

23.17: Amines as Bases

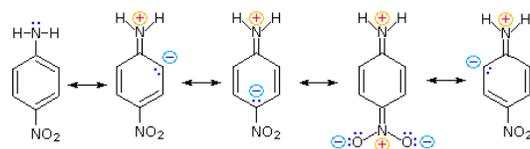
Basicity of Amines

A review of basic acid-base concepts should be helpful to the following discussion. Like ammonia, most amines are Brønsted and Lewis bases, but their base strength can be changed enormously by substituents. It is common to compare basicity's quantitatively by using the pK_a 's of their conjugate acids rather than their pK_b 's. Since $pK_a + pK_b = 14$, **the higher the pK_a the stronger the base**, in contrast to the usual inverse relationship of pK_a with acidity. Most simple alkyl amines have pK_a 's in the range 9.5 to 11.0, and their water solutions are basic (have a pH of 11 to 12, depending on concentration). The first four compounds in the following table, including ammonia, fall into that category.

The last five compounds (colored cells) are significantly weaker bases as a consequence of three factors. The first of these is the hybridization of the nitrogen. In pyridine the nitrogen is sp^2 hybridized, and in nitriles (last entry) an sp hybrid nitrogen is part of the triple bond. In each of these compounds (shaded red) the non-bonding electron pair is localized on the nitrogen atom, but increasing s -character brings it closer to the nitrogen nucleus, reducing its tendency to bond to a proton.

| | | | | | | | | | | |
|----------|------|------|------|--------|-----|-----|-----|-----|------|-----------------|
| Compound | | | | NH_3 | | | | | | $CH_3C\equiv N$ |
| pK_a | 11.0 | 10.7 | 10.7 | 9.3 | 5.2 | 4.6 | 1.0 | 0.0 | -1.0 | -10.0 |

Secondly, aniline and *p*-nitroaniline (first two green shaded structures) are weaker bases due to delocalization of the nitrogen non-bonding electron pair into the aromatic ring (and the nitro substituent). This is the same delocalization that results in activation of a benzene ring toward electrophilic substitution. The following resonance equations, which are similar to those used to explain the enhanced acidity of ortho and para-nitrophenols illustrate electron pair delocalization in *p*-nitroaniline. Indeed, aniline is a weaker base than cyclohexyl amine by roughly a million fold, the same factor by which phenol is a stronger acid than cyclohexanol. This electron pair delocalization is accompanied by a degree of rehybridization of the amino nitrogen atom, but the electron pair delocalization is probably the major factor in the reduced basicity of these compounds. A similar electron pair delocalization is responsible for the very low basicity (and nucleophilic reactivity) of amide nitrogen atoms (last green shaded structure). This feature was instrumental in moderating the influence of amine substituents on aromatic ring substitution, and will be discussed further in the section devoted to carboxylic acid derivatives.

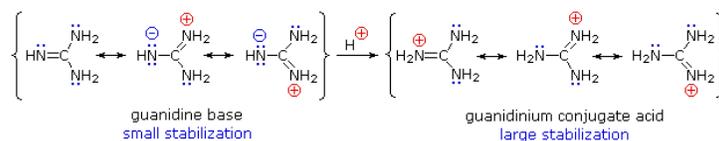


Reduced Basicity of *para*-Nitroaniline due to Electron Pair Delocalization

Conjugated amine groups influence the basicity of an existing amine. Although 4-dimethylaminopyridine (DMAP) might appear to be a base similar in strength to pyridine or *N,N*-dimethylaniline, it is actually more than ten thousand times stronger, thanks to charge delocalization in its conjugate acid. The structure in the gray box shows the locations over which positive charge (colored red) is delocalized in the conjugate acid. This compound is often used as a catalyst for acyl transfer reactions.

Finally, the very low basicity of pyrrole (shaded blue) reflects the exceptional delocalization of the nitrogen electron pair associated with its incorporation in an aromatic ring. Indole ($pK_a = -2$) and imidazole ($pK_a = 7.0$), see above, also have similar heterocyclic aromatic rings. Imidazole is over a million times more basic than pyrrole because the sp^2 nitrogen that is part of one double bond is structurally similar to pyridine, and has a comparable basicity.

Although resonance delocalization generally reduces the basicity of amines, a dramatic example of the reverse effect is found in the compound guanidine ($pK_a = 13.6$). Here, as shown below, resonance stabilization of the base is small, due to charge separation, while the conjugate acid is stabilized strongly by charge delocalization. Consequently, aqueous solutions of guanidine are nearly as basic as are solutions of sodium hydroxide.



The relationship of amine basicity to the acidity of the corresponding conjugate acids may be summarized in a fashion analogous to that noted earlier for acids:

Strong bases have weak conjugate acids, and weak bases have strong conjugate acids.

Important Reagent Bases [Edit section](#)

The significance of all these acid-base relationships to practical organic chemistry lies in the need for organic bases of varying strength, as reagents tailored to the requirements of specific reactions. The common base sodium hydroxide is not soluble in many organic solvents, and is therefore not widely used as a reagent in organic reactions. Most base reagents are alkoxide salts, amines or amide salts. Since alcohols are much stronger acids than amines, their conjugate bases are weaker than amide bases, and fill the gap in base strength between amines and amide salts. In the following table, pK_a again refers to the conjugate acid of the base drawn above it.

| Base Name | Pyridine | Triethyl Amine | Hünig's Base | Barton's Base | Potassium t-Butoxide | Sodium HMDS | LDA |
|-----------|----------|----------------|--------------|---------------|----------------------------|------------------------|--------------------------|
| Formula | | $(C_2H_5)_3N$ | | | $(CH_3)_3CO^{(-)} K^{(+)}$ | $(CH_3)_3SiI_2N^{(-)}$ | $(CH_3)_2CH)_2N^{(-)} I$ |
| pK_a | 5.3 | 10.7 | 11.4 | 14 | 19 | 26 | 35.7 |

Pyridine is commonly used as an acid scavenger in reactions that produce mineral acid co-products. Its basicity and nucleophilicity may be modified by steric hindrance, as in the case of 2,6-dimethylpyridine ($pK_a=6.7$), or resonance stabilization, as in the case of 4-dimethylaminopyridine ($pK_a=9.7$). Hünig's base is relatively non-nucleophilic (due to steric hindrance), and like DBU is often used as the base in E2 elimination reactions conducted in non-polar solvents. Barton's base is a strong, poorly-nucleophilic, neutral base that serves in cases where electrophilic substitution of DBU or other amine bases is a problem. The alkoxides are stronger bases that are often used in the corresponding alcohol as solvent, or for greater reactivity in DMSO. Finally, the two amide bases see widespread use in generating enolate bases from carbonyl compounds and other weak carbon acids.

Contributors

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