^+ \rightarrow CH_3^+ + H_2$$

$$CH_3^+ + 3\,CH_4 \rightarrow (CH_3)_3C^+ + 3H_2$$



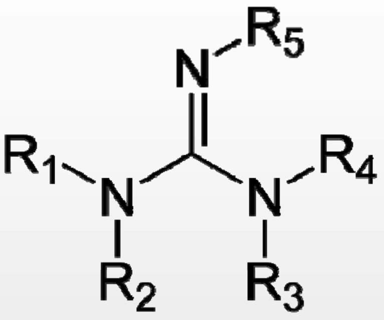
George A. Olah 1927-
The Nobel Prize in Chemistry 1994 for his contribution to carbocation chemistry



Superbase

IUPAC defines superbases simply as a "compound having a very high basicity." The term *superbases* should only be applied to bases resulting from a mixing of two (or more) bases leading to new basic species possessing inherent new properties.

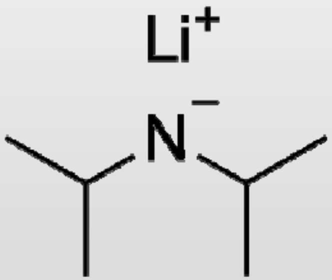
Organic



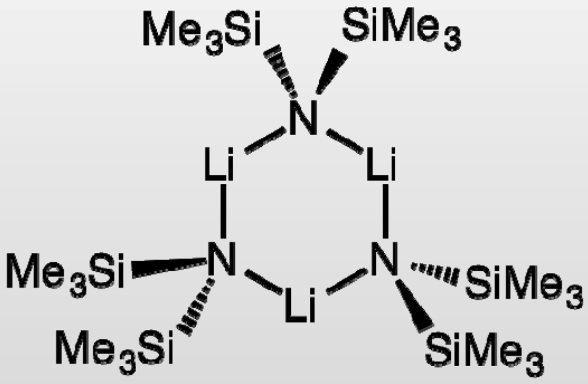
胍

The general structure of a guanidine

Organometallic



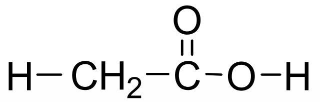
Lithium diisopropylamide
(**LDA**)



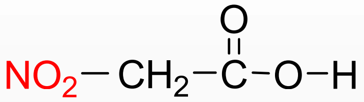
Lithium bis(trimethylsilyl)amide
(LiHMDS)

2.4 The effect of structure on the strengths of acids and bases

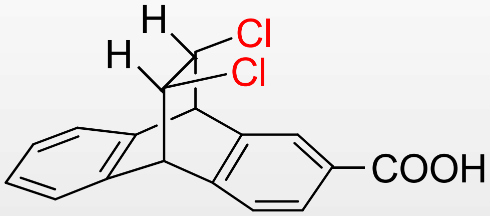
1. Field effects

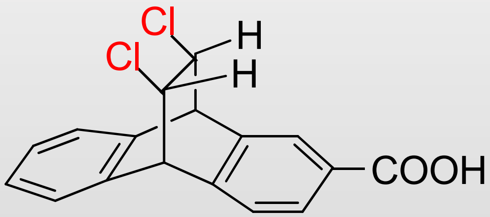


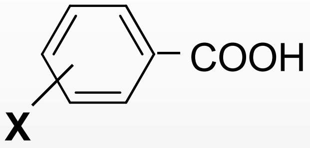
$H-CH_2-\overset{O}{\overset{\|}{C}}-O-H$ pKa = 4.76



$NO_2-CH_2-\overset{O}{\overset{\|}{C}}-O-H$ pKa = 1.68







pKa (50% MeOH/H_2O)

X	pKa
X = H	5.67
3-OMe	5.55
4-OMe	6.02
4-NO_2	4.76
4-Br	5.36
2,6-diphenyl	6.39

Any effect that results in electron withdrawal from a negatively charged center is a stabilizing effect because it spreads the charge.

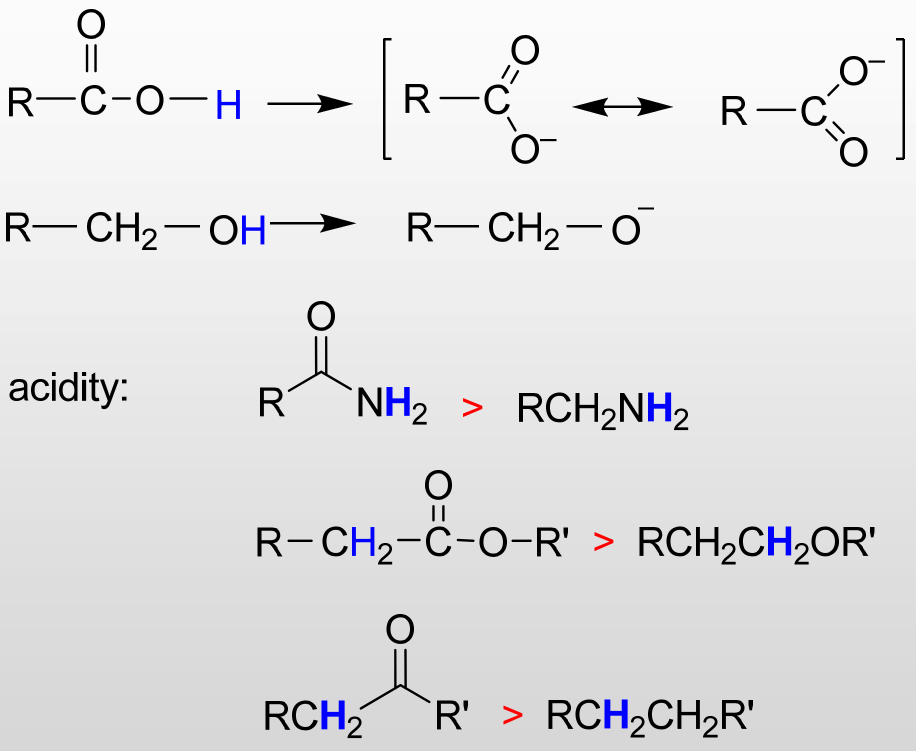
Thus, -*I* groups increase the acidity of uncharged acids such as acetic acid because they spread the negative charge of the anion.

Table 6. pK_a values for some acids

acid	pK_a
HCOOH	3.77
CH_3COOH	4.76
CH_3CH_2COOH	4.88
$CH_3(CH_2)_nCOOH$, n=2-7	4.82- 4.95
$(CH_3)_2CHCOOH$	4.86
$(CH_3)_3CCOOH$	5.05
FCH_2COOH	2.66
$ClCH_2COOH$	2.86
$BrCH_2COOH$	2.86
ICH_2COOH	3.12
$ClCH_2CH_2CH_2COOH$	4.52
$CH_3CHClCH_2COOH$	4.06
$CH_3CH_2CHClCOOH$	2.84
$ClCH_2COOH$	2.86
$Cl_2CHCOOH$	1.29
Cl_3CCOOH	0.65
O_2NCH_2COOH	1.68
$(CH_3)_3N^+CH_2COOH$	1.83
$HOOCCH_2COOH$	2.83
$PhCH_2COOH$	4.31
$^-OOCCH_2COOH$	5.69
$^-O_3SCH_2COOH$	4.05
$HOCH_2COOH$	3.83
$H_2C{=}CHCH_2COOH$	4.35

2. Resonance Effects

Resonance that stabilizes a base but not its conjugate acid results in the acid having a higher acidity than otherwise expected and vice versa.



Hybridization

The energy of a hybrid orbital is lower the more *s* character it contains. It follows that a carbanion at an *sp* carbon is more stable than a corresponding carbanion at an sp^2 carbon.

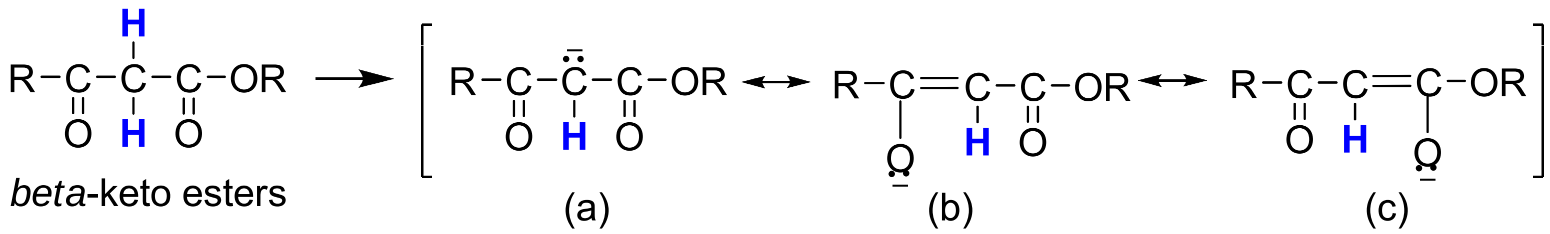
Stability:

$HC{\equiv}C^- > CH_2{=}CH^- > CH_3CH_2^-$

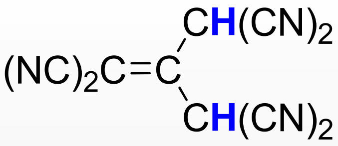
Basicity:

$HC{\equiv}C^- < CH_2{=}CH^- < CH_3CH_2^-$

$ROH > R_2C{=}O$

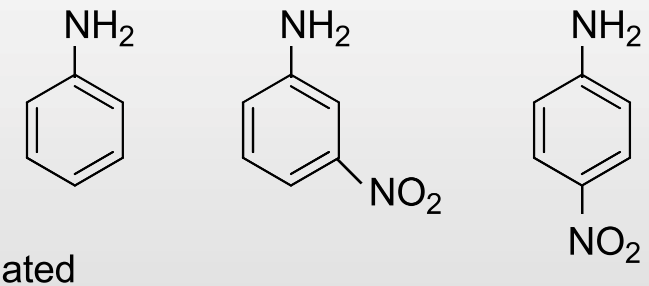


$(NC)_3CH$ pKa -5



$(NC)_2C{=}C(CH(CN)_2)_2$

pKa1 < -8.5
pKa2 -2.5



pK_a of conjugated acid: 4.60 2.47 1.11

Question: Why the basicity of *p*-nitroaniline is weaker than m-nitroaniline still though the *-I* effect should be less because of the greater distance?

In general, resonance effects leads to the same results as field effects. As a result of both resonance and field effects, charge dispersal leads to greater stability.

3. Periodic table correlations

Brønsted acids and bases

(a) Acidity increases and basicity decreases in going from left to right across a row of the periodic table. Electronegativity!

acidity: $CH_4 < NH_3 < H_2O < HF$
basicity: $CH_3^- > NH_2^- > OH^- > F^-$
acidity: $RCOOH >> RCONH_2 >> RCOCH_3$

(b) Acidity increases and basicity decreases in going down a column of the periodic table, despite the decrease in electronegativity.

acidity: $HF < HCl < HBr < HI$; $H_2O < H_2S$
basicity: $NH_3 > PH_3 > AsH_3$
Explanation: the size of the species involved

Exception: acidity order $H_3O^+ > H_3S^+ > H_3Se^+$
although $H_2O < H_2S < H_2Se$

Lewis acidity of the form MX_n: $BCl_3 > AlCl_3$

4. Statistical effects

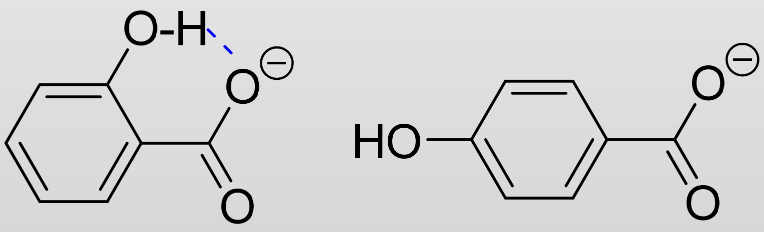
In a symmetric diprotic acid, the first dissociation constant is twice as large as expected since there are two equivalent ionizable hydrogens, while the second constant is only half as large as expected because the conjugate base can accept a proton at two Equivalent sites.

$$K_1/K_2 \approx 4$$

A similar argument holds for molecules with two equivalent basic groups.

5. Hydrogen Bonding

Internal hydrogen bonding can greatly influence acid or base strength.



pKa 2.98 4.58

6. Steric effects

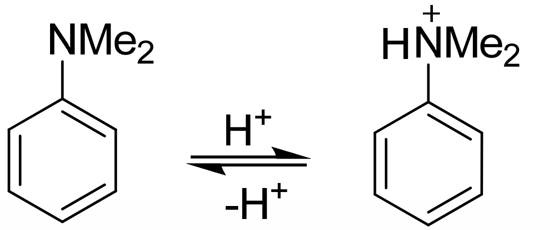
Steric effects are much more common in Lewis acid-base reactions in which larger acids are used.

$$B: + A \rightarrow B\text{—}A$$

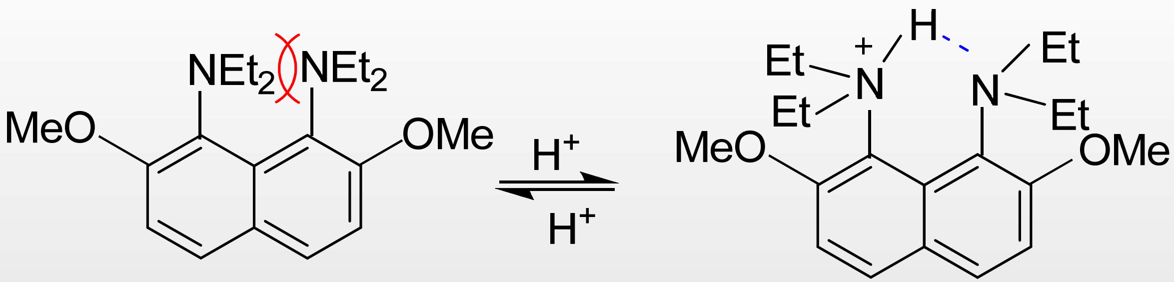
Table 7. Bases listed in increasing order of base strength when compared with certain reference acids

Increasing order of base strength	Reference Acid			
	H^+ or BF_3	**BMe_3**	**$B(CMe_3)_3$**	
↓	NH_3	Et_3N	Me_3N	Et_3N
	Me_3N	NH_3	Me_2NH	Et_2NH
	$MeNH_2$	Et_2NH	NH_3	$EtNH_2$
	Me_2NH	$EtNH_2$	$MeNH_2$	NH_3

Steric effects can also be caused by strain or conformation.

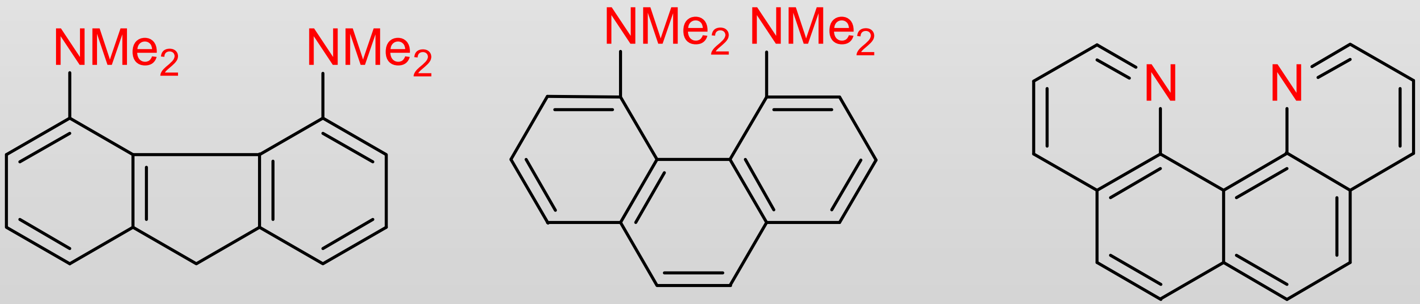


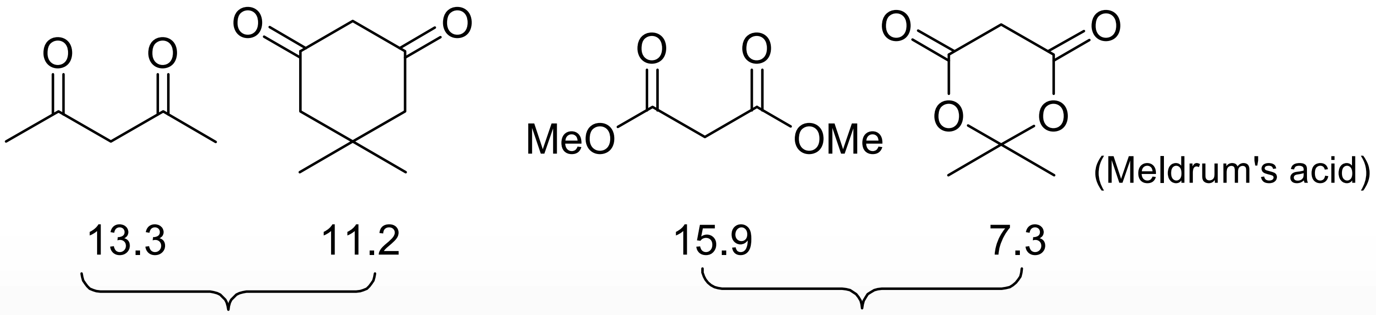
A: N,N-dimethylaniline pKa 5.1



B: 1,8-bis(diethylamino)-
2,7-dimethoxynaphthalene

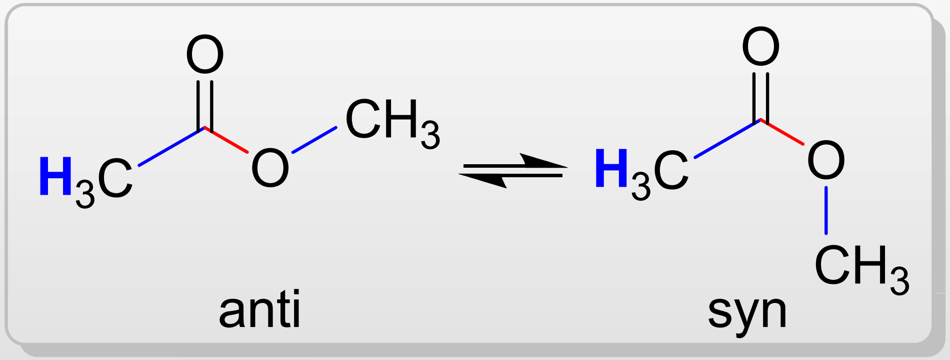
pKa 16.3





pKa 13.3 11.2 15.9 7.3

Δ pKa **2.1** **8.6**



MO calculations: loss of the proton is easier by ~21kJ/mol for the *syn* than for the *anti* conformer of the ester.

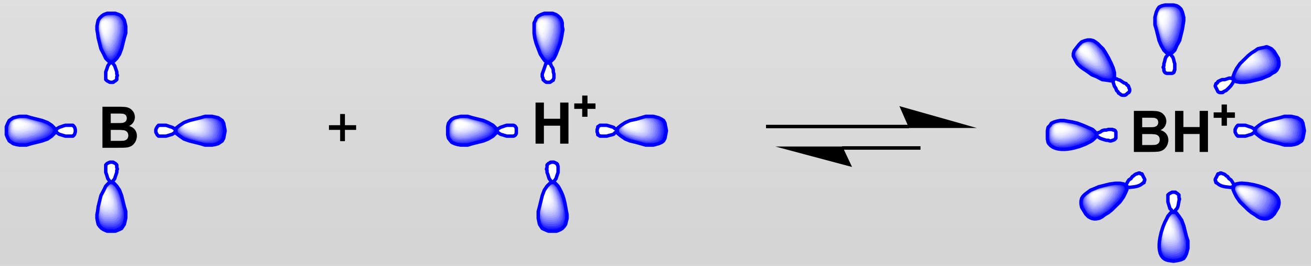
2.4 The effects of the medium on acid and base strength

Structure features are not the only factors that affect acidity and basicity. The same compound can have its acidity or basicity changed when the conditions are changed.

- Temperature effect:

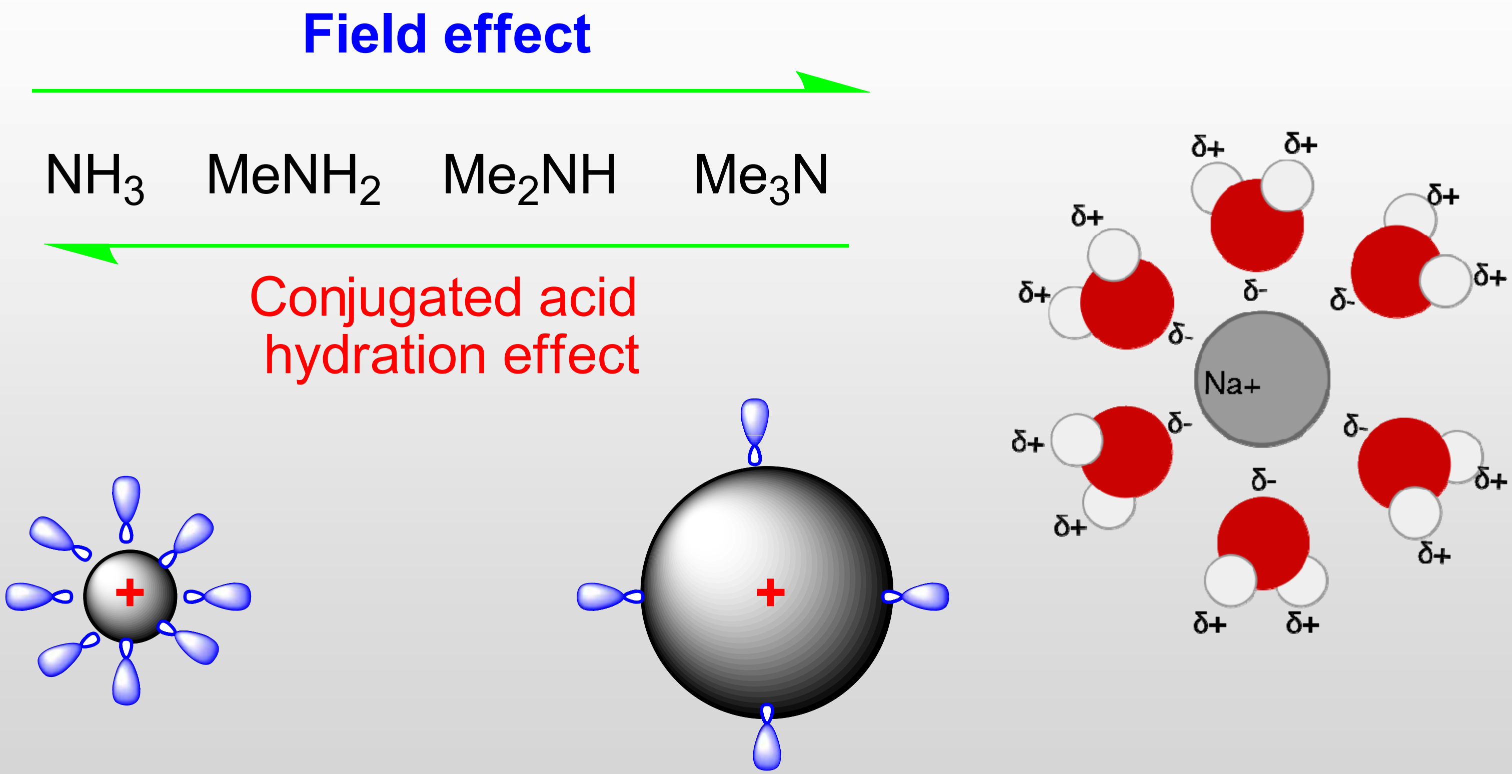
Basicity: >50°C BuOH > H_2O > Bu_2O
1~50°C BuOH > Bu_2O > H_2O
< 1°C Bu_2O > BuOH > H_2O

- Solvation. If a base is more solvated than its conjugated acid, its stability is increased relative to the conjugated acid.



Basicity order (reference acid: H^+):

$NH_3 < Me_3N < MeNH_2 < Me_2NH$



Field effect

NH_3 $MeNH_2$ Me_2NH Me_3N

Conjugated acid
hydration effect

Overview of Chapter 2

2个理论：

Brønsted—Lowry **(布朗斯特-劳里，质子理论)**		**Lewis** **(路易斯，电子理论)**
Brønsted Acid：能够给出H^+	$\subset$	Lewis Acid：有空轨道，能够接受电子对
H_2SO_4, HCl, RCO_2H, Amines, Carbon acids		H^+ and onium ions, metal cations, trigonal planar species, electron poor π-systems
Brønsted Base：能够接受H^+	$\approx$	Lewis Base：有孤对电子
$NH_{3-x}R_x$ $PR_{3-x}A_x$, H^- , F^-, Compounds of O, S, Se and Te, electron rich π-system		

一些概念：

1. pK_a，pK_b, pK_{HB}；特定溶剂（一般是水）
2. 常见化合物的pK_a值
3. 共轭酸、共轭碱

Overview of Chapter 2

软硬酸碱理论

- 硬：体积小、偶极距小、电负性大、氧化态高
- 软：体积大、偶极距大、电负性小、氧化态低

酸碱反应：硬酸＋硬碱；软酸＋软碱

影响酸碱强弱的因素（很复杂！）：

场效应、共轭效应、原子体积（卤素）、氢键、位阻（胺）等

溶剂化效应！