the solution stirred at room temperature overnight. The solution was concentrated under reduced pressure, diluted with water and extracted with methylene chloride. The extract was dried with sodium sulfate and concentrated to dryness. The residue (0.80 g.) was recrystallized from benzene and sublimed for analysis, m.p. 188–189°, $[\alpha]_D$ −87.3°; λ_{max}^{EtOH} 246 (8,400) and 303 mμ (2,100), shld. 312 mμ (1,900); λ_{min} 224 (2,900) and 271 mμ (590).

Anal. Calcd. for $C_{19}H_{26}N_2O$: C, 76.47; H, 8.78; N, 9.39. Found: C, 76.76; H, 8.78; N, 9.50.

SUMMIT, N. J.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS, THE STATE UNIVERSITY]

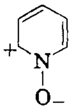
A Comparison of the Structure and Reactivity of Pyridine and Pyridine-1-oxide

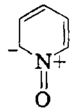
BY RODERICK A. BARNES

RECEIVED OCTOBER 23, 1958

The electron distribution and atom localization energies of pyridine and pyridine-1-oxide have been calculated by the molecular orbital method using a consistent set of parameters for both molecules. The results have been compared with the available experimental data and satisfactory agreement is observed if the resonance integral of the oxygen–nitrogen bond of pyridine-1-oxide is approximately 0.75β.

The resonance or valence-bond method for approximating the true electron distribution works very well for aromatic systems containing no heteroatoms. However, in heterocycles such as pyridine-1-oxide this method may be of doubtful value even for a *qualitative* description. For example, from contributing structures I and II it could be assumed that pyridine-1-oxide has a small negative charge at carbon two because of the somewhat greater stability[1] of structure II; but, whether the contributions of the two structures are really sufficiently different to produce a finite charge at this position could not be predicted with any degree of confidence.


I


II

The failure of the valence-bond procedure for *quantitative* descriptions of heterocycles results from the fact that there is no generally acceptable method for determining exactly the contribution of charged structures such as I and II.[2]

In contrast, the simple molecular orbital method, although subject to some limitations[3] affords a convenient procedure for calculating the charge distribution and relative reactivity of heterocyclic molecules. The main difficulty is in deciding on the correct parameters to be used in the calculations. The ideal situation, in which one set of parameters would serve for a quantitatively accurate description of all heterocycles, is quite unlikely to be operative, but the definition of a set of parameters which give a good qualitative description of a wide variety of heterocycles may be realizable.

The purpose of this paper is to compare the reactivity and electron distribution of pyridine and pyridine-1-oxide, as calculated using a consistent set of parameters for both molecules with the available experimental data. Many of the earlier calculations for systems containing nitrogen atoms assumed that the coulomb integral of nitrogen was represented by $\alpha_N = \alpha_C + 2\beta$, but in this work the suggestion of Coulson[4] that $\alpha_N = \alpha_C + {}^1/_2\beta$ has been followed. Recent calculations by Brown[5] have demonstrated that for attack of the phenyl radical on the pyridine nucleus, only the parameters used here, $\alpha_N = \alpha_C + {}^1/_2\beta$ and $\beta_{CN} = \beta$, produced calculated reactivities which agree with the experimentally observed rate factors.[6] Other calculations for pyridine[7] and pyridine-1-oxide[8] have been made using rather different values for the coulomb integral of nitrogen.

Because there was little basis for choosing a value for the resonance integral of the nitrogen–oxygen bond (β_{NO}), the calculations for pyridine-1-oxide were repeated using three different values covering the range in which the true value is almost certainly located. The charge distributions resulting from these calculations are given Fig. 1.

It is apparent that the change in value of β_{NO} has a profound effect on the charge distribution of pyridine-1-oxide. For the lower value of β_{NO}, the charges on the carbons are much as in pyridine, but at the higher values a part of the negative charge on the oxygen atom appears at positions 2 and 4. In principle it should be possible to determine exactly the value of β_{NO} by calculating the dipole moment for various values of β_{NO}, and comparing it with the experimental value. The part of the moment which arises from the π-electrons is readily calculated, but there is difficulty in deciding on the values to be used for the σ-bond moments, which certainly must vary with the charge on the two atoms of the bond. In spite of this uncertainty, these calculations have been made in a man-

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[1] The smaller separation of charge and the greater number of bonds in II are the reasons for the prediction of its greater stability.

[2] B. Bak, *Acta Chim. Scand.*, **9**, 1355 (1955), has proposed a formula for determining the contribution of charged and uncharged structures from accurate values for the bond lengths, but this procedure has been tested for only a few examples.

[3] R. D. Brown, *Quart. Revs.*, **6**, 63 (1952).

(4) Coulson, "Valence," Oxford University Press, Amen House, London E. C. 4, 1952, p. 242.

(5) R. D. Brown, *J. Chem. Soc.*, 272 (1956).

(6) The only uncertainty about these calculations is that the coefficient *a* of the equation $RT \log k_1/k_2 = a\,(A_2 - A_1)$, which relates rate constants to atom localization energies (A_i), was assumed to be the same for phenyl radicals as for trichloromethyl radicals.

(7) P. Yvan, *Compt. rend.*, **229**, 622 (1949), used $\alpha_N = \alpha_C + \beta$ and $\beta_{CN} = \beta$ but neglected inductive effects.

(8) H. H. Jaffé, THIS JOURNAL, **76**, 3527 (1954), calculated the coulomb integrals $\alpha_N = \alpha_C + 2.004\beta$ and $\alpha_O = \alpha_C + 1.016\beta$ from a relationship he has developed between the coulomb integral and the substituent constants of the Hammett equation; see H. H. Jaffé, *J. Chem. Phys.*, **20**, 279 (1952).

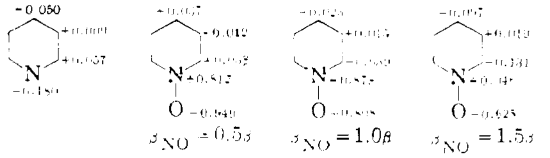

Fig. 1.

ner similar to that of Orgel, Cottrell, Dick and Sutton[9] assuming the length of the nitrogen-oxygen bond to be 1.3 Å.; the σ moment for this bond was calculated from the experimental moment of trimethylamine oxide and therefore also contains a correction factor.

TABLE I

	Compound	π-Moment	σ-Moment	Total	Exptl. moment
1	Pyridine	1.23	0.85	2.08	2.21
2	Pyridine-1-oxide (β_{NO}, 0.5β)	6.47	1.30[a]	5.44	4.28
3	Pyridine-1-oxide (β_{NO}, 1.0β)	4.77	1.30[a]	3.47	4.28
4	Pyridine-1-oxide (β_{NO}, 1.5β)	2.10	1.30[a]	0.80	4.28

[a] This moment is in opposition to the π-moment.

From Table I it may be estimated that when the resonance integral β_{NO} is equal to 0.8β, there would be agreement between the calculated and experimental moments of pyridine-1-oxide.

The aromatic substitution reactions are of greatest interest for these two molecules, and since these are usually rate controlled processes, calculation of the energies of activation would be the ideal way of comparing reactivities. The atom localization energies[10] which may be readily calculated are believed to differ from the true activation energies by a factor which is essentially constant for a given type of substitution reaction. The atom localization energy may be described as the amount of energy required to bring the aromatic molecule into the transition state while still keeping it insulated from any interactions with the approaching reagent. Thus either two, one or zero electrons are localized at a given position depending on whether the reagent is electrophilic, a radical or nucleophilic. In Table II are listed the values in terms of $-\beta$ for the atom localization energies at the three positions for each molecule.

The atom localization energies of benzene, $A_e = A_r = A_n = 2.54$, and naphthalene, $A_e = A_r = A_n = 2.30$, can serve as reference points for the values in the table. It is also noteworthy that for the radical reactions of pyridine a difference in the value of A_r of 0.03β between two positions is equivalent to a factor of two in the rates (at 91°).[5]

The nearly perfect correlation between experimental reactivities and localization energies for attack of phenyl radicals on the pyridine nucleus has already been mentioned. Unfortunately the radical reactions of pyridine-1-oxide have not been sufficiently studied to furnish data for comparison with the calculations. Table II predicts that for all values of β_{NO} the order of reactivity should be $2 > 4 > 3$, the same as for pyridine, with the magnitude of the differences between the positions somewhat greater than for pyridine. These predictions are represented graphically in Fig. 2. In these as well as the other reactions of pyridine-1-oxide, the atom localization energies would be expected to predict a greater reactivity for the 2-position than that observed because the calculations take no account of the steric effect of the oxygen atom of the adjacent nitrogen atom.

TABLE II

ATOM LOCALIZATION ENERGIES

Position	β_{NO}	A_e	A_r	A_n
		Pyridine		
2	..	2.62	2.51	2.40
3	..	2.57	2.54	2.51
4	..	2.69	2.53	2.36
		Pyridine-1-oxide		
2	0.5	2.51	2.47	2.42
3	.5	2.58	2.54	2.50
4	.5	2.60	2.50	2.39
2	1.0	2.22	2.38	2.54
3	1.0	2.59	2.53	2.49
4	1.0	2.34	2.44	2.54
2	1.5	1.92	2.28	2.58
3	1.5	2.60	2.56	2.52
4	1.5	2.09	2.42	2.75

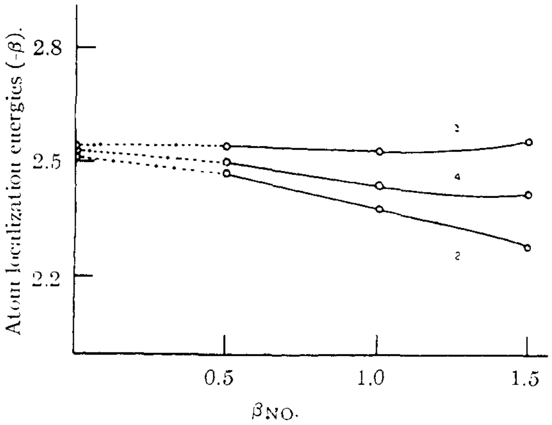

Fig. 2.—Radical substitutions of pyridine-1-oxide (the points at $\beta_{NO} = 0$ are for pyridine and the dotted connecting line has been drawn only to illustrate the relationship between the two substances).

Pyridine is attacked by a variety of nucleophilic reagents, but it is not clear in all of these whether or not the reaction is a true nucleophilic substitution. For example the reaction of an alkyl- or aryllithium probably proceeds by preliminary addition to the 1,2-bond to give an intermediate dihydropyridine which in a subsequent step eliminates lithium hydride to yield the final product.[11] The replacement by a base of the halogen atom of a halopyridine is almost certainly a nucleophilic substitution and the data for these reactions are in substantial agreement with the predictions of the Table II. The 3-halopyridines are about as unreactive as the halobenzenes and the 2- and 4-halopyridines are much

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[9] L. E. Orgel, T. L. Cottrell, W. Dick and L. E. Sutton, *Trans. Faraday Soc.*, **47**, 113 (1951).

[10] The atom localization energy is essentially the same as ΔW which was calculated by Wheland and considered to be a part of the activation energy; see G. W. Wheland, THIS JOURNAL, **64**, 901 (1942).

[11] K. Ziegler and H. Zeiser, *Ber.*, **63**, 1847 (1930).

more reactive. The order of reactivity is predicted to be 4 > 2 > 3 with the difference between the 2- and 4-positions rather small. When 2,4,6-tribromopyridine is treated with sodium methoxide, the 4-bromine atom is replaced first;[12] however, 2,4-dichloropyridine reacts with ammonia to yield a mixture of the two aminochloropyridines.[13]

Figure 3 shows that the order of reactivity predicted for pyridine-1-oxide depends on the value for β_{NO} with four different orders being possibilities. From the rather meager evidence[14–16] it would be presumed that nucleophilic reactions of pyridine-1-oxide proceed about as readily as those of pyridine and that the order of reactivity is probably either 2 > 4 > 3 or 4 > 2 > 3. The latter of these agrees with Fig. 3 provided that the value of β_{NO} is less than 0.825β.

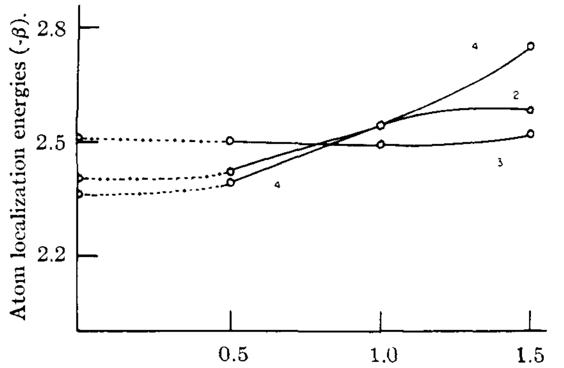

Fig. 3.—Nucleophilic substitutions of pyridine-1-oxide.

The electrophilic substitutions offer a special difficulty because these are almost always conducted in an acid solution in which the pyridine base is in equilibrium with its salt. Thus the reactivity of the salt and its concentration under the experimental conditions must be considered. The formation of a pyridine salt confers a positive charge on the nitrogen atom and thus makes it more electronegative. This may be taken into account in the calculations merely by increasing the coulomb integral of the nitrogen atom. As an illustration, the atom localization energies have been calculated increasing the coulomb integral of the nitrogen atom by 0.5β. Using similar reasoning, the change in the charge on the oxygen atom of pyridine-1-oxide may be accounted for by increasing the coulomb integral of the oxygen atom (also by 0.5β).[17]

Tables II and III predict that for either pyridine or its salt the 3-position is most reactive toward electrophilic substitution. Salt formation should decrease the reactivity at this position slightly while at the 2- and 4-positions the effect is much greater; thus a salt would be expected to yield almost exclusively the 3-isomer. The rather drastic experimental conditions necessary for such reactions as sulfonation, nitration and bromination of pyridine are more nearly in accord with reactivities predicted for a pyridine salt; pyridine base has a localization energy at the 3-position only 0.03β unit greater than benzene.

TABLE III

ATOM LOCALIZATION ENERGIES OF SALTS

Position	β_{NO}	A_e	A_r	A_n
		Pyridine		
2	..	2.85	2.53	2.21
3	..	2.62	2.55	2.48
4	..	2.84	2.55	2.25
		Pyridine-1-oxide		
2	0.5	2.70	2.56	2.39
3	.5	2.58	2.54	2.50
4	.5	2.67	2.51	2.36

The prediction of Table III, that nucleophilic attack should be facilitated by salt formation, has been observed experimentally; aniline reacts with 2-chloropyridine more rapidly in an acid than an alkaline medium.[18]

The most useful reaction of pyridine-1-oxide, its nitration at the 4-position, can be effected much more readily than with pyridine although the reaction is still more difficult than the nitration of benzene.[19] This result agrees with the calculated reactivities only if it is the free base which is being nitrated and if the value of β_{NO} is above 0.53β.[20] For all of the values of β_{NO} (Fig. 4) the reactivity of the 2-position is predicted to be somewhat greater than the 4-position, but as already mentioned, these calculations do not take into account the steric factor decreasing the actual reactivity at the 2-position.

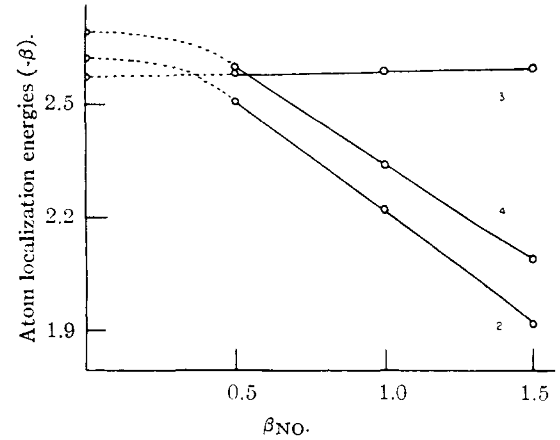

Fig. 4.—Electrophilic substitutions of pyridine-1-oxide.

The sulfonation of pyridine-1-oxide, in contrast to the nitration, is about as difficult as that of pyridine

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[12] H. J. Den Hertog, *Rec. trav. chim.*, **67**, 381 (1948).

[13] H. J. Den Hertog, J. C. M. Schogt, J. de Bruyn and A. de Klerk, *ibid.*, **69**, 673 (1950).

[14] E. Ochia, *J. Org. Chem.*, **18**, 534 (1935).

[15] E. Shaw, J. Bernstein, K. Losee and W. A. Lott, THIS JOURNAL, **72**, 4362 (1950).

[16] M. Colonna and S. Fatutta, *Gazz. chim. ital.*, **83**, 622 (1953).

[17] These changes in the coulomb integrals were arbitrary choices made only to show the direction in which the reactivities would change with salt formation.

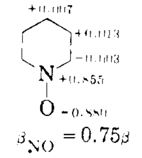
[18] C. K. Banks, THIS JOURNAL, **66**, 1127 (1944).

[19] Pyridine-1-oxide is nitrated by concentrated nitric and sulfuric acids at 130° (3.5 hours) while benzene reacts with the same reagents at 50°; see ref. 14.

[20] If β_{NO} is above 0.6β, the predicted reactivity of pyridine-1-oxide at this position would be greater than benzene (A_r = 2.54). The actual concentration of pyridine-1-oxide base in the nitrating solution may be very low and a valid experimental comparison could be made only with a solution containing an equally low concentration of benzene.

and takes place at the 3-position.[21] The result agrees with Table III if it assumed that under the reaction conditions (fuming sulfuric acid), pyridine-1-oxide is present only in the salt form.

From the correlations with reactivity it can be concluded that the value of β_{NO} for pyridine-1-oxide is between 0.53β and 0.825β and the dipole moment calculations suggest a value nearer the higher of the two. By graphical means the charge distribution and atom localization energies may be determined for pyridine-1-oxide at $\beta_{NO} = 0.75\beta$, which is probably fairly near the true value.



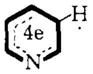
Calculations.—The LCAO procedure described by Coulson[22] was employed.

Pyridine.—The inductive effect of the nitrogen atom was taken into account by using for carbons 2 and 6, $\alpha_{C_{2,6}} = \alpha_C + 0.05\beta$; the other parameters were $\alpha_N = \alpha_C + 0.5\beta$ and $\beta_{CN} = \beta$. For the pyridinium ion the following substitutions were made, $\alpha_N = \alpha_C + 1.0\beta$ and $\alpha_{C_{2,6}} = \alpha_C + 0.1\beta$. The energy levels for the molecular orbitals and the coefficients were determined by solution of the secular equations. The atom localization energies result by subtraction of the total energy of the π-electrons of pyridine from the π-electron energy of the "localized states." As an example, the localized state for electrophilic substitution at the 3-position is shown. For localization at each position a different set of secular equations was solved.

Table IV

Atom Localization Energies of Pyridine-1-oxide ($\beta_{NO} = 0.75\beta$)

Position	A_e	A_r	A_n
2	2.36	2.42	2.48
3	2.58	2.53	2.50
4	2.44	2.47	2.46



Pyridine-1-oxide.—The same procedure was followed as for pyridine. The parameters were: $\alpha_O = \alpha_C + 1.0\beta$, $\alpha_N = \alpha_C + 0.6\beta$ (0.6 instead of 0.5 because of the inductive effect of the oxygen atom), $\alpha_{C_{2,6}} = \alpha_C + 0.06\beta$, $\beta_{CN} = \beta$, $\beta_{NO} = 0.5$, 1.0 and 1.5. For the salt, $\alpha_O = \alpha_C + 1.5\beta$, $\alpha_N = \alpha_C + 0.65\beta$; $\alpha_{C2,6} = \alpha_C + 0.065\beta$, $\beta_{NO} = 0.5\beta$.

New Brunswick, N. J.

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[21] H. S. Mosher and F. J. Welch, This Journal, **77**, 2902 (1955).

[22] Reference 4, pp. 238–256.

[Contribution from the Department of Chemistry, Duke University]

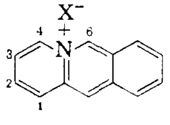
Acridizinium Ion Chemistry. III.[1] Reaction with Bases

By C. K. Bradsher and James H. Jones[2]

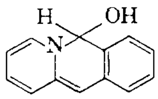
Received October 2, 1958

It has been demonstrated that phenylmagnesium bromide attacks acridizinium bromide at position 6 yielding a dihydro derivative (V) which can be dehydrogenated to a 6-phenylacridizinium salt. In basic media substituted **acridizinium bromides** as well as the parent compound react with potassium cyanide phenylacetonitrile, acetone and acetophenone. It is suggested that in these cases reaction occurs at position 6.

Since the first synthesis of acridizinium salts (I),[3] papers have appeared concerning the photodimerization[4a] of the system as well as its participation as the diene component in the Diels–Alder reaction.[1] To date it appears that no study has been made of the action of bases on the acridizinium ion or on the simple prototype of the series, the quinolizinium ion.[4b] Excellent models for such an investigation are provided by earlier work[5–17] with pyridinium, quinolinium and isoquinolinium salts.



I, X = Br
II, X = $OC_6H_2(NO_2)_3$
III, X = OH



IV

An aqueous solution of acridizinium bromide (I)

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[1] For the previous communication of this series see This Journal, **80**, 933 (1958).

[2] Taken in part from a thesis submitted by James H. Jones in partial fulfillment of the requirements for the Ph.D. degree, Duke University, 1958.

[3] C. K. Bradsher and L. E. Beavers, This Journal, **77**, 4812 (1955).

[4] (a) C. K. Bradsher, L. E. Beavers and J. H. Jones, *J. Org. Chem.*, **22**, 1740 (1957). (b) Added in Proof.—In a recent article (*J. Chem. Soc.*, 3067 (1958)) A. Richards and T. S. Stevens have studied the behavior of bases on both quinolizium and acridizinium salts. It is interesting that under the conditions which they used they were unable to effect the condensation of acridizinium salts with "reactive methylene compounds" in the presence of bases.

[5] J. G. Aston, This Journal, **52**, 5254 (1930); **53**, 1448 (1931).

[6] A. Hantzsch and M. Kalb, *Ber.*, **32**, 3109 (1899).

[7] J. G. Aston and P. A. Lasselle, This Journal, **56**, 426 (1934).

[8] J. G. Aston and C. W. Montgomery, *ibid.*, **53**, 4298 (1931).

[9] J. Meisenheimer and M. Schultze, *Ber.*, **56B**, 1353 (1923).

[10] J. Meisenheimer and E. Stotz and K. Bauer, *ibid.*, **58B**, 2320 (1925).

[11] W. Bradley and S. Jeffrie, *J. Chem. Soc.*, 2770 (1954).

[12] A. Kaufmann, *Ber.*, **51**, 116 (1918).

[13] N. J. Leonard and G. W. Leubner, This Journal, **71**, 3405 (1949).

[14] N. J. Leonard and G. W. Leubner, *ibid.*, **71**, 3408 (1949).

[15] N. J. Leonard, H. A. Dewalt, Jr., and G. W. Leubner, *ibid.*, **73**, 3325 (1951).

[16] N. J. Leonard and R. L. Foster, *ibid.*, **74**, 3671 (1952).

[17] N. J. Leonard and R. L. Foster, *ibid.*, **74**, 2110 (1952).