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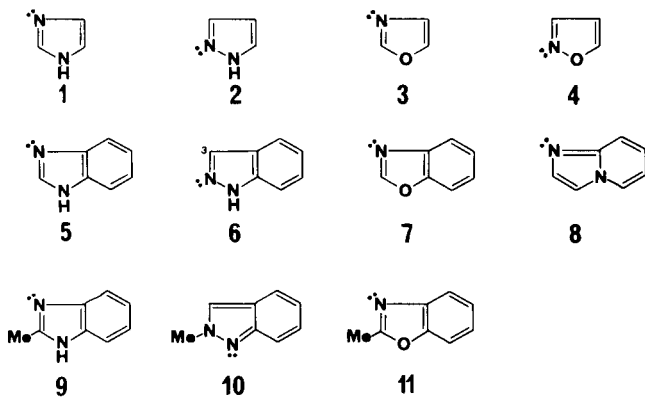
A plot of  $pK_a$  values for eleven azoles and benzazoles *vs* the experimental ionization energy of the nitrogen lone pair shows the existence of three groups of compounds: simple unsubstituted azoles (imidazole, pyrazole, oxazole, isoxazole), unsubstituted benzazoles (benzimidazole, 1*H*-indazole and benzoxazole, including imidazo [1,2-*a*]pyridine) and benzazoles carrying a methyl group  $\alpha$ - to the basic centre (2-methylbenzimidazole, 2-methylindazole and 2-methylbenzoxazole).

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In previous papers of these series [2-4] we have shown that a good correlation exists between  $pK_a$  values (measured in water) and calculated lone pair energies,  $\epsilon_N$ , for pyrazoles and imidazoles. The annelation (imidazole-benzimidazole) [2] and the presence of methyl group  $\alpha$  to the basic center (methylimidazoles and -pyrazoles) [3] causes a decrease in the basicity in water solution, due to steric hindrance and charge dispersion.

We wish to report here an extension to oxygenated derivatives [5], but instead of using calculated  $\epsilon_N$  values we would base our discussion on nitrogen-lone pair vertical ionization energies determined by photoelectron spectroscopy  $LP_N$ (eV). It is well established that for a series of heterocycles (pyridines, imidazoles, *etc.*) [6,7] there is a linear correlation between  $pK_a$ 's and  $LP_N$ .

We have found in the literature the  $pK_a$  and  $LP_N$  values for eleven compounds of the families mentioned above:



It must be stressed that several  $pK_a$  values can be found for each compound (although the dispersion is not large) and even different values for the ionization potentials. Concerning the  $pK_a$ 's it is necessary to take into account the "statistical factor" [3,8] when comparing NH with

*N*-substituted (as **10**) or oxygen derivatives. Since the 1*H*-tautomer is much more stable than the 2*H*-tautomer in indazoles [8], the cation corresponding to compound **6** can lose only one proton (that on N<sub>2</sub>) and thus it must be treated as a *N*-substituted derivative.

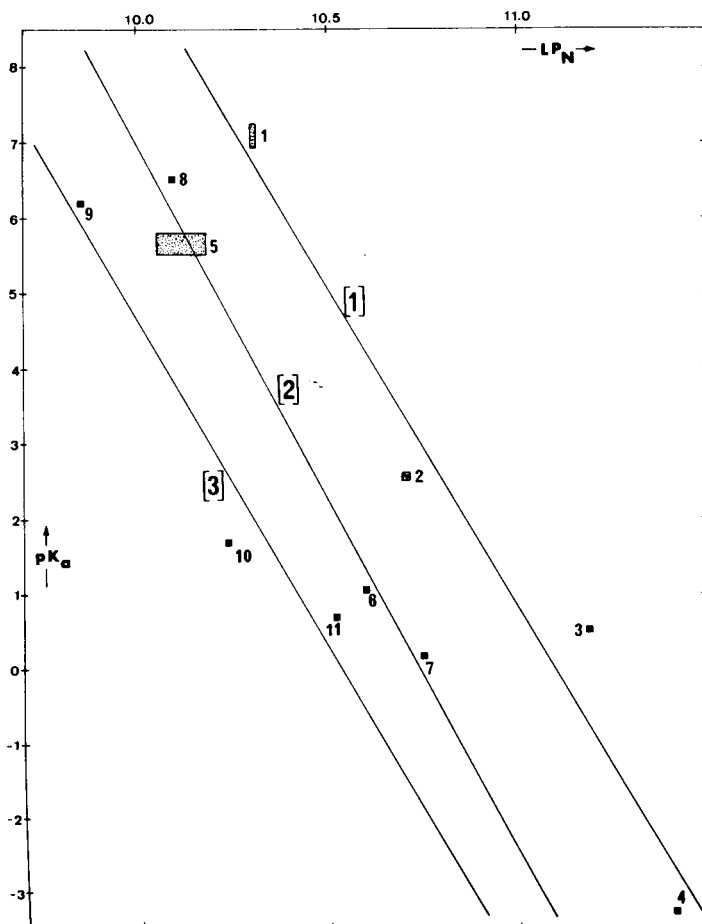


Table  
Experimental Values for Azoles and Benzazoles

Compound	LP <sub>N</sub> (exp) eV	pK <sub>a</sub> (exp) (25°C)	Corrected values
Imidazole <b>1</b>	10.3 [9]	6.95 [13], 7.22 [14]	-
Pyrazole <b>2</b>	10.7 [9]	2.52 [15], 2.56 [14]	-
Oxazole <b>3</b>	11.19 [9]	0.8 [16]	0.5
Isoxazole <b>4</b>	11.41 [9]	-2.97 [18]	-3.27
Benzimidazole <b>5</b>	10.18 [9], 10.05 [10]	5.48 [19], 5.77 [14]	-
Indazole <b>6</b>	10.6 [10]	1.31 [10]	1.01
Benzoxazole <b>7</b>	10.75 [11]	0.5 [21]	0.2
Imidazo[1,2- <i>a</i> ]pyridine <b>8</b>	10.09 [12]	6.79 [22]	6.49
2-Methylbenzimidazole <b>9</b>	9.86 [11]	6.19 [24]	-
2-Methylindazole <b>10</b>	10.24 [9]	2.02 [20]	1.72
2-Methylbenzoxazole <b>11</b>	10.52 [11]	0.99 [21]	0.69

In the figure we plot pK<sub>a</sub> vs LP<sub>N</sub>. Clearly all compounds fall in one of three groups:

- Monocyclic compounds (**1**, **2**, **3**, **4**):

$$pK_a = 93.7 - 8.4 LP_N \quad n = 4, CC^2 = 0.949 \quad [1]$$

- Bicyclic compounds (**5**, **6**, **7**, **8**):

$$pK_a = 101.5 - 9.4 LP_N \quad n = 4, CC^2 = 0.988 \quad [2]$$

-  $\alpha$ -Methyl bicyclic compounds (**9**, **10**, **11**):

$$pK_a = 89.9 - 8.5 LP_N \quad n = 3, CC^2 = 0.934 \quad [3]$$

From these results it can be concluded:

- 1) There is a parallelism between proton affinities (directly related to LP<sub>N</sub> [3]) and aqueous basicities for azoles containing nitrogen and oxygen.
- 2) The annelation decreases the aqueous basicity by about 2.8 pK<sub>a</sub> units (at 10.5 eV).
- 3) The presence of a methyl group  $\alpha$  to the basic nitrogen further decreases the basicity by about 2.0 pK<sub>a</sub> units (at 10.5 eV) [25].

In the vapour phase the intrinsic basicity will follow the LP<sub>N</sub> values, and as benzimidazole is experimentally more "basic" than imidazole in the vapour phase [2], indazole and benzoxazole should be stronger bases than pyrazole and oxazole, respectively.

#### REFERENCES AND NOTES

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[22] Value determined at 20° [23].

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[25] It is interesting that using Eq (3) (which corresponds to  $\alpha$ -methyl bicyclic compounds) we find for 3 Cl-indazole (LP<sub>N</sub>(exp) = 10.80 eV [10]) a "corrected" value of pK<sub>a</sub> = -1.9, which coincides with the "corrected" experimental value of -1.97 [20]