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Some Studies in Molecular Orbital Theory

II. Ionization Constants in Heteroaromatic Amines and Related Compounds*

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The relative basicities of a series of mono-aza-aromatic amines are calculated by a very simple application of LCAO molecular orbital theory. Rough quantitative agreement between theory and experiment is obtained if the heterocyclic nitrogen atom is supposed to take up the proton; on the other hand, if the amine group is assumed to add the proton in the first ionization, the observed basicities are negatively correlated with theory.

It is also shown how the qualitative differences in reactivity between methyl-aza-hydrocarbons and between heteroaromatic phenols may be understood in similar very simple terms.

1. INTRODUCTION

IN recent years much valuable experimental data¹⁻³ has been obtained as to the basic strengths of aromatic amines. In particular, a comprehensive collection of data has been published by Albert, Goldacre, and Phillips,¹ who recorded ionization constants for 120 heterocyclic bases belonging to 30 different, completely unsaturated ring systems. These authors assumed that in heterocyclic amines such as the amino-pyridines, the first proton adds to the heterocyclic nitrogen atom rather than to the amino group; and on this assumption they interpreted their results qualitatively in terms of resonance possibilities in the amine and its cation.

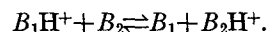
In this paper the ionization constants given by Albert, Goldacre, and Phillips will be discussed quantitatively in terms of LCAO molecular orbital theory. Attention will be confined to those bases which are derived from cata-condensed hydrocarbons by replacing a CH group by N, and attaching an NH₂ at some external position. The results confirm the view that the heterocyclic nitrogen adds the first proton; and quantitative calculation shows that the observed differences in basicity are mainly caused by differences in resonance energy, in agreement with Albert, Goldacre, and Phillips.

In interpreting the experimental results theoretically, first-order perturbation theory has been used, for two reasons: (1) because it minimizes the number of unknown parameters that have to be introduced into the calculations—indeed, only one unknown parameter enters into the final results; and (2) because the use of perturbation theory tremendously simplifies the mathematics.

2. POSTULATES

Any comparison of the dissociation constants of two bases B_1 and B_2 in a given solvent at a given tempera-

ture amounts to a consideration of the equilibrium



Hammett⁴ has discussed in detail how the equilibrium constant for such a reaction is related to the kinetic and potential energies of reaction. Let

$$\Delta G^0 = -RT \log K$$

be the standard free energy change in the reaction, K being the equilibrium constant. Then, as Hammett points out, if the partition functions of the species B_1H^+ , B_1 , B_2H^+ , and B_2 are related by the equation

$$\frac{f_{B_1H^+}}{f_{B_1}} = \frac{f_{B_2H^+}}{f_{B_2}},$$

it is possible to use ΔG^0 as a measure of the potential energy change ΔE_P occurring in the reaction. (Strictly speaking, this would only be true in a solvent of infinite dielectric constant, and electrostatic interaction terms should be taken into account; but these will be less important the more alike the charge distributions in B_1H^+ and B_2H^+ .)

Now for bases of the type discussed in this paper, the change in potential energy ΔE_P will be principally due to the difference in unsaturation energy between the species on the right-hand side of the equation and those on the left. For simplicity it will be assumed that strict equality holds, that is:

$$\Delta E_P = \Delta \mathcal{E}_2 - \Delta \mathcal{E}_1,$$

where $\Delta \mathcal{E}_2$ is the difference in unsaturation energy between B_2H^+ and B_2 , and $\Delta \mathcal{E}_1$ is defined similarly. This assumption cannot be entirely correct, but it is a reasonable initial hypothesis, and may be tested by its consequences.

In order to establish a connection with the experimental data, it is further necessary to assume that Hammett's condition holds, i.e., that f_{BH^+}/f_B has the same value for all the bases considered; this amounts to

* L. P. Hammett, *Physical Organic Chemistry* (McGraw-Hill Book Company, Inc., New York, 1940).

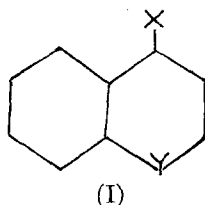
* Work done under ONR, Task Order IX of Contract N6ori-20, with the University of Chicago.

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¹ Albert, Goldacre, and Phillips, *J. Chem. Soc.* 2240 (1948).

² A. Albert and R. J. Goldacre, *J. Chem. Soc.* 706 (1946).

³ A. Albert and R. J. Goldacre, *J. Chem. Soc.* 454 (1943).



saying that the entropies of ionization of heteroaromatic amines are roughly equal. This is an optimistic assumption, but cannot be avoided, as no entropy data are available at present.

The above postulates may be summarized in the equations

$$\Delta\epsilon_2 - \Delta\epsilon_1 \simeq \Delta E_F \simeq \Delta G^0 = -RT \log K$$

$$= 2.3RT(pKa_1 - pKa_2)$$

or, dropping suffixes,

$$2.3RTpKa = \text{const.} - \Delta\epsilon.$$

3. METHOD OF CALCULATING $\Delta\epsilon$

The principle of the method is to assume that the wave function for the π -electrons in a conjugated molecule containing one or two heteroatoms is the same as in the "parent" hydrocarbon—that is, the hydrocarbon with the same arrangement of atomic p orbitals and the same number of π -electrons. The unsaturation energy ϵ of the heteromolecule is then obtained from the π -wave function of the parent hydrocarbon by first-order perturbation theory, assuming that structural differences between the heteromolecule and its parent hydrocarbon may be regarded as perturbations applied to the Hamiltonian of the latter.

The procedure is probably best illustrated by an example. Consider the set of molecules (I) where X stands for H, CH₃, CH₂⁻, NH₂, or NH₃⁺, and Y stands for CH, N, NH⁺, or NR⁺. If hyperconjugation is neglected, the molecules with X=H, CH₃, or NH₃⁺ have naphthalene (II) as their parent hydrocarbon, whereas those with X=CH₂⁻ or NH₂ are derived from the carbanion (III). Now it is known⁵ that if r is an atom in a conjugated system, and if the Coulomb integral of atom r is altered by a small amount $\delta\alpha_r$, then the change in unsaturation energy of the system is given by

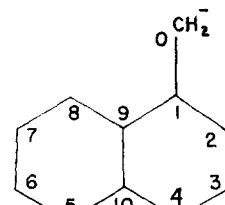
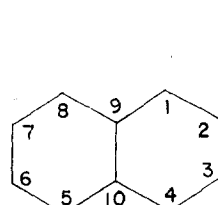
$$\delta\epsilon = q_r \delta\alpha_r,$$

where q_r is the π -electron density at position r . It follows that on passing from (II) or (III) to one of the heteromolecules (I), the change in unsaturation energy can be

TABLE I. Unsaturation energies in molecules of Type (I).

X =	H or CH ₃	NH ₃ ⁺	CH ₂ ⁻	NH ₂
Y = CH	ϵ_0	$\epsilon_0 + z$	ϵ_1	$\epsilon_1 + q_0 y$
N	$\epsilon_0 + x$	$\epsilon_0 + x + z$	$\epsilon_1 + q_4 x$	$\epsilon_1 + q_4 x + q_0 y$
NH ⁺ or NR ⁺	$\epsilon_0 + y$	$\epsilon_0 + y + z$	$\epsilon_1 + q_4 y$	$\epsilon_1 + q_4 y + q_0 y$

⁵ C. A. Coulson and H. C. Longuet-Higgins, Proc. Roy. Soc. A191, 39 (1947).



expressed in terms of the electron densities in the parent hydrocarbon and the changes in Coulomb integral at the affected atoms.

The π -electron densities are known to be unity at every position in naphthalene;⁶ but the π -electron densities in (III) will not necessarily be equal to one, and their values at the CH₂⁻ group and the four-position may be denoted by q_0 and q_4 , respectively. Then, if ϵ_0 and ϵ_1 denote the unsaturation energies of (II) and (III), the unsaturation energies of the molecules (I) will be as listed in Table I.

In Table I, x denotes the difference in Coulomb integral between aromatic CH and N, y denotes the difference in Coulomb integral between

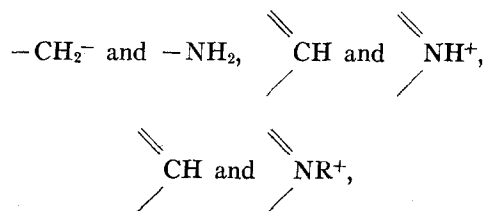


TABLE II. Changes in unsaturation energy for some ionization reactions.

(1)		$\Delta\epsilon = y - x$
(2)		$\Delta\epsilon = \begin{cases} \epsilon_0 - \epsilon_1 \\ +z - q_0 y \end{cases}$
(3)		$\Delta\epsilon = q_4(y - x)$
(4)		$\Delta\epsilon = \begin{cases} \epsilon_0 - \epsilon_1 \\ +x + z \\ -q_4 x - q_0 y \end{cases}$
(5)		$\Delta\epsilon = \begin{cases} \epsilon_1 - \epsilon_0 \\ +x + z \\ +q_4 y - y \end{cases}$

⁶ C. A. Coulson and S. Rushbrooke, Proc. Camb. Phil. Soc. 36, 193 (1940).

TABLE III. Base strengths of some heterocyclic systems.

Base	pK_a in aqueous solution	pK_a in 50 percent aqueous ethanol
Pyridine	5.23	—
Quinoline	4.94	—
Acridine	5.60	4.11*
Isoquinoline	5.14	—
5,6-benzquinoline	5.15	3.90
6,7-benzquinoline	5.05	3.84
7,8-benzquinoline	4.25	3.15
Phenanthridine	—	3.30
3,4-benzacridine	4.70	4.16
2,3-benzacridine	—	4.52
1,2-benzacridine	—	3.45

* This figure is taken from Albert and Goldacre (see reference 2).

and z is the change in Coulomb integral of an aromatic CH group when the H atom is replaced by $-\text{NH}_3^+$.

(It is assumed that methyl substitution does not affect appreciably the Coulomb integral of aromatic carbon.)

From Table I it is possible to deduce $\Delta\mathcal{E}$, the change in unsaturation energy in some ionization reactions; and Table II gives values of $\Delta\mathcal{E}$ for five different possible ionizations.

(In reactions (3) and (5) the species on the right-hand side have important resonance structures in which the charges are disposed in a different way from that shown in Table II. However, this fact is irrelevant when these reactions are discussed in terms of molecular orbital theory: the additional stabilization arising from such resonance is implicit in the expressions given for $\Delta\mathcal{E}$.)

The data in Table II lead to some interesting conclusions. For reaction (1) the change in \mathcal{E} is seen to be independent of \mathcal{E}_0 and \mathcal{E}_1 ; and is simply equal to the difference in Coulomb integral between the groups

N and NH^+ . The essential reason for this is that in

naphthalene the π -electron density is unity at the four-position, and this is a special case of the Coulson-Rushbrooke theorem⁶ that in any hydrocarbon containing no odd-membered rings the π -electron density is unity at every position. It follows from this theorem that to a first approximation the value of $\Delta\mathcal{E}$ and hence of pK_a should be the same for all mono-aza-derivatives of such hydrocarbons under given conditions. Table III gives the pK_a values for all the alternant aza-hydrocarbons so far studied experimentally; the data are taken from Albert, Goldacre, and Phillips,¹ and refer to 20°C. It will be seen that apart from acridine, which has a high value of pK_a in water but not in aqueous alcohol, the figures in the two columns of Table III show little variation. The observed differences are relatively small when compared to those occurring in the amino-derivatives discussed below, and may be in part due to differences in activity coefficient, associated with the large

differences in solubility between the various bases.⁷ In any case, discrepancies would be expected in view of the severe approximations made in Section 2.

Another important feature of Table II is that it provides a theoretical basis for deciding whether, in a given series of amines, ionization involves the heterocyclic nitrogen atom or the amine group. Craig and Short,⁸ from a study of electronic absorption spectra, established that in the amino-acridines it is the nuclear nitrogen atom which first adds a proton; but it is not known how widely this is true for heteroaromatic amines. Consider, for example, the various aza-derivatives of 1-naphthylamine, all of which have the carbanion (III) as their parent hydrocarbon. (The following argument would not hold for the various amino-quinolines, as these are not all derived from the same parent hydrocarbon.) If the ionization of r -aza-1-naphthylamine is represented by Eq. (3) in Table II, then $\Delta\mathcal{E}$, is given by

$$\Delta\mathcal{E}_r = q_r(y-x),$$

where q_r is the π -electron density at position r in (III).

Now NH^+ is more electron-attracting than N , so $y-x$ is negative; hence a plot of $\Delta\mathcal{E}_r$ against q_r for various values of r should have a negative slope. But by hypothesis

$$2.3RTpK_a = \text{const.} - \Delta\mathcal{E},$$

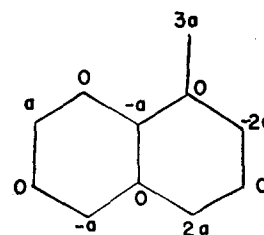
so if Eq. (3) represents the ionization correctly, a plot of pK_a against q_r should have a positive slope. Suppose, on the contrary, that the ionization of r -aza-1-naphthylamine is correctly represented by Eq. (4). In this case we have

$$\Delta\mathcal{E} = \mathcal{E}_0 - \mathcal{E}_1 + x + z - q_r x + q_0 y.$$

Here all the terms except q_r are the same for different values of r , so the last equation may be written

$$\Delta\mathcal{E} = -q_r x + \text{const.}$$

But N attracts electrons more strongly than CH , so x is negative, and a plot of pK_a against q_r should have a



(IV)

$$(20a^2 = 1.)$$

⁷ Kolthoff, Lingane, and Larson, J. Am. Chem. Soc. **60**, 2512 (1938).

⁸ D. P. Craig and L. N. Short, J. Chem. Soc. 419 (1945).

TABLE IV. Values of net charge and acidity constant for some aza-1-naphthylamines.

Amine	$q_r - 1$	pK_a in water at 20°
2-aza-1-naphthylamine (1-amino-isoquinoline)	0.200	7.62
4-aza-1-naphthylamine (α -amino-quinoline)	0.200	9.17
5-aza-1-naphthylamine (5-amino-quinoline)	0.050	5.46
8-aza-1-naphthylamine (8-amino-quinoline)	0.000	3.99

negative slope. Therefore, in order to distinguish between the possibilities (3) and (4), it is only necessary to determine whether a plot of pK_a against q_r has a positive or a negative slope, assuming, of course, that the ionization proceeds by the same mechanism for the different amines in the series.

4. CALCULATION OF q_0 AND q_r

Before discussing the other ionizations formulated in Table II, we shall show how the electron densities q_0 and q_r may be calculated for the carbanions of Type (III). The calculation is made extremely simple by the following general theorems:⁹

(i) In a singly ionized carbanion containing no odd-membered rings, the net negative charge $q_r - 1$ at atom r is given by

$$q_r - 1 = (c_r^0)^2,$$

TABLE V.

Serial No.	Amine	Parent carbanion	$(q_r - 1)$	pK_a in water at 20°C	Anomaly (if any)
12	2-amino-pyridine	A	1/7=0.143	6.86	Ortho
13	3-amino-pyridine	A	0=0.000	5.98	—
14	4-amino-pyridine	A	1/7=0.143	9.17	—
16	2-amino-quinoline	C	4/17=0.235	7.34	Ortho
17	3-amino-quinoline	C	0=0.000	4.95	—
18	4-amino-quinoline	B	4/20=0.200	9.17	—
19	5-amino-quinoline	B	1/20=0.050	5.46	—
20	6-amino-quinoline	C	0=0.000	5.63	—
21	7-amino-quinoline	C	1/17=0.059	6.65	—
22	8-amino-quinoline	B	0=0.000	3.99	Peri
26	5-amino-acridine	D	4/14=0.286	9.99	—
27	4-amino-acridine	E	4/42=0.095	6.04	—
28	3-amino-acridine	F	0=0.000	5.88	—
29	2-amino-acridine	F	4/34=0.118	8.04	—
30	1-amino-acridine	E	0=0.000	4.40	Peri
36	8-amino-1-aza-phenanthrene	H	1/54=0.019	5.20	—
38	5-amino-1-aza-phenanthrene	L	0=0.000	5.03	—
46	3-amino-1-aza-anthracene	F	0=0.000	4.78	—
54	9-amino-phenanthridine	G	16/56=0.286	7.31	Ortho
60	1-amino-isoquinoline	B	4/20=0.200	7.62	Ortho
64	8-amino-2,3-benzacridine	Q	9/99=0.091	7.42	—
75	8-amino-1,2-benzacridine	P	9/102=0.088	6.72	—

⁹ H. C. Longuet-Higgins, Paper I of this series, J. Chem. Phys. 18, 265 (1950).

TABLE VI.

Serial No.	Amine	Parent carbanion	$(q_r - 1)$	pK_a at 20°C in 50 percent ethanol	Anomaly (if any)
26	5-amino-acridine	D	4/14=0.286	9.45*	—
27	4-amino-acridine	E	4/42=0.095	5.50*	—
28	3-amino-acridine	F	0=0.000	5.03*	—
29	2-amino-acridine	F	4/34=0.118	7.61*	—
30	1-amino-acridine	E	0=0.000	3.59*	Peri
32	4-amino-1-aza-phenanthrene	L	9/51=0.176	7.99	—
36	8-amino-1-aza-phenanthrene	H	1/54=0.019	4.10	—
37	7-amino-1-aza-phenanthrene	J	0=0.000	4.02	—
41	4-amino-1-aza-acridine	E	9/42=0.214	8.75	—
46	3-amino-1-aza-acridine	F	0=0.000	3.73	—
48	1-amino-4-aza-phenanthrene	H	9/54=0.167	7.68	—
54	9-amino-phenanthridine	G	16/56=0.286	6.75	Ortho
62	5-amino-3,4-benzacridine	M	36/144=0.250	8.41	—
63	7-amino-3,4-benzacridine	P	0=0.000	5.03	—
64	8-amino-3,4-benzacridine	Q	9/99=0.091	6.51	—
68	5-amino-2,3-benzacridine	R	36/120=0.300	9.72	—
70	7-amino-2,3-benzacridine	S	0=0.000	5.38	—
73	5-amino-1,2-benzacridine	N	36/156=0.231	8.13	—
74	7-amino-1,2-benzacridine	Q	0=0.000	4.05	—
75	8-amino-1,2-benzacridine	P	9/102=0.088	5.97	—

where $\psi^0 = \sum_r c_r^0 \phi_r$ is the highest occupied molecular orbital.

(ii) If the carbanion contains an odd number of p atomic orbitals, the orbital ψ^0 has zero binding energy, and, furthermore, the coefficients c_r^0 have non-zero

TABLE VII.

Serial No.	Amine	Parent carbanion	$(q_r - 1)$	pK_a at 20°C in 50 percent ethanol	Anomaly (if any)
33	4-amino-2-methyl-1-aza-phenanthrene	L	9/51=0.176	8.45	—
35	2-amino-4-methyl-1-aza-phenanthrene	J	9/46=0.195	6.51	Ortho
42	4-amino-2-methyl-1-aza-anthracene	E	9/42=0.214	9.45	—
49	1-amino-3-methyl-4-aza-phenanthrene	H	9/54=0.167	7.96	—
50	3-amino-1-methyl-4-aza-phenanthrene	K	9/49=0.184	6.02	Ortho
51	9-amino-3-methyl-4-aza-phenanthrene	G	0=0.000	5.23	—
52	8-amino-3-methyl-4-aza-phenanthrene	H	0=0.000	4.75	—
55	2-amino-9-methyl-phenanthridine	J	1/46=0.022	5.66	—
56	7-amino-9-methyl-phenanthridine	J	0=0.000	5.23	—

values only at those atoms r which bear a formal charge in one or more of the principal resonance structures.

As an illustration, consider again the carbanion (III). To calculate the π -electron densities we must first find the coefficients c_r^0 . By (ii), these coefficients will vanish at positions 1, 3, 6, 8, and 10, as these are separated from the CH_2^- group by odd numbers of bonds, and therefore cannot bear a negative charge in any of the principal resonance structures. Now, as is well known,¹⁰ the coefficients c_r in a MO must satisfy the equations

$$-\epsilon c_r + \sum_{s \neq r} \beta_{rs} c_s = 0, \text{ for all positions } r,$$

where ϵ is the binding energy and β_{rs} is the resonance integral between orbitals ϕ_r and ϕ_s . For the orbital ψ^0 , ϵ is zero; so the equations become

$$\sum_{s \neq r} \beta_{rs} c_s^0 = 0, \text{ for all } r.$$

Further, β_{rs} will have roughly the same value β for all bonded pairs of atoms, and will be zero if r and s are not bonded. It follows that for each atom r , the coefficients c_s^0 at the adjacent atoms must add up to zero. Returning to the example (III), we see that if the coefficient c_7^0 equals a , the other coefficients c_r^0 must be as shown in (IV). The normalization condition requires that $20a^2 = 1$, so that $a = 1/(20)^{1/2}$. Therefore in (III) the net charges are: 9/20 at the CH_2 group, 4/20 at the 2 and 4 positions, 1/20 at the 5, 7, and 9 positions, and zero elsewhere.

5. RELATION BETWEEN q_r AND pK_a

Table IV gives a comparison between the acidity constants of various aza-1-naphthylamines, determined by

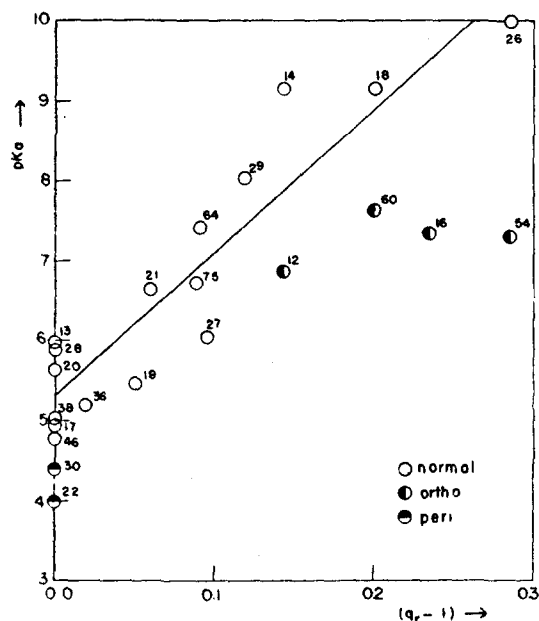


Fig. 1.

¹⁰ C. A. Coulson and H. C. Longuet-Higgins, Proc. Roy. Soc. A192, 16 (1947).

Albert, Goldacre, and Phillips, and the appropriate values of $q_r - 1$, determined in the previous section. The function pK_a is seen to increase with q_r , except that the first amine is less basic than the second, and this exception may be explained as an "ortho" anomaly in 1-amino-isoquinoline. It follows from the argument of Section 3, that the proton adds to the heterocyclic nitrogen atom rather than to the amino group.

Tables V-VII give values of $q_r - 1$ and pK_a for a wide variety of amines, derived from eleven different heteroaromatic ring systems. The first column gives the serial number allotted to each amine by Albert, Goldacre, and Phillips. The letter in the third column denotes which of the carbanions in the Appendix is the "parent" hydrocarbon; the fourth column gives the net charge $q_r - 1$ obtained from this carbanion; the fifth column gives the experimental pK_a value. All the values of pK_a are taken from Albert, Goldacre, and Phillips,¹ except for those marked with an asterisk, which are taken from Albert and Goldacre.² The measurements were all made at 20°C; those in Table V refer to aqueous solution, and those in Tables VI and VII to solution in 50 percent ethanol. All the amines considered contain just one NH_2 group and one heterocyclic nitrogen atom, and are derived from even-membered ring systems; the amines in Table VII contain also a methyl group attached to the aromatic system, but amines containing other side groups have not been considered. Within the field defined by these restrictions, all the available experimental data are presented in Tables V-VII; and Figs. 1-3 give the same data plotted in graphical form.

DISCUSSION OF RESULTS

Although the points in Figs. 1-3 are somewhat scattered, there does seem to be a roughly linear relationship

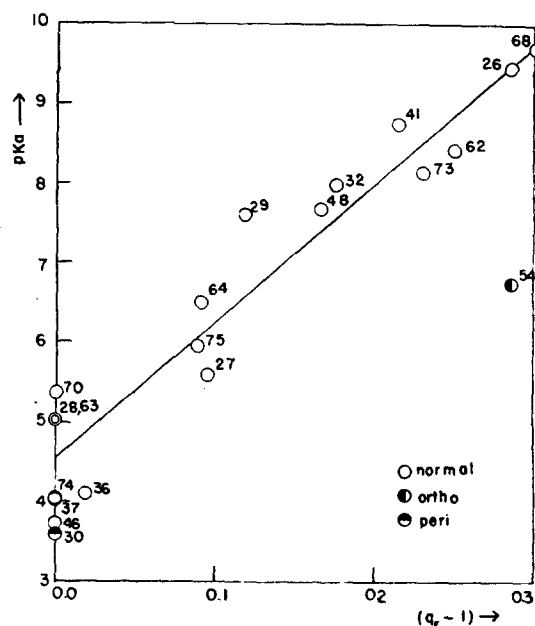


Fig. 2.

between pK_a and q_r for those amines in which the NH_2 group is not too close to the heterocyclic nitrogen atom. The bases which deviate most widely from the general trend are, almost without exception, those in which the NH_2 group is either in the *ortho* or in the *peri* position with respect to the nuclear nitrogen; and, as suggested by Albert and Goldacre,² this anomaly is probably an instance of the well-known and widely occurring "ortho effect." With this comment, such anomalous molecules will be dismissed from further consideration. The straight lines in Figs. 1-3 have been drawn to give the

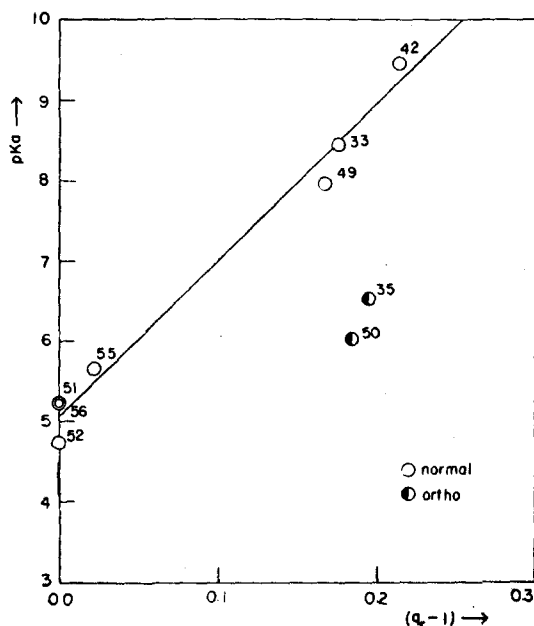


FIG. 3.

best general fit with the remaining points; the fact that these lines have a positive rather than a negative slope is strong evidence that the ionization of the amines in Tables V-VII involves the nuclear nitrogen rather than the NH_2 group, as anticipated earlier.

In judging the present simple theory by the data given in Figs. 1-3, it must be remembered that many serious approximations have been made in establishing the correlation between q_r and pK_a . Quite apart from the usual errors inherent in simple LC AO MO theory, it cannot, for instance, be correct to regard the replacement of CH_2^- by NH_2 as a small perturbation; also addition of the proton to the nuclear nitrogen atom will certainly modify the π -wave function considerably, and introduce second-order corrections to the energy. However, there is a compensating factor which makes the former assumption, at least, less drastic than it would otherwise be. This factor is the influence of the charge at an atom on its Coulomb integral. If the charges in 1-naphthylamine, for instance, are anywhere near those calculated for the carbanion (III), the excess electron density at the nitrogen atom will reduce its electron

affinity considerably, perhaps to a value which hardly differs from the value for aromatic carbon; and the charge distribution calculated for (III) may even be a better approximation for the amine than for the carbanion.

Again, it cannot be strictly correct to assume that the difference in free energy of ionization between two bases, is equal to the difference between their values of $\Delta\mathcal{E}$: differences in entropy of ionization and electrostatic energy terms should really be taken into consideration. So it would be naïve to expect a precise linear relation between the theoretical q_r and the experimental pK_a ; indeed, when all the possible errors are considered, it is encouraging that the observed correlation is as good as it is.

One other point may be noted here, as it illustrates the fundamental agreement between qualitative resonance theory and molecular orbital theory. The form of the zero-energy MO ψ^0 demands that the net charge $q_r - 1$ be zero at every atom separated from the amino group by an odd number of bonds. Therefore all amines, in which there is an odd number of bonds between the heterocyclic atom and the amino group, should have approximately the same base strength, in agreement with qualitative resonance theory. This expectation is roughly confirmed by the experimental results.

CALCULATION OF $y-x$

From the slope of the graphs in Figs. 1-3, it is possible to obtain an order of magnitude for $y-x$, the difference

in Coulomb integral between heterocyclic N and

heterocyclic NH^+ . The theoretical slope is determined by the equations

$$\begin{aligned}(q_r - q_r')(y - x) &= \Delta\mathcal{E} - \Delta\mathcal{E}' \\ &= \Delta F - \Delta F' = RT \log_e K_a / K_a' \\ &= -2.3RT(pK_a - pK_a'),\end{aligned}$$

where primed and unprimed quantities refer to two different bases. The observed slopes of the three lines are 18, 18, and 20 \log_{10} per unit of charge. It follows that

$$(y-x)/(2.3RT) = 18,$$

whence $y-x$ is approximately 24,000 cal./mole. The usual value assigned to β , the carbon-carbon resonance integral, is 20,000 cal./mole, so $y-x$ is approximately 1.2β . The probable error in this figure is large, perhaps ± 20 percent, but the value may be found useful in later computations.

RELATED REACTIONS

There are other important types of reaction that can be discussed in terms of the theoretical ideas put

forward in this paper. Consider, for example, the ionization of methyl groups attached to heteroaromatic systems. This process is represented by reaction (5) in Table II, and involves a change in unsaturation energy given by

$$\Delta\mathcal{E} = \mathcal{E}_1 - \mathcal{E}_0 + q_r y - y - z.$$

This equation implies that ionization of a methyl group attached to a heteroaromatic system proceeds more easily the greater the charge q_r at the heteroatom. But, as shown already, q_r is positively correlated with the basic strength of the corresponding heteroaromatic amine. Therefore, given a series of s -amino- r -aza-derivatives (where s is fixed and r varies), it may be predicted that the more basic the amino-derivative, the more easily ionized will be the CH_3 group of the corresponding methyl derivative, especially when the nuclear nitrogen atom is quaternated. This has been known as a qualitative fact for some time: for example, the high reactivity of the N -methyl-4-methyl-quinolinium ion is naturally interpreted as due to easy ionization of the 4-methyl group; but there seem to be no quantitative data at present to confirm or contradict the prediction that the values of $\Delta\mathcal{E}$ for the two types of reaction should be linearly related.

Or again, consider the ionization of a heteroaromatic phenol. There is good evidence that the $-\text{O}^-$ group conjugates much more strongly with an aromatic system than the $-\text{OH}$ group; and this is presumably due to the high electron affinity of OH relative to O^- , which makes structures involving $=\text{O}$ more stable than those involving $=\text{OH}^+$. Denote by v the change in Coulomb integral of a CH group when the H atom is replaced by OH , and denote by w the difference in Coulomb integral between $-\text{CH}_2^-$ and $-\text{O}^-$. Then, by similar arguments

to those of Section 3, the change in unsaturation energy on ionization of an r -aza-phenol is given by

$$\begin{aligned}\Delta\mathcal{E} &= (\mathcal{E}_1 + q_0 w + q_r x) - (\mathcal{E}_0 + v + x) \\ &= \mathcal{E}_1 - \mathcal{E}_0 + q_r x + q_0 w - x - v.\end{aligned}$$

That is, in a series of r -aza-derivatives of a given aromatic phenol, the acidity of the OH group will be greater the greater the electron density at the r -position. Now the greater q_r , the greater also the basicity of the heterocyclic nitrogen atom; and indeed it is found that in molecules such as 4-hydroxy-pyridine or 5-hydroxy-acridine, for which the value of q_r in the parent carbanion is high, the phenolic proton actually migrates from the OH group to the nuclear nitrogen atom, giving a pyridone or acridone. As yet, very little quantitative data is available as to the ionization constants of heteroaromatic phenols; from the theoretical standpoint such data would be of great interest.

CONCLUSION

The perturbation theory outlined here makes it possible to calculate relative rate constants and equilibrium constants for many types of reaction without having to solve completely the secular equations. For example, in calculating $\Delta\mathcal{E}$ for each amine in Tables V-VII it was only necessary to find atomic orbital coefficients c_r^0 for a molecular orbital of zero binding energy; the net charge $q_r - 1$ was then obtained simply by squaring the appropriate coefficient. As already shown, these atomic orbital coefficients may be written down with great rapidity, and herein lies the usefulness of the method.

In the next paper of this series we shall show how these atomic orbital coefficients can be used in calculating transition state energies for the substitution reactions of aromatic and heteroaromatic systems.

(See page 282 for Appendix of this paper.)

APPENDIX

Zero-Energy Molecular Orbitals in Some Carbanions

