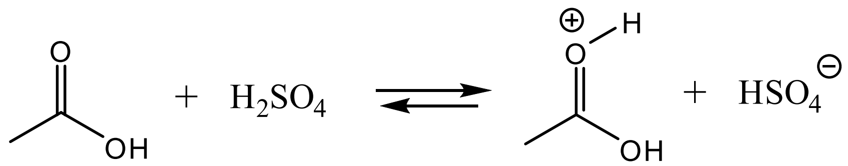
Brønsted acid-base chemistry

- Brønsted acid --- proton donor

$$HA + B \rightleftharpoons A^{\ominus} + BH^{\oplus} \quad \text{(Eq. 4.1)}$$

- Brønsted base --- proton acceptor

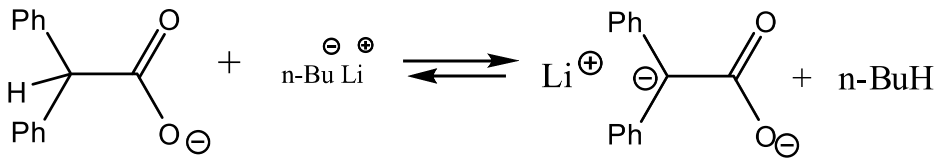


(Eq. 4.2)

Bronsted base

- Conjugate base

- Conjugate acid



(Eq. 4.3)

Bronsted acid

** **Any molecule containing hydrogen is a potential Brønsted acid, whereas any molecule at all is a potential Brønsted base.**

Acid and base in diluted aqueous solutions

$$HA + H_2O \rightleftharpoons A^{\ominus} + H_3O^{\oplus} \qquad \text{(Eq. 4.4)}$$

$$Ka = \frac{[H_3O^+][A^-]}{[HA]} \qquad \text{(Eq. 4.5)}$$

$$pKa = -lgKa \qquad \text{(Eq. 4.6)}$$

$$pH = pKa + lg\left(\frac{[A^-]}{[HA]}\right) \qquad \text{(Eq. 4.7)}$$

pKa of H_3O^+ is -1.74, in diluted aqueous solutions, it is the strongest acid
--- any acid stronger than H_3O^+ is fully dissociated in water

p*K*a of various acids

Acid	Base	Approximate pK_a (relative to water)
Super Acids		
$HF{-}SbF_5$	SbF_6^-	
$FSO_3H{-}SbF_5{-}SO_3$		
$FSO_3H{-}SbF_5$		
FSO_3H	FSO_3^-	
RNO_2H^+	RNO_2	−12
$ArNO_2H^+$	$ArNO_2$	−11
$HClO_4$	ClO_4^-	−10
HI	I^-	−10
$RCNH^+$	RCN	−10
$R{-}C(={}^{+}OH){-}H$	$R{-}C(=O){-}H$	−10
H_2SO_4	HSO_4^-	
HBr	Br^-	−9
$Ar{-}C(={}^{+}OH){-}OR$ [24]	$Ar{-}C(=O){-}OR$	−7.4
HCl	Cl^-	−7
RSH_2+	RSH	−7
$Ar{-}C(={}^{+}OH){-}OH$ [24]	$Ar{-}C(=O){-}OH$	−7
$Ar{-}C(={}^{+}OH){-}H$	$Ar{-}C(=O){-}H$	−7
$R{-}C(={}^{+}OH){-}R$	$R{-}C(=O){-}R$	−7
$ArSO_3H$	$ArSO_3^-$	−6.5

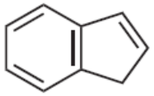
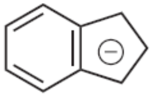
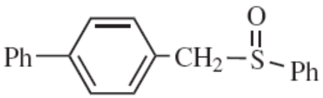
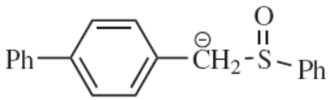
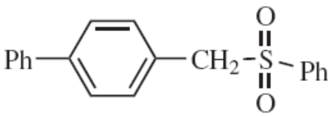
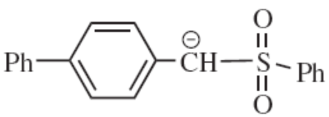
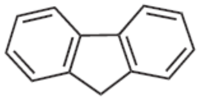
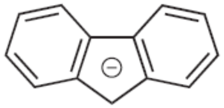
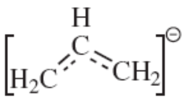
Acid	Base	Approximate pK_a (relative to water)
$R{-}C(={}^{+}OH){-}OR$ [24]	$R{-}C(=O){-}OR$	−6.5
$ArOH_2^+$	ArOH	−6.4
$R{-}C(={}^{+}OH){-}OH$ [24]	$R{-}C(=O){-}OH$	−6
$Ar{-}C(={}^{+}OH){-}R$	$Ar{-}C(=O){-}R$	−6
$Ar{-}\overset{+}{O}(H){-}R$	$Ar{-}O{-}R$	−6
$CH(CN)_3$	$^-C(CN)_3$	−5
Ar_3NH^+	Ar_3N	−5
$H{-}C(={}^{+}OH){-}H$	$H{-}C(=O){-}H$	−4
$R{-}\overset{+}{O}(H){-}R$	$R{-}O{-}R$	−3.5
$R_3COH_2^+$	R_3COH	−2
$R_2CHOH_2^+$	R_2CHOH	−2
$RCH_2OH_2^+$	RCH_2OH	−2

p*K*a of various acids

Acid	Base	Approximate pK_a (relative to water)
H_3O^+	H_2O	**−1.74**
$Ar-C(=\overset{+}{O}H)-NH_2$ [24]	$Ar-C(=O)-NH_2$	−1.5
HNO_3	NO_3^-	−1.4
$R-C(=\overset{+}{O}H)-NH_2$ [24]	$R-C(=O)-NH_2$	−0.5
$Ar_2NH_2^+$	Ar_2NH	1
HSO_4^-	SO_4^{2-}	**1.99**
HF	F^-	**3.17**
HONO	NO_2^-	**3.29**
$ArNH_3^+$	$ArNH_2$	3-5
$ArNR_2H^+$	$ArNR_2$	3-5
RCOOH	$RCOO^-$	4-5
$HCOCH_2CHO$	HCOC−HCHO	5
H_2CO_3 [42]	HCO_3^-	**6.35**
H_2S	HS^-	**7.00**
ArSH	ArS^-	6–8

Acid	Base	Approximate pK_a (relative to water)
$CH_3COCH_2COCH_3$ [44]	$CH_3COC{-}HCOCH_3$	9
HCN	CN^-	9.2
NH_4^+	NH_3	**9.24**
ArOH	ArO^-	8–11
RCH_2NO_2	$RC{-}HNO_2$	10
R_3NH^+	R_3N	10–11
RNH_3^+	RNH_2	10–11
HCO_3^-	CO_3^{2-}	**10.33**
RSH	RS^-	10–11
$R_2NH_2^+$	R_2NH	11
$N{\equiv}CCH_2C{\equiv}N$	$N{\equiv}CC{-}HC{\equiv}N$	11
CH_3COCH_2COOR	$CH_3COC{-}HCOOR$	11
$CH_3SO_2CH_2SO_2CH_3$	$CH_3SO_2C{-}HSO_2CH_3$	12.5
$EtOOCCH_2COOEt$	EtOOCC−HCOOEt	13
CH_3OH	CH_3O^-	15.2
H_2O	OH^-	**15.74**
		16
RCH_2OH	RCH_2O^-	16
RCH_2CHO	RC−HCHO	16
R_2CHOH	R_2CHO^-	16.5
R_3COH	R_3CO^-	17
$RCONH_2$	$RCONH^-$	17
$RCOCH_2R$	RCOC−HR	19-20 [56]

p*K*a of various acids

Acid	Base	Approximate pK_a (relative to water)
		20
		20.08[a]
		18.91[a]
		23
$ROOCCH_2R$	$ROOCC{-}HR$	24.5
$RCH_2C{\equiv}N$	$RC{-}HC{=}N$	25
$HC{\equiv}CH$	$HC{\equiv}CC^-$	25
Ph_2NH	PH_2N^-	24.95[b]
$EtOCOCH_3$	$EtOCOCH_2^-$	25.6
$PhNH_2$	$PhNH^-$	30.6[b]
Ar_3CH	Ar_3C^-	31.5
Ar_2CH_2	Ar_2CH^-	33.5
H_2	H^-	35
NH_3	NH_2^-	38
$PhCH_3$	$PhCH_2^-$	40
$CH_2{=}CHCH_3$		43
PhH	Ph^-	43

Acid	Base	Approximate pK_a (relative to water)
$CH_2{=}CH_2$	$CH_2{=}CH^-$	44
cyclo-C_3H_6	*c*-$C_3H_5^-$	46
CH_4[72]	CH_3^-	48
C_2H_6	$C_2H_5^-$	50
$(CH_3)_2CH_2$[72]	$(CH_3)_2CH^-$	51
$(CH_3)_3CH$[72]	$(CH_3)_3C^-$	

[a] pK_a in THF.
[b] pK_a in DMSO.

The leveling effect

- An acid stronger than the conjugate acid of the solvent can not exist in that solvent
- A base stronger than the conjugate base of the solvent can not exist in that solvent

Relative acidities of acids can be determined in various solvents and scaled to a consistent set of values for a single solvent (pKa relative to an aqueous solution)

Acids in concentrated aqueous solutions

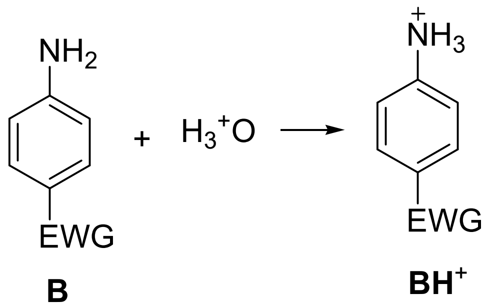
Acidity function *vs* pH

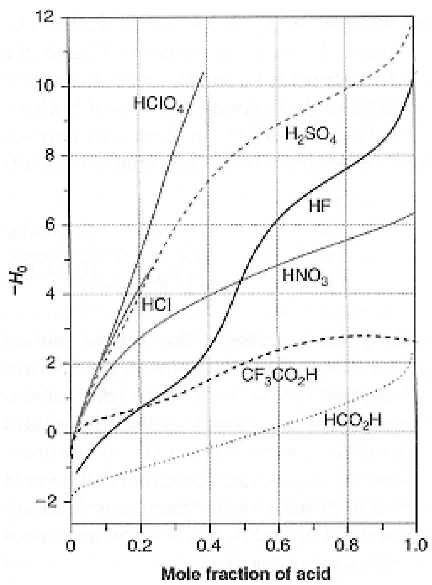
Acidity function: a measurement of the effective ability of the concentrated solution to donate protons to an organic compound

pH: the ability of a diluted acid solution to donate protons

- **Hammett acidity function:**

H_0=pKa + lg([B]/[BH^+])





H_0 values for mixtures of several different acids in water as a function of their mole fractions. The data come from Cox, R. A., and Yates, K. "Acidity Functions: An Update." *Can. J. Chem.*, 61, 2225 (1983).

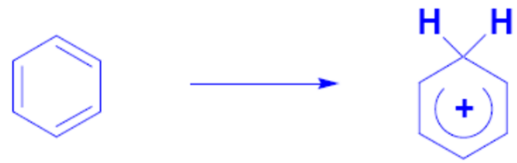
Super acids

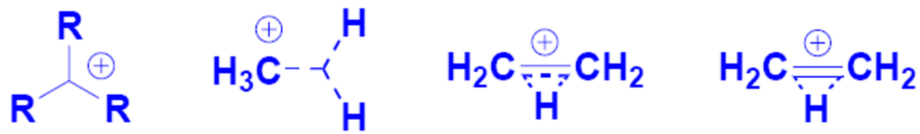
- Acid with H_o<-12
- The extreme of strongly acidic solutions are those formed from BF_3, PF_5, AsF_5 and especially SbF_5 in liquid HF, often diluted with FSO_3H and SO_2ClF.
- Acids of the extremely non-nucleophilic and non-coordinating anions BF_4^-, PF_6^-, AsF_6^-, and SbF_6^-
- Such solution can protonate bases as weak as benzene and alkane to create persistent carbenium ions.

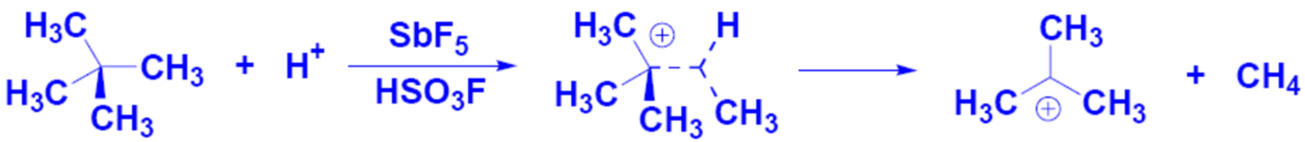
Carbenium ions created by super acids

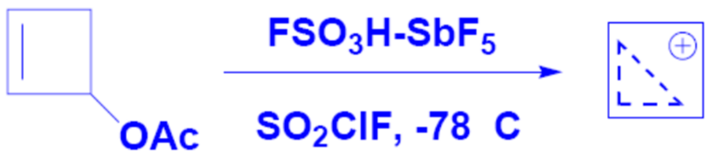
HSO_3F, HSO_3F-SbF_5, HF-SbF_5

$$ROH \longrightarrow R^+$$









Acid and base in nonaqueous systems

- pKa values change significantly when measured in different solvents

Table 4.1
pK_as of Various Acids in Differing Solvents

Acid	Solvent				
	H_2O	CH_3OH	DMSO	DMF	CH_3CN
CH_3CO_2H	4.76	9.5	12.6	13.5	
p-$NO_2C_6H_4OH$	7.15	11.4	11.0	12.6	21
$PhNH_3^+$	4.6		3.2	4.2	

Acid and base in nonaqueous systems

- Solvation has a large influence in altering the intrinsic ability of a compound to act as a proton donor

Table 4.2

pK_a Values for Various Acids in Water and DMSO*

Acid	pK_a (water)	pK_a (DMSO)
HBr	−9	0.9
HCl	−8	1.8
HF	3.2	15
Picric acid	0.4	0.0
Acetic acid	4.75	12.3
Phenol	10.0	18.0
Methanol	15.5	29.0
Water	15.57	32
HCN	9.1	12.9
$CH_2(CN)_2$	11.0	11.0

*Bordwell, F. G. "Equilibrium Acidities in Dimethyl Sulfoxide Solution." *Acc. Chem. Res.*, **21**, 456 (1988).

Strengths of BrØnsted acids and bases

Do you know the right answers to questions like:

- What base to use for a base-initiated reaction?
- What acid to use to remove a protecting group?
- Conditions to generate reactive carbanion intermediate?

How?

- pK_a values of common structures (all standard pK_as are referenced to water!)
- The ability to predict relative acid or base strength!

Predicting relative acidities

Guiding principles for predicting relative acidities

- When the acids being compared are neutral (HA) and create negative conjugate bases (A^-), it is most convenient to predict the relative acidities by examining the relative stabilities of the anionic conjugate bases. The acid with the most stable conjugate base A^- will be the strongest acid.

- When the acids being compared are cationic (HA^+) and create neutral conjugate bases (A), it is most convenient to predict the relative acidities by examining the relative stabilities of the acids themselves. The acid HA^+ that is the most stable will be the weakest acid.

Predicting relative acidities

Important factors related to acidity

- **Electronegativity effect**
- **Inductive effects**
- **Electrostatic effects**
- **Resonance**
- **Aromaticity/antiaromaticity**
- **Solvation**
- **Hybridization effects**
- **Polarizability**
- **Bond strengths**
- **Steric effects**