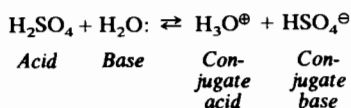


3

The strengths of acids and bases

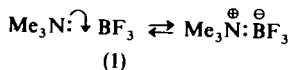
- 3.1 ACIDS, p. 54:
3.1.1 pK_a , p. 54; 3.1.2 The origin of acidity in organic compounds, p. 55; 3.1.3 The influence of the solvent, p. 56; 3.1.4 Simple aliphatic acids, p. 57; 3.1.5 Substituted aliphatic acids, p. 59; 3.1.6 Phenols, p. 61; 3.1.7 Aromatic carboxylic acids, p. 62; 3.1.8 Dicarboxylic acids, p. 63; 3.1.9 pK_a and temperature, p. 64.
- 3.2 BASES, p. 65:
3.2.1 pK_b , pK_{BH^+} and pK_a , p. 65; 3.2.2 Aliphatic bases, p. 66; 3.2.3 Aromatic bases, p. 69; 3.2.4 Heterocyclic bases, p. 72.
- 3.3 ACID/BASE CATALYSIS, p. 74:
3.3.1 Specific and general acid catalysis, p. 74; 3.3.2 Specific and general base catalysis, p. 75.

Modern electronic theories of organic chemistry have been highly successful in a wide variety of fields in correlating behaviour with structure, not least in accounting for the relative strengths of organic acids and bases. According to the definition of Arrhenius, acids are compounds that yield hydrogen ions, H^+ , in solution while bases yield hydroxide ions, OH^- . Such definitions are reasonably adequate if reactions in water only are to be considered, but the acid/base relationship has proved so useful in practice that the concepts of both acids and bases have become considerably more generalised. Thus Brønsted defined acids as substances that would give up protons, i.e. *proton donors*, while bases were *proton acceptors*. The first ionisation of sulphuric acid in aqueous solution is then looked upon as:



Here water is acting as a base by accepting a proton, and is thereby converted into its so-called *conjugate acid*, H_3O^+ , while the acid, H_2SO_4 , by donating a proton is converted into its *conjugate base*, HSO_4^- .

The more generalised picture provided by Lewis, who defined acids as molecules or ions capable of coordinating with unshared electron pairs, and bases as molecules or ions which have such unshared electron pairs available for coordination, has already been referred to (p. 29). Lewis acids include such species as boron trifluoride (1) which reacts with trimethylamine to form a solid salt (m.p. 128°):

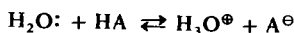


Other common examples are aluminium chloride, tin(IV) chloride, zinc chloride, etc. We shall, at this point, be concerned essentially with proton acids, and the effect of structure on the strength of a number of organic acids and bases will now be considered in turn. Compounds in which it is a C—H bond that is ionised will be considered subsequently (p. 270), however.

3.1 ACIDS

3.1.1 pK_a

The strength of an acid, HA, in water, i.e. the extent to which it is dissociated, may be determined by considering the equilibrium:

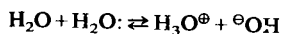


Then the equilibrium constant, in water, is given by:

$$K_a \approx \frac{[\text{H}_3\text{O}^{\oplus}][\text{A}^{\ominus}]}{[\text{HA}]}$$

The $[\text{H}_2\text{O}]$ term is incorporated into K_a because water is present in such excess that its concentration does not change significantly. It should be emphasised that K_a , the *acidity constant* of the acid in water, is only approximate (as above) if concentrations are used instead of the more correct activities; it is a reasonable assumption, however, provided the solution is fairly dilute. The acidity constant is influenced by the composition of the solvent in which the acid is dissolved (see below) and by other factors, but it does, nevertheless, serve as a useful guide to comparative acid strength. In order to avoid writing negative powers of 10, K_a is generally converted into pK_a ($pK_a = -\log_{10} K_a$); thus while K_a for ethanoic (acetic) acid in water at 25° is 1.79×10^{-5} , $pK_a = 4.76$. The smaller the numerical value of pK_a , the stronger the acid to which it refers.

Very weak acids, those with pK_a greater than ≈ 16 , will not be detectable as acids at all in water, as the $[\text{H}_3\text{O}^{\oplus}]$ they will produce therein will be less than that produced by the autolysis of water itself:



Their relative acidities (pK_a s) thus cannot be measured in water at all. Further, when acids are sufficiently strong (low enough pK_a), they will all be essentially fully ionised in water, and will thus all appear to be of the same strength, e.g. HCl, HNO₃, HClO₄, etc. This is known as the *levelling effect* of water.

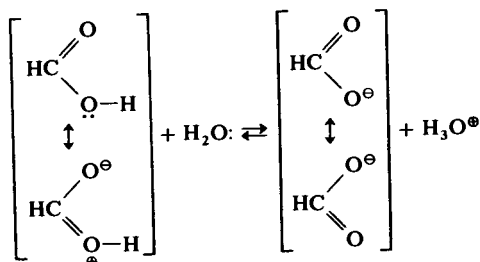
The range of comparative pK_a measurement can, however, be extended by, in the first case, providing a stronger, and the latter case a weaker, base than H₂O as solvent. By carrying out measurements in a range of solvents of increasing basicity (and by using an acid that is near the bottom limit of the acidity range in one solvent and near the top of the range in the next as a common reference in each case) it is possible to carry determination of acid strengths on down to acids as weak as methane ($pK_a \approx 43$).

3.1.2 The origin of acidity in organic compounds

Among the factors that may influence the acidity of an organic compound, HA, are:

- The strength of the H—A bond.
- The electronegativity of A.
- Factors stabilising A[⊖] compared with HA.
- The nature of the solvent.

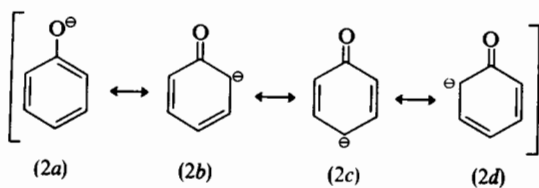
Of these (a) is not normally found to be a limiting factor, but the effect of (b) is reflected in the fact that the pK_a of methanol, CH₃O—H, is ≈ 16 while that of methane, CH₃—H, is ≈ 43 , oxygen being considerably more electronegative than carbon. By contrast the pK_a of methanoic (formic) acid is 3.77. This is in part due to the electron-withdrawing carbonyl group enhancing the electron affinity of the oxygen atom to which the incipient proton is attached, but much more important is (c): the stabilisation possible in the resultant methanoate anion compared with the undissociated methanoic acid molecule:



There is extremely effective delocalisation, with consequent stabilisation, in the methanoate anion involving as it does two canonical structures of identical energy, and though delocalisation can take

place in the methanoic acid molecule also, this involves separation of charge and will consequently be much less effective as a stabilising influence (*cf.* p. 20). The effect of this differential stabilisation is somewhat to discourage the recombination of proton with the methanoate anion, the equilibrium is to this extent displaced to the right, and methanoic acid is, by organic standards, a moderately strong acid.

With alcohols there is no such factor stabilising the alkoxide anion RO^\ominus , relative to the alcohol itself, and alcohols are thus very much less acidic than carboxylic acids. With phenols, however, there is again the possibility of relative stabilisation of the anion (2), by delocalisation of its negative charge through interaction with the π orbitals of the aromatic nucleus:



Delocalisation also occurs in the undissociated phenol molecule (*cf.* p. 23) but, involving charge separation, this is less effective than in the anion (2), thus leading to some reluctance on the part of the latter to recombine with a proton. Phenols are indeed found to be stronger acids than alcohols (the $\text{p}K_a$ of phenol itself is 9.95) but considerably weaker than carboxylic acids. This is due to the fact that delocalisation of the negative charge in the carboxylate anion involves structures of identical energy content (see above), and of the centres involved two are highly electronegative oxygen atoms; whereas in the phenoxide anion (2) the structures involving negative charge on the nuclear carbon atoms are likely to be of higher energy content than the one in which it is on oxygen and, in addition, of the centres involved here only one is a highly electronegative oxygen atom. The relative stabilisation of the anion, with respect to the undissociated molecule, is thus likely to be less effective with a phenol than with a carboxylic acid, leading to the lower relative acidity of the former.

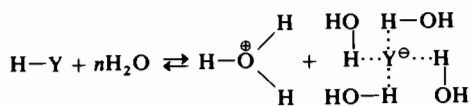
3.1.3 The influence of the solvent

Despite the above discussion on the influence of internal structural features on a compound's acidity, the real determining role is often exerted by the solvent, and this is particularly the case when, as commonly, the solvent is water.

Water has the initial disadvantage as an ionising solvent for organic compounds that some of them are insufficiently soluble in their unionised form to dissolve in it in the first place. That limitation apart,

water is a singularly effective ionising solvent on account (a) of its high dielectric constant ($\epsilon = 80$), and (b) of its ion-solvating ability. The first property exerts its effect because the higher the dielectric constant (polarity) of a solvent the lower the electrostatic energy of any pairs of ions present in it will be: the more readily will such ion pairs thus be formed, the more stable will they be in solution, and the less ready will they be, therefore, to recombine with each other.

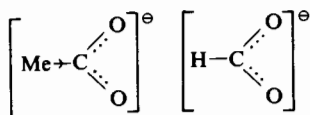
Ions in solution strongly polarise nearby solvent molecules, thereby collecting a solvation envelope of solvent molecules around them: the greater the extent to which this can take place, the greater the stabilisation of the ion, which is in effect stabilising itself by spreading or delocalising its charge. The peculiar effectiveness of water, as an ion-solvating medium, arises from the fact that H_2O is extremely readily polarised, and also relatively small in size; because of this it can solvate, and thereby stabilise, both cations and anions. The effect is particularly marked with anions for powerful 'hydrogen-bonded' type solvation can occur (see below). Similar H-bonded type solvation cannot in general occur with cations, but in the particular case of acids, the initial cation, H^\oplus , can also solvate through hydrogen bonding with the solvent water molecules:



Alcohols, just so long as they are not too bulky, e.g. MeOH , share something of water's abilities and, for example, HCl is found to be a strong acid in methanol also. It should not, however, be forgotten that the prime requirement of the solvent is that it should be capable of functioning as a base: the weaker the base, the smaller the dissociation of the acid. Thus we find that in, for example, methylbenzene (toluene) HCl occurs as such, i.e. it is almost wholly undissociated.

3.1.4 Simple aliphatic acids

The replacement of the non-hydroxylic hydrogen atom of methanoic acid by an alkyl group might be expected to produce a weaker acid, as the electron-donating inductive effect of the alkyl group would reduce the residual electron affinity of the oxygen atom carrying the incipient proton, and so reduce the strength of the acid. In the alkyl-substituted anion the increased electron availability on oxygen would serve to promote its recombination with proton, as compared with the methanoate anion/methanoic acid system:



We should thus expect the equilibrium to be shifted to the left compared with that for methanoic acid/methanoate anion, and it is in fact found that the pK_a of ethanoic acid is 4.76, compared with 3.77 for methanoic acid. However, the degree of structural change effected in so small a molecule as methanoic acid by replacement of H by CH_3 makes it doubtful whether so simple an argument is really valid; it could well be that the relative solvation possibilities in the two cases are markedly affected by the considerably different shapes of, as well as by the relative charge distribution in, the two small molecules.

It is important to remember that the value of the acidity constant, K_a , of an acid is related to the standard free energy change for the ionisation, ΔG^\ominus , by the relation

$$-\Delta G^\ominus = 2.303RT \log K_a$$

and that ΔG^\ominus includes both enthalpy and entropy terms:

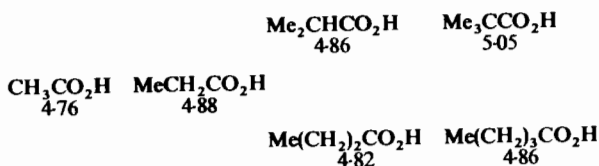
$$\Delta G^\ominus = \Delta H^\ominus - T\Delta S^\ominus$$

Thus it is found for the ionisation of ethanoic acid in water at 25° ($K_a = 1.79 \times 10^{-5}$) that $\Delta G^\ominus = 27.2 \text{ kJ (6.5 kcal)}$, $\Delta H^\ominus = -0.5 \text{ kJ (-0.13 kcal)}$, and $\Delta S^\ominus = -92 \text{ J (-22 cal) deg}^{-1}$ [i.e. $T\Delta S^\ominus = -27.6 \text{ kJ (-6.6 kcal)}$]; while for methanoic acid ($K_a = 17.6 \times 10^{-5}$) the corresponding figures are: $\Delta G^\ominus = 21 \text{ kJ (5.1 kcal)}$, $\Delta H^\ominus = -0.3 \text{ kJ (-0.07 kcal)}$, and $\Delta S^\ominus = -74 \text{ J (-18 cal) deg}^{-1}$ [i.e. $T\Delta S^\ominus = -21.3 \text{ kJ (-5.17 kcal)}$]. The surprisingly small ΔH^\ominus values almost certainly arise from the fact that the energy required for dissociation of the O—H bond in the undissociated carboxylic acids is cancelled out by that evolved in solvating the resultant ions.

The differing ΔG^\ominus s, and hence the differing K_a s, for the two acids thus result from the different values of the two entropy (ΔS^\ominus) terms. There are two species on each side of the equilibrium and differences in translational entropy on dissociation will thus be small. However, the two species are neutral molecules on one side of the equilibrium and ions on the other. The main feature that contributes to ΔS^\ominus is thus the solvation sheaths of water molecules that surround RCO_2^\ominus and $\text{H}_3\text{O}^\oplus$, and the consequent restriction, in terms of increased orderliness, that is thereby imposed on the solvent water molecules; the increase in orderliness not being quite so great as might have been expected as there is already a good deal of orderliness in liquid water itself. The difference in strength between methanoic and ethanoic acids thus does indeed relate to the differential solvation of their anions, as was suggested above.

Further substitution of alkyl groups in ethanoic acid has much less effect than this first introduction and, being now essentially a second-order effect, the influence on acid strength is not always regular, steric

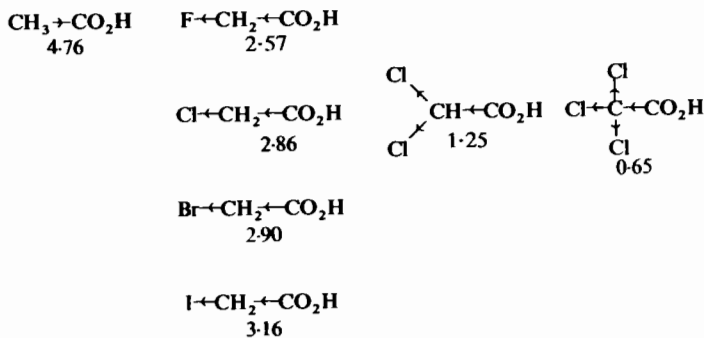
and other influences playing a part; pK_a values are observed as follows:



If there is a doubly bonded carbon atom adjacent to the carboxyl group the acid strength is increased. Thus propenoic (acrylic) acid, $\text{CH}_2=\text{CHCO}_2\text{H}$, has a pK_a of 4.25 compared with 4.88 for the saturated analogue, propanoic acid. This is due to the fact that the unsaturated α -carbon atom is sp^2 hybridised, which means that electrons are drawn closer to the carbon nucleus than in a saturated, sp^3 hybridised atom due to the rather larger s contribution in the sp^2 hybrid. The result is that sp^2 hybridised carbon atoms are less electron-donating than saturated sp^3 hybridised ones, and so propenoic acid though still weaker than methanoic acid is stronger than propanoic. The effect is much more marked with the sp hybridised carbon atom of a triple bond, thus the pK_a of propynoic (propionic) acid, $\text{HC}\equiv\text{CCO}_2\text{H}$, is 1.84. An analogous situation occurs with the hydrogen atoms of ethene and ethyne; those of the former are little more acidic than the hydrogens in ethane, whereas those of ethyne are sufficiently acidic to be readily replaceable by a number of metals (*cf.* p. 272).

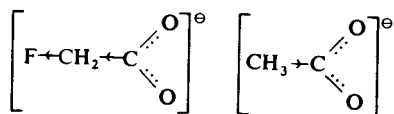
3.1.5 Substituted aliphatic acids

The effect of introducing electron-withdrawing substituents into simple aliphatic acids is more marked. Thus halogen, with an inductive effect acting in the opposite direction to alkyl, might be expected to increase the strength of an acid so substituted, and this is indeed observed as pK_a values show:



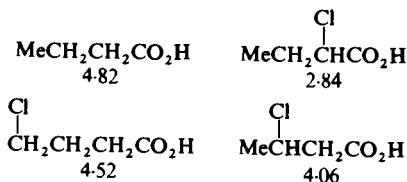
The relative effect of the different halogens is in the expected order, fluorine being the most electronegative (electron-withdrawing) and producing a hundredfold increase in strength of fluoroethanoic acid as compared with ethanoic acid itself. The effect is very much greater than that produced, in the opposite direction, by the introduction of an alkyl group, and the introduction of further halogens still produces large increases in acid strength: trichloroethanoic is thus a very strong acid.

Here again it is important to remember that K_a (and hence pK_a) is related to ΔG^\ominus for the ionisation, and that ΔG^\ominus includes both ΔH^\ominus and ΔS^\ominus terms. In this series of halogen-substituted ethanoic acids ΔH^\ominus is found to differ little from one compound to another, the observed change in ΔG^\ominus along the series being due largely to variation in ΔS^\ominus . This arises from the substituent halogen atom effecting delocalisation of the negative charge over the whole of the anion,



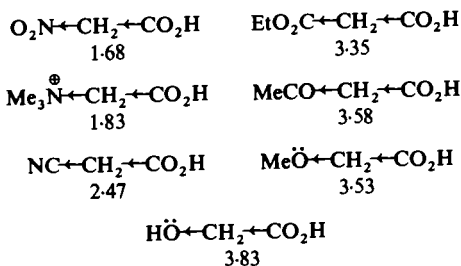
the latter thus imposes correspondingly less powerful restriction on the water molecules surrounding it than does the unsubstituted ethanoate anion whose charge is largely concentrated, being confined substantially to CO_2^\ominus . There is therefore a smaller decrease in entropy on ionisation of the halogen-substituted ethanoic acids than with ethanoic acid itself. This is particularly pronounced with $\text{CF}_3\text{CO}_2\text{H}$ (pK_a 0.23) for whose ionisation $\Delta G^\ominus = 1.3$ kJ (0.3 kcal) compared with 27.2 kJ (6.5 kcal) for $\text{CH}_3\text{CO}_2\text{H}$, while the ΔH^\ominus values for these two acids differ very little from each other.

The introduction of a halogen atom further away from the carboxyl group than the adjacent α -position has much less influence. Its inductive effect quickly dies away down a saturated chain, with the result that the negative charge becomes progressively less spread, i.e. more concentrated, in the carboxylate anion. The acid thus increasingly resembles the corresponding simple aliphatic acid itself, as the following pK_a values show:



Other electron-withdrawing groups, e.g. $\text{R}_3\text{N}^\oplus$, CN , NO_2 , SO_2R , CO , CO_2R increase the strength of simple aliphatic acids, as also do

hydroxyl and methoxyl groups. The unshared electrons on the oxygen atoms of the last two groups are not able to exert a mesomeric effect, in the opposite direction to their inductive effect, owing to the intervening saturated carbon atoms. All this is seen in the pK_a values:



3.1.6 Phenols

Analogous effects can be observed with substituted phenols, the presence of electron-withdrawing groups in the nucleus increasing their acidity. In the case of a nitro substituent, the inductive effect would be expected to fall off with distance on going o - \rightarrow m - \rightarrow p -nitrophenol, but there would also be an electron-withdrawing mesomeric effect when the nitro group is in the o - or p -, but not in the m -position; and this too would promote ionisation by stabilisation (though delocalisation) of the resultant anion. We might therefore expect o - and p -nitrophenols to be more acidic than the m -compound which is, in fact, found to be the case. Introduction of further NO_2 groups promotes acidity markedly, thus 2,4,6-trinitrophenol (picric acid) is found to be a very strong acid:

C_6H_5OH	pK_a 9.95	
$o-O_2NC_6H_4OH$	7.23	
$m-O_2NC_6H_4OH$	8.35	
$p-O_2NC_6H_4OH$	7.14	
$2,4-(O_2N)_2C_6H_3OH$	4.01	
$2,4,6-(O_2N)_3C_6H_2OH$	1.02	

Here again ΔH^{\ominus} is found to vary only very slightly between o -, m - and p -nitrophenols, the differing ΔG^{\ominus} values observed for the three arising from differences in the $T\Delta S^{\ominus}$ terms, i.e. from variations in the solvation patterns of the three anions, due to the differing distribution of negative charge in them.

The effect of introducing electron-donating alkyl groups into the benzene nucleus is found to be small:

C_6H_5OH	pK_a 9.95
$o-MeC_6H_4OH$	10.28
$m-MeC_6H_4OH$	10.08
$p-MeC_6H_4OH$	10.19

The resulting substituted phenols are very slightly weaker acids, but the effect is marginal and irregular, indicating that the effect of such substituents in destabilising the phenoxide ion, by disturbing the interaction of its negative charge with the delocalised π orbitals of the aromatic nucleus, is small, as might have been expected.

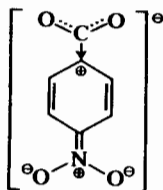
3.1.7 Aromatic carboxylic acids

Benzoic acid, with a pK_a of 4.20, is a stronger acid than its saturated analogue cyclohexane carboxylic acid ($pK_a = 4.87$); suggesting that a phenyl group, like a double bond, is here less electron-donating—compared with a saturated carbon atom—towards the carboxyl group, due to the sp^2 hybridised carbon atom to which the carboxyl group is attached (*cf.* p. 59). The introduction of alkyl groups into the benzene nucleus has very little effect on the strength of benzoic acid (*cf.* similar introduction in phenols, p. 61),

	pK_a
$C_6H_5CO_2H$	4.20
$m\text{-Me}C_6H_4CO_2H$	4.24
$p\text{-Me}C_6H_4CO_2H$	4.34

but electron-withdrawing groups increase its strength, the effect, as with the phenols, being most pronounced when they are in the *o*- and *p*-positions:

	pK_a
$C_6H_5CO_2H$	4.20
$o\text{-}O_2NC_6H_4CO_2H$	2.17
$m\text{-}O_2NC_6H_4CO_2H$	3.45
$p\text{-}O_2NC_6H_4CO_2H$	3.43
$3,5\text{-}(O_2N)_2C_6H_3CO_2H$	2.83



The particularly marked effect with *o*-NO₂ may be due to the very short distance over which the powerful inductive effect is operating, but some direct interaction between the adjacent NO₂ and CO₂H groups cannot be ruled out.

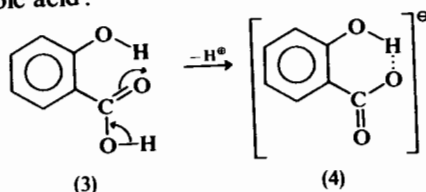
The presence of groups such as OH, OMe, or halogen having an electron-withdrawing inductive effect, but an electron-donating mesomeric effect when in the *o*- and *p*-positions, may, however, cause the *p*-substituted acids to be weaker than the *m*- and, on occasion, weaker even than the unsubstituted acid itself, e.g. *p*-hydroxybenzoic acid:

	pK_a of $XC_6H_4CO_2H$				
	H	Cl	Br	OMe	OH
<i>o</i> - 4.20	2.94	2.85	4.09	2.98	
<i>m</i> - 4.20	3.83	3.81	4.09	4.08	
<i>p</i> - 4.20	3.99	4.00	4.47	4.58	

It will be noticed that this compensating effect becomes more pronounced in going $\text{Cl} \approx \text{Br} \rightarrow \text{OH}$, i.e. in increasing order of readiness with which the atom attached to the nucleus will part with its electron pairs.

It is important to emphasise, however, that here—as in the cases above—it is probably the effect of differing charge distributions in the anions on their patterns of solvation, i.e. on the TAS^\ominus term relating to the degree of ordering induced locally in the assembly of solvent molecules, that is responsible for the observed differences in $\text{p}K_a$.

The behaviour of *o*-substituted acids is, as seen above, often anomalous. Their strength is sometimes found to be considerably greater than expected due to direct interaction between the adjacent groups. Thus intramolecular hydrogen bonding (cf. p. 36) stabilises the anion (4) from *o*-hydroxybenzoic (salicylic) acid (3) by delocalising its charge, an advantage not shared by its *m*- and *p*-isomers, nor by *o*-methoxybenzoic acid:



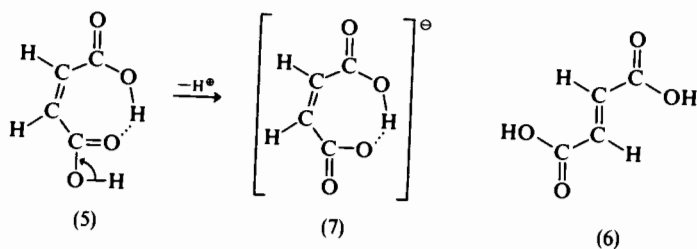
Intramolecular hydrogen bonding can, of course, operate in the undissociated acid as well as in the anion, but it is likely to be considerably more effective in the latter than in the former—with consequent relative stabilisation—because the negative charge on oxygen in the anion will lead to stronger hydrogen bonding. The effect is even more pronounced where hydrogen bonding can occur with hydroxyl groups in both *o*-positions, and 2,6-dihydroxybenzoic acid is found to have $\text{p}K_a = 1.30$.

3.1.8 Dicarboxylic acids

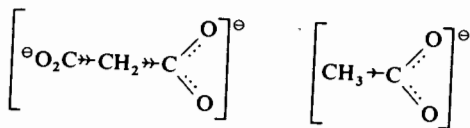
As the carboxyl group itself has an electron-withdrawing inductive effect, the presence of a second such group in an acid might be expected to make it stronger, as shown by the following $\text{p}K_a$ values:

HCO_2H	$\text{HO}_2\text{CCO}_2\text{H}$
3.77	1.23
$\text{CH}_3\text{CO}_2\text{H}$	$\text{HO}_2\text{CCH}_2\text{CO}_2\text{H}$
4.76	2.83
$\text{CH}_3\text{CH}_2\text{CO}_2\text{H}$	$\text{HO}_2\text{CCH}_2\text{CH}_2\text{CO}_2\text{H}$
4.88	4.19
$\text{C}_6\text{H}_5\text{CO}_2\text{H}$	$\text{HO}_2\text{CC}_6\text{H}_4\text{CO}_2\text{H}$
4.17	<i>o</i> -2.98
	<i>m</i> -3.46
	<i>p</i> -3.51

The effect is very pronounced, but falls off sharply as soon as the carboxyl groups are separated by more than one saturated carbon atom. *Cis*-butenedioic(maleic) acid (5, $pK_a^1 = 1.92$) is a much stronger acid than *trans*-butenedioic(fumaric) acid (6, $pK_a^1 = 3.02$), due to the intramolecular hydrogen bonding that can take place with the former, but not with the latter, leading to relative stabilisation of the *cis* (maleate, 7) mono-anion (*cf.* *o*-hydroxybenzoic acid above):



The second dissociation of *trans*-butenedioic acid ($pK_a^2 = 4.38$) occurs more readily than that of the *cis*-acid ($pK_a^2 = 6.23$), however, because of the greater difficulty in removing a proton from the negatively charged cyclic system in the anion (7) derived from the latter. Ethanedioic(oxalic), propane-1,3-dioic(malonic) and butane-1,4-dioic(succinic) acids are each weaker in their second dissociations than methanoic, ethanoic and propanoic acids, respectively. This is because the second proton has to be removed from a negatively charged species containing an electron-donating substituent, i.e. CO_2^\ominus , which might be expected to destabilise the anion with respect to the undissociated acid, as compared with the unsubstituted system:



3.1.9 pK_a and temperature

We have already seen (p. 56) that the K_a , and hence pK_a , value for an acid is not an intrinsic attribute of the species itself, because it varies from one solvent to another: the value depending on the overall system of which the acid is a constituent. Values are normally quoted for aqueous solution, unless otherwise specified, because most data are available for that solvent. Most values are also quoted as at 25° , again because most data were obtained at this temperature. A constant temperature has to be specified as K_a , an equilibrium constant, varies with temperature. We have been concerned above with the *relative*

acidity of various categories of acids, and in trying to correlate relative acidity sequences with structure in a rational way—with some degree of success. It is, however, pertinent to point out that not only do individual K_a values vary with temperature, they also vary *relative* to each other: thus ethanoic is a weaker acid than $\text{Et}_2\text{CHCO}_2\text{H}$ below 30° , but a stronger acid above that temperature. Such reversals of relative acidity with change of temperature are found to be fairly common; it thus behoves us not to split too many fine hairs about correlating relative acidity with structure at 25° !

3.2 BASES

3.2.1 $\text{p}K_b$, $\text{p}K_{\text{BH}^\oplus}$ and $\text{p}K_a$

The strength of a base, $\text{B}:$, in water, may be determined by considering the equilibrium:

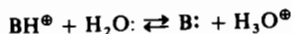


The equilibrium constant in water, K_b , is then given by:

$$K_b \approx \frac{[\text{BH}^\oplus][\ominus\text{OH}]}{[\text{B}]}$$

The $[\text{H}_2\text{O}]$ term is incorporated into K_b , because water is present in such excess that its concentration does not change significantly; here again, concentrations can commonly be used instead of the more correct activities provided the solution is reasonably dilute.

It is, however, now more usual to describe the strength of bases also in terms of K_a and $\text{p}K_a$, thereby establishing a single continuous scale for both acids and bases. To make this possible we use, as our reference reaction for bases, the equilibrium

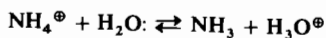


for which we can then write,

$$K_a \approx \frac{[\text{B}][\text{H}_3\text{O}^\oplus]}{[\text{BH}^\oplus]}$$

where K_a (and $\text{p}K_a$) is a measure of the acid strength of the conjugate acid, BH^\oplus , of the base, $\text{B}:$. This measure of the readiness with which BH^\oplus will part with a proton is, conversely, a measure of the lack of readiness with which the base, $\text{B}:$, will accept one: the stronger BH^\oplus is as an acid, the weaker $\text{B}:$ will be as a base. Thus the smaller the numerical value of $\text{p}K_a$ for BH^\oplus , the weaker $\text{B}:$ is as a base. When using $\text{p}K$ to quote the strength of a base, $\text{B}:$, $\text{p}K_{\text{BH}^\oplus}$ should actually be specified but it has become common—though incorrect—to write it simply as $\text{p}K_a$.

Taking as an example NH_4^{\oplus} , with a $\text{p}K_a$ value of 9.25,



it is found that $\Delta G^{\ominus} = 52.7 \text{ kJ (12.6 kcal)}$, $\Delta H^{\ominus} = 51.9 \text{ kJ (12.4 kcal)}$, and $\Delta S^{\ominus} = -2.9 \text{ J (-0.7 cal) deg}^{-1}$ [i.e. $T\Delta S^{\ominus} = -0.8 \text{ kJ (-0.2 kcal)}$] at 25° . Thus the position of the above equilibrium is effectively determined by ΔH^{\ominus} , the effect of ΔS^{\ominus} being all but negligible: a result that is in marked contrast to the behaviour of many acids as we have seen above (p. 58). The reason for the small effect of ΔS^{\ominus} is that here there is one charged species (a positive ion) on each side of the equilibrium, and these ions have closely comparable effects in restricting the solvent water molecules that surround them, so that their entropies of solvation tend to cancel each other out.

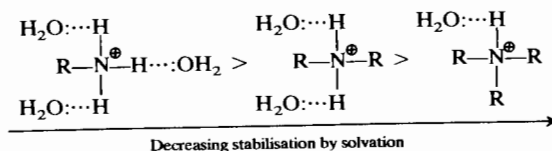
3.2.2 Aliphatic bases

As increasing strength in nitrogenous bases is related to the readiness with which they are prepared to take up protons and, therefore, to the availability of the unshared electron pair on nitrogen, we might expect to see an increase in basic strength on going: $\text{NH}_3 \rightarrow \text{RNH}_2 \rightarrow \text{R}_2\text{NH} \rightarrow \text{R}_3\text{N}$, due to the increasing inductive effect of successive alkyl groups making the nitrogen atom more negative. An actual series of amines was found to have related $\text{p}K_a$ values as follows, however:

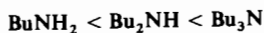
$\text{Me} \rightarrow \text{NH}_2$	$\begin{array}{c} \text{Me} \searrow \\ \text{NH} \\ \nearrow \text{Me} \end{array}$	$\begin{array}{c} \text{Me} \searrow \\ \text{Me} \rightarrow \text{N} \\ \nearrow \text{Me} \end{array}$
10.64	10.77	9.80
NH_3 9.25		
$\text{Et} \rightarrow \text{NH}_2$	$\begin{array}{c} \text{Et} \searrow \\ \text{NH} \\ \nearrow \text{Et} \end{array}$	$\begin{array}{c} \text{Et} \searrow \\ \text{Et} \rightarrow \text{N} \\ \nearrow \text{Et} \end{array}$
10.67	10.93	10.88

It will be seen that the introduction of an alkyl group into ammonia increases the basic strength markedly as expected. The introduction of a second alkyl group further increases the basic strength, but the net effect of introducing the second alkyl group is very much less marked than with the first. The introduction of a third alkyl group to yield a tertiary amine, however, actually decreases the basic strength in both the series quoted. This is due to the fact that the basic strength of an amine in water is determined not only by electron-availability on the

nitrogen atom, but also by the extent to which the cation, formed by uptake of a proton, can undergo solvation, and so become stabilised. The more hydrogen atoms attached to nitrogen in the cation, the greater the possibilities of powerful solvation *via* hydrogen bonding between these and water:

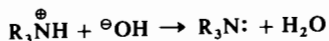


Thus on going along the series, $\text{NH}_3 \rightarrow \text{RNH}_2 \rightarrow \text{R}_2\text{NH} \rightarrow \text{R}_3\text{N}$, the inductive effect will tend to *increase* the basicity, but progressively less stabilisation of the cation by hydration will occur, which will tend to *decrease* the basicity. The *net* effect of introducing successive alkyl groups thus becomes progressively smaller, and an actual changeover takes place on going from a secondary to a tertiary amine. If this is the real explanation, no such changeover should be observed if measurements of basicity are made in a solvent in which hydrogen-bonding cannot take place; it has, indeed, been found that in chlorobenzene the order of basicity of the butylamines is



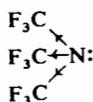
though their related $\text{p}K_a$ values in water are 10.61, 11.28 and 9.87.

Tetraalkylammonium salts, e.g. $\text{R}_4\text{N}^{\oplus}\text{I}^{\ominus}$, are known, on treatment with moist silver oxide, AgOH , to yield basic solutions comparable in strength with the mineral alkalis. This is readily understandable for the base so obtained, $\text{R}_4\text{N}^{\oplus}\text{OH}^{\ominus}$, is bound to be completely ionised as there is no possibility, as with tertiary amines, etc.,



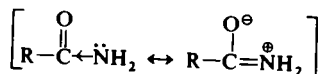
of reverting to an unionised form.

The effect of introducing electron-withdrawing groups, e.g. Cl , NO_2 , close to a basic centre is to decrease the basicity, due to their electron-withdrawing inductive effect (*cf.* substituted anilines below, p. 70); thus the amine

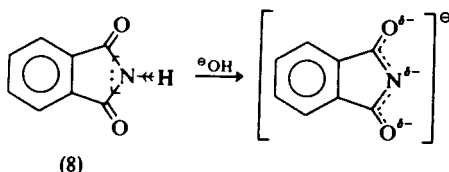


is found to be virtually non-basic, due to the three powerfully electron-withdrawing CF_3 groups.

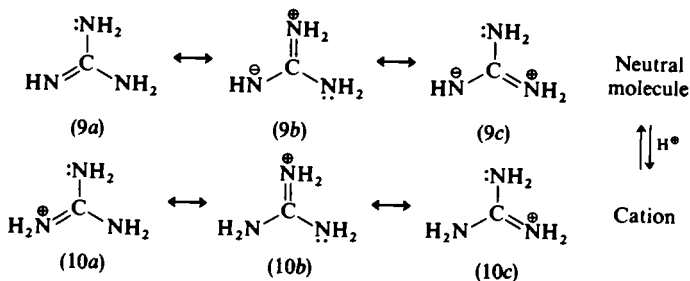
The change is also pronounced with $C=O$, for not only is the nitrogen atom, with its electron pair, bonded to an electron-withdrawing group through an sp^2 hybridised carbon atom (*cf.* p. 59), but an electron-withdrawing mesomeric effect can also operate:



Thus amides are found to be only very weakly basic in water [pK_a for ethanamide(acetamide) is ≈ 0.5], and if two $C=O$ groups are present the resultant imides, far from being basic, are often sufficiently acidic to form alkali metal salts, e.g. benzene-1,2-dicarboximide (phthalimide, 8):

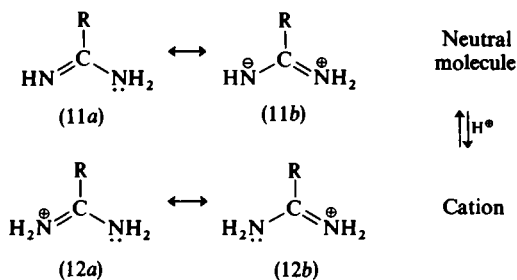


The effect of delocalisation in *increasing* the basic strength of an amine is seen in guanidine, $HN=C(NH_2)_2$ (9), which, with the exception of the tetraalkylammonium hydroxides above, is among the strongest organic nitrogenous bases known, with a related pK_a of ≈ 13.6 . Both the neutral molecule, and the cation, $H_2N^+=C(NH_2)_2$ (10), resulting from its protonation, are stabilised by delocalisation;



but in the cation the positive charge is spread symmetrically by contribution to the hybrid of three exactly equivalent structures of equal energy. No comparably effective delocalisation occurs in the neutral molecule (in which two of the contributing structures involve separation of charge), with the result that the cation is greatly stabilised with respect to it, thus making protonation 'energetically profitable' and guanidine an extremely strong base.

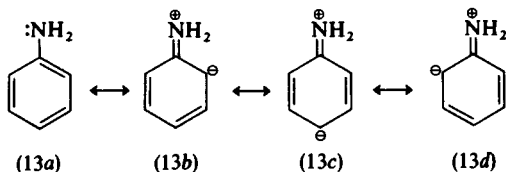
A somewhat analogous situation occurs with the amidines, $\text{RC}(=\text{NH})\text{NH}_2$ (11):



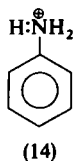
While stabilisation by delocalisation in the cation (12) would not be expected to be as effective as that in the guanidine cation (10) above, ethanamidine, $\text{CH}_3\text{C}(=\text{NH})\text{NH}_2$ ($\text{p}K_{\text{a}} = 12.4$), is found to be a much stronger base than ethylamine, MeCH_2NH_2 ($\text{p}K_{\text{a}} = 10.67$).

3.2.3 Aromatic bases

The exact reverse of the above is seen with aniline (13), which is a very weak base ($\text{p}K_{\text{a}} = 4.62$) compared with ammonia ($\text{p}K_{\text{a}} = 9.25$) or cyclohexylamine ($\text{p}K_{\text{a}} = 10.68$). In aniline the nitrogen atom is again bonded to an sp^2 hybridised carbon atom but, more significantly, the unshared electron pair on nitrogen can interact with the delocalised π orbitals of the nucleus:



If aniline is protonated, any such interaction, with resultant stabilisation, in the anilinium cation (14) is prohibited, as the electron pair on N is no longer available:



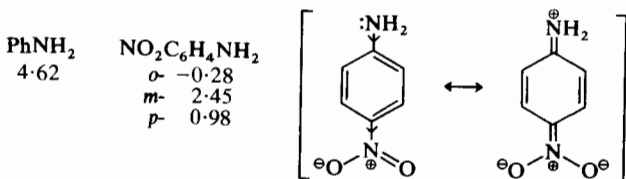
The aniline molecule is thus stabilised with respect to the anilinium cation, and it is therefore 'energetically unprofitable' for aniline to take up a proton; it thus functions as a base with the utmost reluctance ($pK_a = 4.62$, compared with cyclohexylamine, $pK_a = 10.68$). The base-weakening effect is naturally more pronounced when further phenyl groups are introduced on the nitrogen atom; thus diphenylamine, Ph_2NH , is an extremely weak base ($pK_a = 0.8$), while triphenylamine, Ph_3N , is by ordinary standards not basic at all.

Introduction of alkyl, e.g. Me, groups on to the nitrogen atom of aniline results in small increases in pK_a :

$\text{C}_6\text{H}_5\text{NH}_2$	$\text{C}_6\text{H}_5\text{NHMe}$	$\text{C}_6\text{H}_5\text{NMe}_2$	$\text{MeC}_6\text{H}_4\text{NH}_2$
4.62	4.84	5.15	o - 4.38 m - 4.67 p - 5.10

Unlike on such introduction in aliphatic amines (p. 66), this small increase is progressive: suggesting that cation stabilisation through hydrogen-bonded solvation, responsible for the irregular behaviour of aliphatic amines, here has less influence on the overall effect. The major determinant of basic strength in alkyl-substituted anilines remains mesomeric stabilisation of the aniline molecule (13) with respect to the cation (14); borne out by the irregular effect of introducing Me groups into the o -, m - and p -positions in aniline. Similar irregular effects on the pK_a of phenol were observed when Me groups were introduced into its o -, m - and p -positions (p. 61).

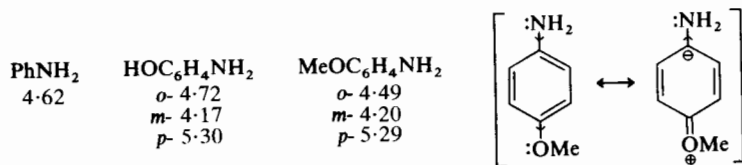
A group with a more powerful (electron-withdrawing) inductive effect, e.g. NO_2 , is found to have rather more influence. Electron-withdrawal is intensified when the nitro group is in the o - or p -position, for the interaction of the unshared pair of the amino nitrogen with the delocalised π orbital system of the benzene nucleus is then enhanced. The neutral molecule is thus stabilised even further with respect to the cation, resulting in further weakening as a base. Thus the nitro-anilines are found to have related pK_a values:



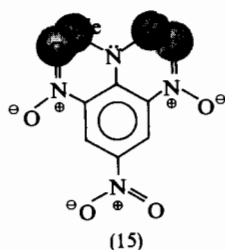
The extra base-weakening effect, when the substituent is in the o -position, is due in part to the short distance over which its inductive effect is operating, and also to direct interaction, both steric and by hydrogen bonding, with the NH_2 group (*cf.* the case of o -substituted benzoic acids, p. 63). o -Nitroaniline is such a weak base that its salts

are largely hydrolysed in aqueous solution, while 2,4-dinitroaniline is insoluble in aqueous acids, and 2,4,6-trinitroaniline resembles an amide; it is indeed called picramide and readily undergoes hydrolysis to picric acid (2,4,6-trinitrophenol).

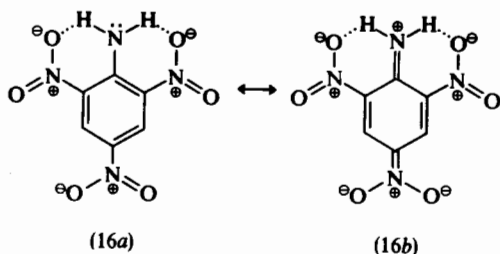
With substituents such as OH and OMe that have unshared electron pairs, an electron-donating, i.e. base-strengthening, mesomeric effect can be exerted from the *o*- and *p*-, but not from the *m*-position, with the result that the *p*-substituted aniline is a stronger base than the corresponding *m*-compound. The *m*-compound is a weaker base than aniline itself, due to the electron-withdrawing inductive effect exerted by the oxygen atom in each case. As so often, the effect of the *o*-substituent remains somewhat anomalous, due to direct interaction with the NH₂ group by both steric and polar effects. The substituted anilines are found to have related pK_a values as follows:




An interesting case is provided by 2,4,6-trinitro-*N,N*-dimethylaniline (15) and 2,4,6-trinitroaniline (16), where the former is found to be about 40,000 times (ΔpK_a 4·60) stronger a base than the latter (by contrast *N,N*-dimethylaniline and aniline itself differ very little in basic strength). This is due to the fact that the NMe₂ group is sufficiently large to interfere sterically with the very large NO₂ groups in both *o*-positions. Rotation about ring-carbon to nitrogen bonds allows the O atoms of NO₂ and the Me groups of NMe₂ to move out of each other's way, but the *p* orbitals on the N atoms are now no longer parallel to the *p* orbitals of the ring-carbon atoms. As a consequence, mesomeric shift of the unshared electron pair on NMe₂ to the oxygen atoms of the NO₂ groups, *via* the *p* orbitals of the ring-carbon atoms (*cf.* p. 70), is inhibited, and the expected base-weakening—by mesomeric electron-withdrawal—does not take place (*cf.* p. 27). The base-weakening influence of the three nitro groups in (15) is thus confined essentially to their inductive effects:



In 2,4,6-trinitroaniline (16), however, the NH_2 group is sufficiently small for no such limitation to be imposed; hydrogen-bonding between the oxygen atoms of the *o*- NO_2 groups and the hydrogen atoms of the NH_2 group may indeed help to hold these groups in the required, planar, orientation. The *p* orbitals may thus assume a parallel orientation, and the strength of (16) as a base is enormously reduced by the powerful electron-withdrawing mesomeric effect of the three NO_2 groups:



3.2.4 Heterocyclic bases

Pyridine, , is an aromatic compound (*cf.* p. 18), the N atom is sp^2 hybridised, and contributes one electron to the 6π ($4n + 2$, $n = 1$) system; this leaves a lone pair of electrons available on nitrogen (accommodated in an sp^2 hybrid orbital), and pyridine is thus found to be basic ($\text{p}K_a = 5.21$). It is, however, a very much weaker base than aliphatic tertiary amines (e.g. Et_3N , $\text{p}K_a = 10.75$), and this weakness is found to be characteristic of bases in which the nitrogen atom is multiply bonded. This is due to the fact that as the nitrogen atom becomes progressively more multiply bonded, its lone pair of electrons is accommodated in an orbital that has progressively more *s* character. The electron pair is thus drawn closer to the nitrogen nucleus, and held more tightly by it, thereby becoming less available for forming a bond with a proton, with consequent decline in the basicity of the compound (*cf.* p. 59). On going $\text{>N:} \rightarrow \text{>N:} \rightarrow \text{>N:}$ in, for example, $\text{R}_3\text{N:} \rightarrow \text{C}_5\text{H}_5\text{N:} \rightarrow \text{RC}\equiv\text{N:}$, the unshared pairs are in sp^3 , sp^2 and sp orbitals, respectively, and the declining basicity is reflected in the two $\text{p}K_a$ values quoted above, and in the fact that the basicity of alkyl cyanides is very small indeed (MeCN , $\text{p}K_a = -4.3$).

With quinuclidine (17), however, the unshared electron pair is



(17)

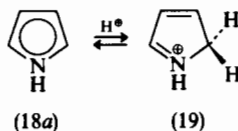
again in an sp^3 orbital and its related pK_a (10.95) is found to be very little different from that of triethylamine (10.75).

Pyrrole (18) is found to exhibit some aromatic character (though this is not so pronounced as with benzene or pyridine), and does not behave like a conjugated diene as might otherwise have been expected:



(18)

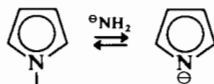
For such aromaticity to be achieved, six π electrons ($4n + 2$, $n = 1$) from the ring atoms must fill the three bonding molecular orbitals (*cf.* p. 17). This necessitates the contribution of two electrons by the nitrogen atom and, though the resultant electron cloud will be deformed towards nitrogen because of the more electronegative nature of that atom as compared with the four carbons, nitrogen's electron pair will not be readily available for taking up a proton (18a):



(18a)

(19)

Protonation, if forced upon pyrrole, is found to take place not on nitrogen but on the α -carbon atom (19). This occurs because incorporation of the nitrogen atom's lone pair of electrons into the aromatic $6\pi e$ system leaves the N atom positively polarised; protons tend to be repelled by it, and are thus taken up by the adjacent α -carbon atom. The basicity situation rather resembles that already encountered with aniline (p. 70) in that the cation (19) is destabilised with respect to the neutral molecule (18a). The effect is much more pronounced with pyrrole, however, for to function as a base it has to lose all aromatic character, and consequent stabilisation: this is reflected in its related pK_a (-0.27) compared with aniline's of 4.62, i.e. pyrrole is a very weak base indeed. It can in fact function as an acid, albeit a very weak one, in that the H atom of the NH group may be removed by strong bases, e.g. ${}^{\ominus}\text{NH}_2$; the resultant anion (20) then retains the aromatic character of pyrrole, unlike the cation (19):



(18a)

(20)