WHICH BASE NEEDS TO BE USED TO DEPROTONATE A GIVEN BRONSTED ACID? QUANTITATIVE APPROACH

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ABSTRACT

A simple quantitative evaluation of the positions of equilibria for the acid-base reactions is presented with emphasis on the organic chemistry. The method is applied for deprotonation of Bronsted C-H, N-H and O-H acids. *[African Journal of Chemical Education—AJCE 13(1), January 2023]*

DEPROTONATION OF BRONSTED ACIDS

Deprotonation of Bronsted acids is a frequent operation to get anions (or nucleophiles). Considering a range of the pKas of the acids, a practical question arises which base is capable to deprotonate a given acid and to what extent. Surprisingly, this issue is not treated quantitatively in the organic chemistry textbooks with sufficient attention and the thermodynamic criteria are not presented to answer this question.

Let´s take a trivial example of primary school chemistry:

$$NaOH + HCl \longrightarrow NaCl + H_2O \quad (1)$$
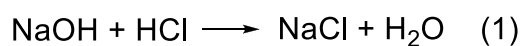
and let´s ask why this reaction occurs from a thermodynamic standpoint and why this reaction is written as going from the left to the right only, and if it is exergonic or endergonic? To answer this one must use a version of the fundamental Gibbs equation:
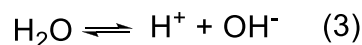
$$\Delta G^0 = -1.36 \log K$$

If $\log K > 0$, or positive, then $\Delta G^0 < 0$, or negative, so the free energy content of the products is smaller that this of the substrates and the reaction is exergonic and spontaneous and goes as written from the left to the right. How can one evaluate the ΔG° of the reaction (1)? To do this, it is necessary to re-write the reaction (1) as shown below.

$$H^+ + \cancel{Cl^-} + \cancel{Na^+} + OH^- \longrightarrow \cancel{Na^+} + \cancel{Cl^-} + H_2O \quad (2)$$
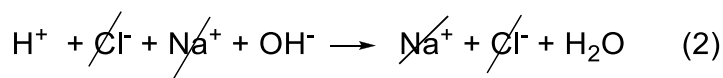
Since both Cl^- and Na^+ are present on both sides of the equation, they can be cancelled and

$$K = \frac{[H_2O]}{[H^+][OH^-]}$$

The numerical value of K can be easily evaluated since it is a reciprocal value of the known dissociation constant of water K´ (reaction 3):

$$H_2O \rightleftharpoons H^+ + OH^- \quad (3)$$

$$K´ = \frac{[H^+][OH^-]}{[H_2O]} \quad pKa \sim 16; \ K´ = 10^{-16}$$

and thus,

$$K = \frac{1}{K´} = 10^{16}$$

Since the K of the reaction (1) is big and positive, the associated Gibbs free energy is highly negative.

$$\Delta G^0 = -1.36 \ (\log 10^{16}) = -21.7 \text{kcal/mol}$$

As a conclusion, the reaction (1) is exergonic and goes to the right as written.
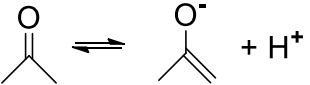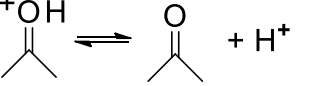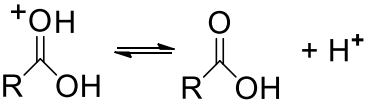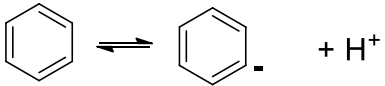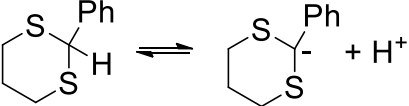
The same reasoning can be extended to the organic substrates. A purpose of the present didactic text is to apply this thinking to the other acid-base reactions and to show how to choose a necessary strength of a base to deprotonate a given acid and to calculate the equilibrium constant. Attention will be given to the Bronsted acids.

The following acids/bases will be used throughout this text and their associated pKas values are shown in the Table 1.[1,2] Besides the reference 1 and 2, the internet data bases can be consulted.[3] The pKas presented in these references very slightly, but are consistent. It should be pointed out that evaluation of the strength of very strong acids with negative pKas varies contingent upon a method of evaluation and consequently, their pKas should be treated only as approximate

values. For instance, protonation of diethyl ether furnishes the conjugated Bronsted acid which has pKa between -0.30 and –6.2.[1] Likewise, protonation of the carbonyl group of acetone furnishes the conjugated acid which has its pKa between -0.24 and -7.2.[4,5] The same uncertainty about the pKas applies to very weak acids.

It should be pointed out that the dissociations shown in the Table 1 represent strictly speaking the processes in a gas phase, because no bases are shown to pick up the liberated proton. The dissociations in gas phases are highly endergonic since the charges are separated without any solvation, as shown by the theoretical calculations.[6]. Nevertheless, such treatments of the behavior of the acids are very convenient and represent a kind of the "half-reactions", the other half is a binding of a proton by the conjugated base of the other acid. This will be shown below in details.

Table 1. A list of the pKas of acids

	pKa
$\overset{+}{N}H_4 \rightleftharpoons NH_3 + H^+$	9
$Et_3\overset{+}{N}H \rightleftharpoons Et_3N + H^+$	10.7
$NH_3 \rightleftharpoons NH_2^- + H^+$	32
$iPr_2NH \rightleftharpoons iPr_2N^- + H^+$	36
$H_2O \rightleftharpoons HO^- + H^+$	~16
$H_3\overset{+}{O} \rightleftharpoons H_2O + H^+$	-1.7
$R\overset{+}{O}H_2 \rightleftharpoons ROH + H^+$	-2.5
$PhOH \rightleftharpoons PhO^- + H^+$	10

 19.2

 -5

 16-17

 -6

$RCO_2H \rightleftharpoons RCO_2^- + H^+$	~5
$CH_4 \rightleftharpoons H_3C^- + H^+$	~50
$Bu\text{-}H \rightleftharpoons Bu^- + H^+$	~50
$HC{\equiv}CH \rightleftharpoons HC{\equiv}C^- + H^+$	25
$H_2C{=}CH_2 \rightleftharpoons H_2C{=}CH^- + H^+$	44

 43

 30

| $Cl_3CH \rightleftharpoons Cl_3H^- + H^+$ | 15.5 |
| $H_2 \rightleftharpoons H^- + H^+$ | 35 |

60

A problem to solve is which base is able to remove a proton from a given acid and what is the equilibrium constant and the associated Gibbs free energy. Let´s consider a reaction (4), attempted deprotonation of acetylene using KOH.

$$HC{\equiv}CH + \cancel{K}^{+}\,{}^{-}OH \rightleftharpoons HC{\equiv}C^{-}\cancel{K}^{+} + H_2O \quad (4)$$
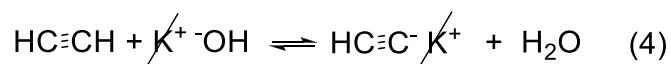
As in the reaction (1) the potassium cations can be cancelled since they are present on both sites of the equation, and the equilibrium constant has a form (5).

$$K = \frac{[HC{\equiv}C^{-}][H_2O]}{[HC{\equiv}CH][OH^{-}]} \quad (5)$$

To evaluate it quantitatively, one has to apply a trick of multiplication by $1=[H^{+}]/[H^{+}]$ and to re-write it as follow.

$$K = K{\cdot}1 = K\frac{[H^{+}]}{[H^{+}]} = \frac{[HC{\equiv}C^{-}][H^{+}]}{[HC{\equiv}CH]}\frac{[H_2O]}{[H^{+}]\,[OH^{-}]} = 10^{-9} \quad (6)$$

dissociation constant of
acetylene, $pKa=25$, $K=10^{-25}$

association of H^{+} and OH^{-}, $K=10^{16}$

$$\Delta G° = -1.36(-9) = 12.2 kca/mol$$

The association of H^{+} and OH^{-} has been already treated in the reaction (1) and (2). We can see that the overall equilibrium constant of the reaction (6) can be easily derived from two "half-reactions" shown in the Table 1, and that it is very small, and its logarithm is negative. Consequently, the Gibbs free energy is positive, and the process does not advance to the right. At equilibrium there will be much more acetylene and KOH than the acetylide anion and water. KOH is definitely not

strong enough to remove a proton from acetylene. A reaction in the opposite direction is in fact favored, which is deprotonation of water molecule by the acetylide anion, and it has an equilibrium constant of 10^9.

Attempted deprotonation of acetylene by commonly used bases like ammonia or triethylamine, which are approximately of the same strength, is also unsuccessful as shown below (reaction 7).

$$HC \equiv CH + NH_3 \rightleftharpoons HC \equiv C^- + \overset{+}{N}H_4 \quad\quad (7)$$

$$K = \frac{[HC \equiv C^-][H^+]}{[HC \equiv CH]} \quad \frac{[NH_4^+]}{[NH_3][H^+]} = 10^{-25} \cdot 10^9 = 10^{-16}$$
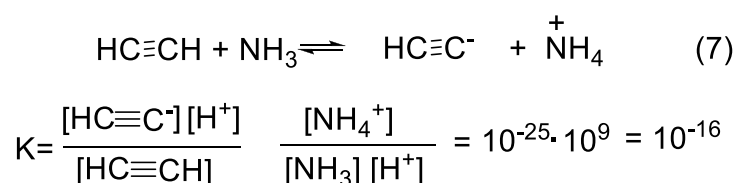
For triethylamine the same equilibrium constant would be $10^{-14.3}$, very small indeed. As a conclusion, both ammonia and triethylamine are also too weak to deprotonate acetylene appreciably. Evidently a stronger base is needed to get acetylide. Let´s use sodium amide, $NaNH_2$, where a basic part is NH_2^-, a conjugated base of ammonia, which is a very weak acid, so NH_2^- is a very strong base (reaction 8).

$$HC \equiv CH + NaNH_2 \rightleftharpoons HC \equiv C^- Na^+ + NH_3 \quad\quad (8)$$
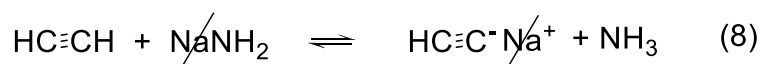
One must not confuse two processes (A) and (B) shown below.

$$NH_4^+ \rightleftharpoons NH_3 + H^+ \quad pKa\ 9 \quad (A)$$
$$NH_3 \rightleftharpoons NH_2^- + H^+ \quad pKa\ 32 \quad (B)$$
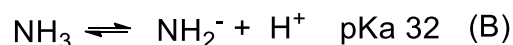
The process (A) depicts acidic properties of the ammonium cation and indicates, that its conjugated base, ammonia, is a moderately strong base, whereas the process (B) shows ammonia as a very weak acid, which implies that its conjugated base is very strong. We will use exactly the last base in an attempt to get acetylide anion.

The equilibrium constant for the reaction (8) has a form of (9):

$$K = \frac{[HC\equiv C^-][NH_3]}{[HC\equiv CH][NH_2^-]} \qquad (9)$$

After multiplication by $[H^+]/[H^+]$ we get (10) which can be evaluated quantitatively using the "half-reactions" from the Table 1.

$$K = \frac{[HC\equiv C^-][H^+]}{[HC\equiv CH]} \cdot \frac{[NH_3]}{[H+][^-NH_2]} = 10^{-25}10^{32} = 10^7 \qquad (10)$$

dissociation, $K=10^{-25}$ association, $K=10^{32}$
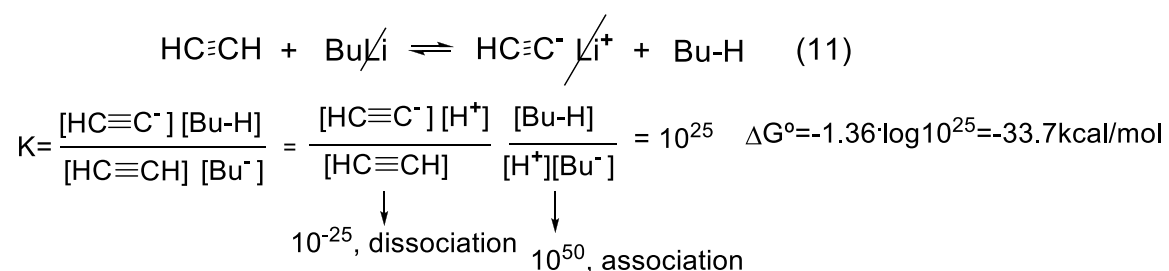
One can now evaluate of the Gibbs free energy:

$$\Delta G^o = -1.36 \cdot \log 10^7 = -10.5 \text{kcal/mol}$$

The process (8) is exergonic and proceeds to the right. High numerical value of K means that the reaction (8) is for practical reasons irreversible and quantitative.

As a conclusion, sodium amide is a base adequately strong to deprotonate acetylene and this process is exergonic.

The same sort of evaluation can be performed using the other bases like methyl lithium, MeLi and butyllithium, BuLi. Both are the strongest bases in use since the hydrocarbons are the weakest acids known. The basic part of both reagents is an anion R⁻, a conjugated base of hydrocarbons (methane or butane; pKas= ~50), without any stabilization of the negative charge, which is localized on the carbon atom. The factors which control acidity are presented in any organic textbook. Briefly, the electronegativity, the polarizability and the stabilization by resonance are essential to stabilize the negative charge of a conjugated base after departure of a proton.

The equation (11) represents deprotonation of acetylene by butyllithium.

$$HC{\equiv}CH \ + \ Bu{-}Li \ \rightleftharpoons \ HC{\equiv}C^- \ Li^+ \ + \ Bu\text{-}H \quad (11)$$

$$K = \frac{[HC{\equiv}C^-]\,[Bu\text{-}H]}{[HC{\equiv}CH]\,[Bu^-]} = \frac{[HC{\equiv}C^-]\,[H^+]}{[HC{\equiv}CH]}\frac{[Bu\text{-}H]}{[H^+][Bu^-]} = 10^{25} \quad \Delta G° = -1.36{\cdot}log10^{25} = -33.7 \text{kcal/mol}$$

$$10^{-25}, \text{dissociation} \qquad 10^{50}, \text{association}$$

The process depicted in the equation (11) has very big equilibrium constant and is practically quantitative, irreversible and highly exergonic. The other strong bases like PhLi, MeLi, *t*BuLi or iPr$_2$NLi (LDA), etc. can also be used for this purpose. It can be seen that the alkyllithiums are excellent bases for deprotonations in general.

A generalization can be made already at this point. During any acid-base reaction there is always an acid-substrate (which we want to deprotonate) and an acid-product, a conjugated acid of a base used for deprotonation. If a given reaction is supposed to go from the left to the right and be

exergonic, the acid-product must be weaker than the acid-substrate. To say this in the other words, the base-product must be weaker than the base-substrate. This is seen in the reaction (11): the acid-product (butane) is weaker than the acid-substrate, acetylene, so the process goes as written. Obviously, the base-product, acetylide, is weaker than the base-substrate, Bu^-. The opposed can be seen in the reactions (4) and (7). In (4) the acid-product (water, pKa ~16) is stronger than the acid-substrate (acetylene, pKa 25) and the reaction is endergonic and does not go to the right. Likewise, in (7) the acid-product (NH_4^+) is stronger than the acid-substrate, acetylene, and the base-product (acetylide) is stronger than the base-substrate (ammonia). For this reason, the reaction (7) does not progress to the right since it is endergonic. For practical reasons it is enough to compare the strengths of both participating acids only since their pKas are tabulated, whereas the strengths of the bases must be inferred from the strengths of their conjugated acids which is less convenient.

The other strong base used in a common practice is lithium diisopropylamide or LDA. This reagent can be prepared by deprotonation of diisopropylamine (reaction 12) which is very weak acid (pKa ca 36), so very strong base (BuLi or MeLi) is needed. The calculations which show that such reaction functions well and that the associated equilibrium constant is big, are shown below.

$$i\text{Pr}_2\text{NH} + \text{BuLi} \rightleftharpoons i\text{Pr}_2\text{NLi} + \text{Bu-H} \quad (12)$$

$$K = \frac{[i\text{Pr}_2\text{N}^-][\text{H}^+]}{[i\text{Pr}_2\text{NH}]} \quad \frac{[\text{Bu-H}]}{[\text{Bu}^-][\text{H}^+]} = 10^{14}$$

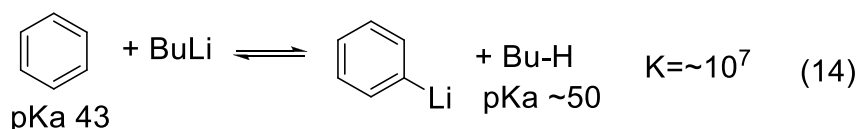dissociation $\quad$ association
$K = 10^{-36}$ $\qquad$ $K = 10^{50}$

Considering a fact that CH_4 and butane have approximately the same pKas (~50), methyl lithium can be a replacement in the reaction (12).

To get the LDA though, one must have the bases like BuLi or MeLi. Both cannot be prepared by direct deprotonation of methane or butane, since there are no bases strong enough for this purpose, so indirect approach must be used, which is a metalation (reaction 13).

$$\text{R-X} + 2\text{Li} \longrightarrow \text{RLi} + \text{LiX} \quad (13)$$
$$\text{X: Cl, Br, I}$$
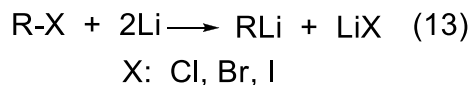
In this way the strongest bases known can be prepared. Since the C-Li bonds are partially covalent, one can increase their ionic character and consequently the strength of the alkyl lithiums by addition of 1,2-tetramethylethylenediamine (TMEDA) or 1,2-dimethoxyethane. Both of these compounds form strong complexes with lithium cation and increase a strength of the anion as a base by increasing its distance between Li and the anionic C center. Also, the organolithiums tend to become monomeric after such treatment, which additionally increases their basic properties. This is illustrated by deprotonation of benzene by BuLi (reaction 14) with and without addition of TMEDA.

$$\text{(benzene, pKa 43)} + \text{BuLi} \rightleftharpoons \text{(phenyllithium, Li)} + \text{Bu-H (pKa ~50)} \quad K=\sim10^7 \quad (14)$$

Even though the reaction (14) should go to the right as evidenced by a favorable equilibrium constant, the yield the phenyllithium is small (ca 5%), but increases to 76% after addition of TMEDA (ref. [2], p.723). Obviously, phenyllithium can be prepared by metalation of phenyl halides. Likewise, direct obtention of vinyllithium by deprotonation of ethylene by BuLi or MeLi should be possible as shown in the reaction (15). However, this reaction would be complicated by the anionic polymerization initiated by addition of BuLi to ethylene.[7] The methods to obtain vinyllithium are presented in the reference [8].

$$CH_2=CH_2 \text{ (pKa 44)} + BuLi \rightleftharpoons CH_2=CHLi + Bu\text{-}H \text{ (pKa ~50)} \quad K=\sim10^6 \quad (15)$$
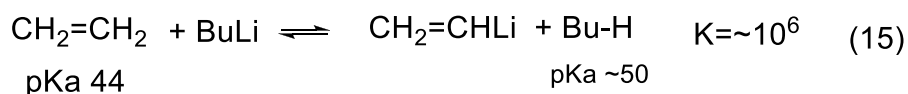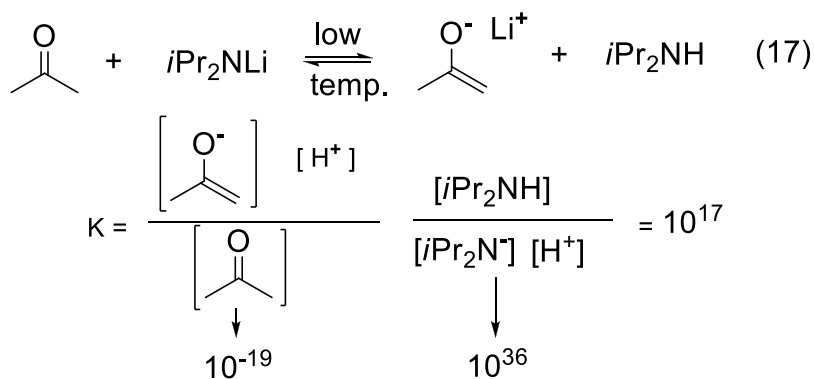
It should be pointed out that the Grignard reagents are also basic and capable to react with the Bronsted acids. Nevertheless, due to higher electronegativity of Mg (1.31, vs. Li, 0.98, Pauling scale), the C-MgX bonds are less polarized and more covalent than the C-Li bonds, and consequently, the Grignard reagents are less basic than the corresponding alkyllithiums. Nevertheless, the RMgX can be used interchangeably with RLi in certain cases as shown in the reaction 16.

$$RC{\equiv}CH + R'MgX \rightleftharpoons RC{\equiv}C^- \ ^+MgX + R'H \quad K=10^{25} \quad (16)$$

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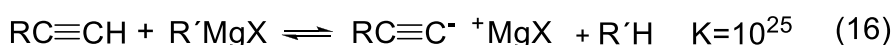
To perform the evaluation of K of the reaction (16) it was assumed that the RMgX is as strong as the RLi which obviously contradicts a statement above. In general, exact evaluation of the strength of the very weak acids is subjected to experimental errors, so quantitative differentiation of the strength of their conjugated bases neutralized by different cations is difficult, and in the first approximation it was assumed that both RLi and RMgX are of the same strength. At this point it should be mentioned that the Gilman reagents, R_2CuLi, are less basic than RMgX and RLi due to the electronegativity of the copper (1.9 in the Pauling scale). This means that the C-Cu bonds are weakly polarized and with little anionic character. The same applies to the other organometallics like R_2Cd and R_2Zn (electronegativity of both is ca 1.7).

Additionally, a distinction must be made between the nucleophilic bases and the non-nucleophilic bases. This can be illustrated by obtention of the enolate derived from acetone (pKa ~19). As presented above, any conjugated base of the acid which has its pKa>19 will do the job, for example the LDA (pKa of *i*Pr$_2$NH is 36) as shown in the reaction (17). It can be seen that the LDA is sufficiently strong to deprotonate a molecule of acetone to form its enolate and that this process is practically quantitative and irreversible.

$$K = \frac{\left[\begin{array}{c} O^- \\ \end{array}\right] [H^+]}{\left[\begin{array}{c} O \\ \end{array}\right]} \cdot \frac{[i\text{Pr}_2\text{NH}]}{[i\text{Pr}_2\text{N}^-] [H^+]} = 10^{17}$$

$$10^{-19} \qquad\qquad 10^{36}$$

If BuMgX or BuLi were used for the same purpose, the outcome would be different as shown in the reaction (18).
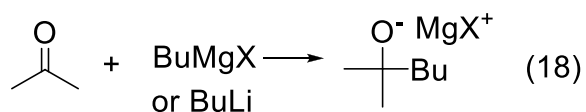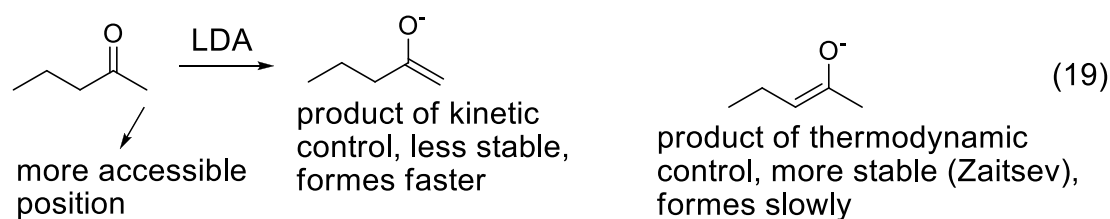
The main process would be the addition to the carbonyl group and a reduction of a carbonyl group by the hydride anion coming from BuMgX (ref [2], p.714) omitted for clarity. The deprotonation would not occur. This is an illustration of the nucleophilic character of the bases. The pair of electrons present in a given base can be used to remove a proton from a molecule (basic property) or can be transferred to a carbon atom (nucleophilic property). The addition to the carbonyl group is much faster than deprotonation, so both BuMgBr and BuLi behave like nucleophiles in the reaction (18). They are nucleophilic bases. At the same time, both BuLi and BuMgX do not add to the terminal carbon-carbon triple bonds, so the outcome of the reaction (11) and (16) is the same and deprotonation only takes place. If a steric bulk of the R group in the organometallics increases, like

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in Ph$_3$CLi or (CH$_3$)$_3$CLi, the resulting compounds are unable to approach the carbonyl groups and to form the C-C bond. It is much easier for them to abstract a proton and to act as a base only, so they behave like non-nucleophilic bases. In general, the non-nucleophilic bases are sterically crowded and remove protons from the more accessible positions which permits to achieve regioselectivity. The structures of frequently used non-nucleophilic bases are shown below.
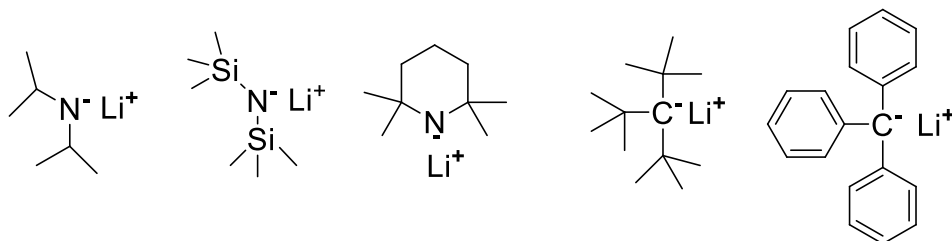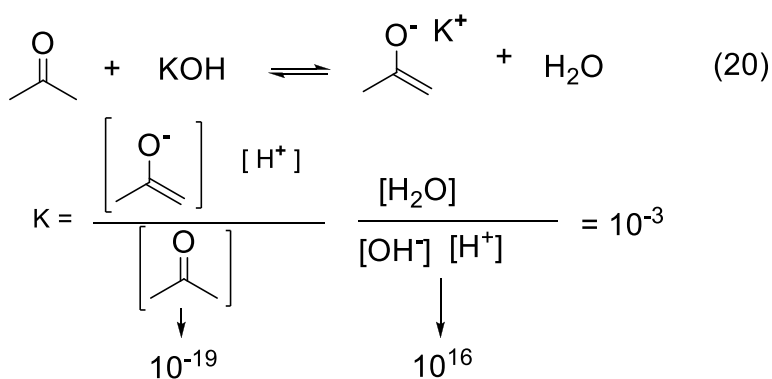

The non-nucleophilic base can be small however, like in the case of the sodium hydride, NaH. Its basic moiety is H$^-$, a very small anion, which is practically free of the nucleophilic properties. For this reason, NaH will deprotonate enolizable ketones or aldehydes to form the enolates, without addition to the carbonyl groups.

Let's return to deprotonation of ketones. As shown in the reaction (17), LDA is strong enough to form the enolate of acetone quantitatively. Considering its steric bulk, it removes protons selectively from the more accessible positions of the ketones which are not symmetrical like in the reaction (19). The same process can be conducted with any other sterically crowded non-nucleophilic bases.

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product of kinetic control, less stable, formes faster

more accessible position

product of thermodynamic control, more stable (Zaitsev), formes slowly

(19)

If KOH or NaOH (bases much weaker than LDA) were used for a purpose of deprotonation of acetone, the enolate would also be formed, but in equilibrium with unreacted acetone. Position of the equilibrium would be shifted towards the substrate, and the product (the enolate) would be present only in small concentration (reaction 20).

(20)

$$K = \frac{\left[\begin{array}{c} O^- \\ \end{array} \right] [H^+]}{\left[\begin{array}{c} O \\ \end{array} \right]} \cdot \frac{[H_2O]}{[OH^-] \, [H^+]} = 10^{-3}$$
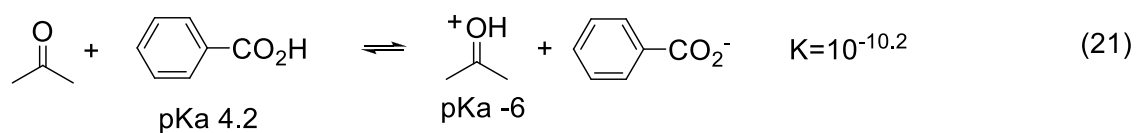
10^{-19} 10^{16}

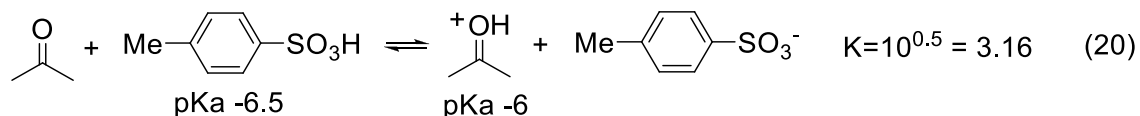The presence of both enolate (a nucleophile) and unreacted acetone (electrophile) implies that an aldol reaction would take place. In contrast, the use of the LDA permits quantitative deprotonation, so the unreacted substrate is absent, and subsequent addition of the other carbonyl compound permits a cross-aldol reaction with full control of which component acts as a nucleophile and as an electrophile.
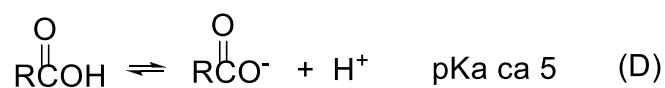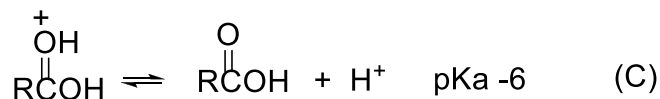
A complication arises however when the enolates derived from ketones react with enolizable aldehydes. It should be remembered that the aldehydes RCH$_2$CHO are stronger acids than the ketones. For example, ethanal has its pKa of ca 16, propanal of ca 17.3, whereas acetone has pKa of ca 19, so the ketone-derived enolate (a base) can deprotonate an aldehyde. Consequently, two enolates will be present as shown in the reaction (19), which may complicate a cross-aldol reaction. It is not our intention to discuss such specific cases.
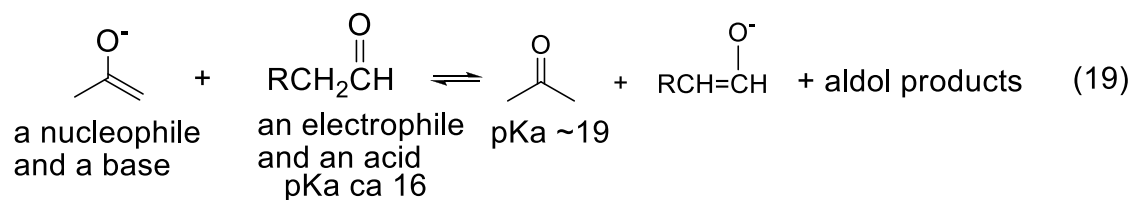
The carbonyl groups present in carboxylic acids, aldehydes or ketones among the other compounds, are very weak bases as evidenced by their negative pKas of their conjugated acids as shown in the Table 1. In many reactions like esterification or formation of acetals or ketals, protonation of the carbonyl group is the first step. To achieve a reasonable concentration of the reactive species one must use very strong acids like p-toluenesulfonic acid (pKa -6) or even stronger, like sulfuric acid or trifluoromethanesulfonic acid. Weak acids like AcOH or BzOH do not function. A comparison of protonation of acetone by strong and weak acid is shown in the reaction (20) and (21), respectively.

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$$\text{Me}-\underset{\text{pKa -6.5}}{\overset{\text{O}}{\underset{\|}{}}} + \text{Me}-\langle\rangle-\text{SO}_3\text{H} \rightleftharpoons \underset{\text{pKa -6}}{\overset{+\text{OH}}{}} + \text{Me}-\langle\rangle-\text{SO}_3^- \quad K=10^{0.5}=3.16 \quad (20)$$

$$\underset{\text{pKa 4.2}}{\overset{\text{O}}{\underset{\|}{}}} + \langle\rangle-\text{CO}_2\text{H} \rightleftharpoons \underset{\text{pKa -6}}{\overset{+\text{OH}}{}} + \langle\rangle-\text{CO}_2^- \quad K=10^{-10.2} \quad (21)$$

It is clearly seen that a benzoic acid (or any weak acid, like acetic acid, pKa 4.7) is unsuitable as a catalyst for ketal/acetal formation since a concentration of the reactive protonated species is negligibly low and that the process of protonation is highly endergonic. For the same reason formation of esters from carboxylic acids and alcohols requires strong acids to initiate the process by protonation of weakly basic (pKa -6) carbonyl group present in the $-\text{CO}_2\text{H}$ moiety. As in the case of ammonia (reactions (A) and (B)), one must not confuse the processes depicted in (C) and (D) which illustrate a capacity of a carbonyl group of a carboxylic acid to accept/lose a proton, and a capacity of a carboxyl group to lose a proton, respectively.

$$\overset{+\text{OH}}{\underset{}{\text{RCOH}}} \rightleftharpoons \overset{\text{O}}{\underset{}{\text{RCOH}}} + \text{H}^+ \quad \text{pKa -6} \quad (C)$$

$$\overset{\text{O}}{\underset{}{\text{RCOH}}} \rightleftharpoons \overset{\text{O}}{\underset{}{\text{RCO}^-}} + \text{H}^+ \quad \text{pKa ca 5} \quad (D)$$

It should be stressed again, that a carbonyl group is a very weak base, whereas a carboxyl group is a reasonably strong acid.

The conversion of aldehydes into ketones can be performed via inversion of polarity at the carbonyl group also known as "umpolung". The first stage of this procedure is deprotonation of dithioacetals.

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Considering weakly acidic character of dithioacetals, very strong bases must be used as shown in the reaction (22).
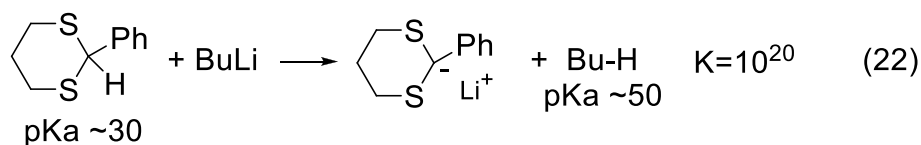

The Wittig reaction is frequently used in the organic synthesis and requires conversion of the phosphonium salts to form the ylides. Considering structures of the ylides (stabilized or non-stabilized), bases of various strength should be used to achieve deprotonation of the phosphonium salts as shown in the reaction (23) and (24) for the formation of the stabilized and non-stabilized ylides, respectively. It can be noticed that formation of the stabilized ylide from the more acidic phosphonium salt, requires less basic conditions (reaction 23). In fact, a base weaker than NaOH, like Na_2CO_3 can be used.
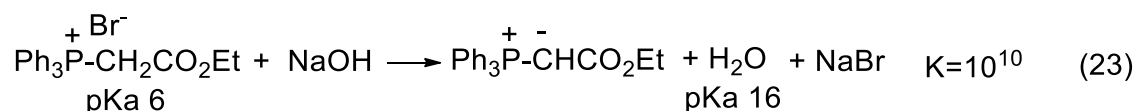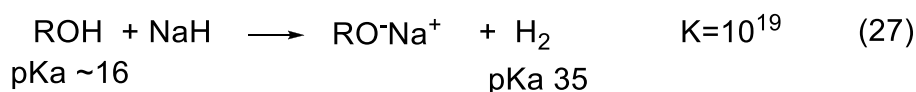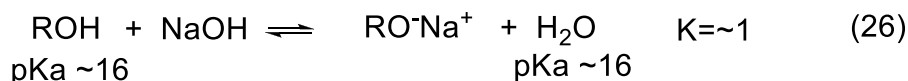

To get ylides from less acidic phosphonium salts, stronger bases like NaH or BuLi are used (reaction 24).
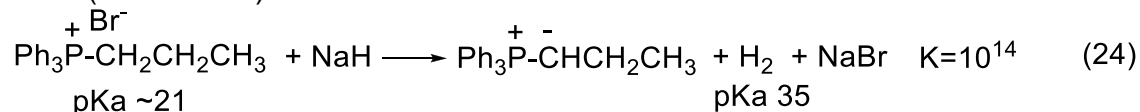
Deprotonation of the phenolic hydroxyl groups (pKa ~10) goes well with NaOH or KOH as shown in the reaction (25).

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$$\text{ArOH} + \text{NaOH} \rightleftharpoons \text{ArO}^-\text{Na}^+ + \text{H}_2\text{O} \qquad K=10^4 \qquad (25)$$

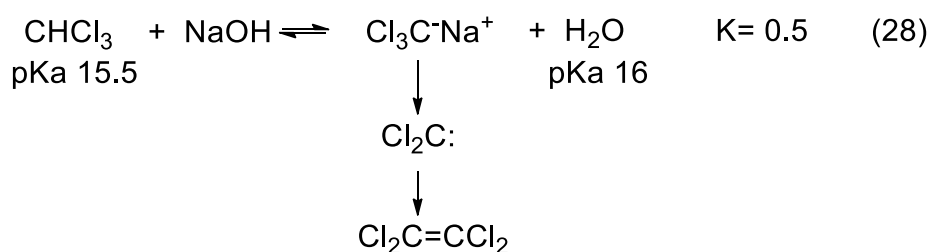pKa ~10   pKa~16
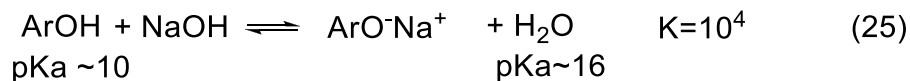
In contrast, deprotonation of hydroxyl groups present in alcohols (pKa ~16) in the same conditions furnishes mixtures of the unreacted alcohol and the alcoholate (reaction 26). Application of the stronger base like sodium hydride however, yields the alcoholate anion only as shown in the reaction (27).

$$\text{ROH} + \text{NaOH} \rightleftharpoons \text{RO}^-\text{Na}^+ + \text{H}_2\text{O} \qquad K=\sim1 \qquad (26)$$

pKa ~16   pKa ~16

$$\text{ROH} + \text{NaH} \longrightarrow \text{RO}^-\text{Na}^+ + \text{H}_2 \qquad K=10^{19} \qquad (27)$$

pKa ~16   pKa 35

Big differences of the associated Ks should be noticed in the reaction (26) and (27). The last example is deprotonation of chloroform, a common solvent used in extractions. Neutralization of such extracts by bases is routinely performed. Some care must be exercised to use NaOH or KOH for this purpose. CHCl$_3$ is reasonably strong acid and can be substantially deprotonated by bases like NaOH (reaction 28).

$$\text{CHCl}_3 + \text{NaOH} \rightleftharpoons \text{Cl}_3\text{C}^-\text{Na}^+ + \text{H}_2\text{O} \qquad K= 0.5 \qquad (28)$$

pKa 15.5   pKa 16

$$\downarrow$$

$$\text{Cl}_2\text{C}:$$

$$\downarrow$$

$$\text{Cl}_2\text{C}=\text{CCl}_2$$

The trichloromethyl anion formed losses the Cl^- to form dichlorocarbene, which can rapidly dimerize to form tetrachloroethylene with liberation of substantial amount of heat due to formation of the strong carbon-carbon double bond. This may result in increase of pressure in a separatory funnel and even an explosion. Thus, for safety reasons the acidic chloroform extracts must be neutralized by bases with care. Looking from a different standpoint, formation of dichlorocarbene is desirable to obtain dichlorocyclopropanes by addition to C=C double bonds.

CONCLUDING REMARKS

A simple method of quantitative evaluation of the positions of the equilibria of the acid-base reactions is shown, which is based on the known pKas of the acids. To illustrate this approach a series of the acid-base processes are presented to evaluate quantitatively how strong the base should be used to achieve a reasonable concentration of the deprotonated acid. Deprotonation is frequently performed in research to get nucleophiles and yet, a quantitative treatment of the acid-base reactions is neglected in the organic chemistry textbooks just like the issue of the oxidation states of the carbon atoms, which we have addressed before.[9] Rather vague statements are used whenever preparation of the acetylide anions for example, is needed, like "strong base should be used". It must be stated that strength of a base is a relative term. For instance, water is sufficiently strong base to deprotonate HCl ($H_2O + HCl \rightarrow H_3O^+ + Cl^-$; $K = 10^{5.3}$), whereas is a weak base to deprotonate a phenolic hydroxyl group (PhOH + $H_2O \rightarrow PhO^- + H_3O^+$; $K=10^{-11.7}$). Conversely, there is no need to use NaH or LDA to

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obtain phenolate ion since NaOH is very good for this purpose, but LDA is indispensable to obtain various types of the enolates. Thus, it seems a good idea from a didactic standpoint to present a method of evaluation of a given acid-base process quantitatively rather than to depend on words which do not transmit any quantitative meaning. We believe that the present text may be useful as a supplementary material to study the introduction to organic chemistry.

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