white crystals, m.p. 90–91°. The infrared spectrum of this substance was also typical of substituted melamines. This together with the analyses indicated that the solid is N^2-diphenyl-N^4,N^6-bis(diethyl)melamine.

Anal. Calcd. for $C_{23}H_{30}N_6$: C, 70.73; H, 7.74; N, 21.52 Found: C, 70.88; H, 7.90; N, 21.28.

ST. LOUIS 77, MO.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF SAN DIEGO STATE COLLEGE]

Acidity Constants of Some Arylimidazoles and Their Cations

HAROLD WALBA AND ROBERT W. ISENSEE

Received December 8, 1960

A comparative study of the thermodynamic acidity constants, both $pK°_a$ and $pK°_{a+}$, of imidazole, the mono- and di-C-phenylimidazoles, benzimidazole, and 2-phenylbenzimidazole is presented.

This paper is a continuation of our study of the effect of phenylation on the acidity of some amphiprotic arylimidazoles. In our earlier work[1,2] the acidity of the neutral molecules was studied; in this work their basicity or the acidity of their cations is considered. Of interest here is the effect of protonation on the role of the phenyl group. Added to the list of compounds studied is 4,5-diphenylimidazole, which, with phenyl groups on adjacent carbons, is of steric interest. To favor the cancelling out of procedural and systematic errors when making comparisons by difference, we have determined all acidity constants but one in our laboratory. The value not determined was that for the cation of imidazole which was not amenable to study by the method used.

EXPERIMENTAL

Calculation of the thermodynamic constants. The negative logarithm of the thermodynamic acidity constant of the neutral molecules, $pK°_a$, was calculated from the experimentally determined hydrolysis constants of the anions by the known relationship

$$pK°_a = pK°_w - pK°_h \qquad (1)$$

where $K°_w$ is the thermodynamic ionization product of water and $K°_h$ the thermodynamic hydrolysis constant of the anion. We have shown[1] that with 2-phenylbenzimidazole there is, within error of measurements, a linear relationship between pK_h and ionic strength, I_c, given by the equation

$$pK_h = pK_h° - mI_c^{1/2} \qquad (2)$$

where m is the slope. Following the same procedures that were used with 2-phenylbenzimidazole, we find that benzimidazole and 2,4(or 2,5)-diphenylimidazole give a slope of 0.10 which is the same slope to two significant figures found for 2-phenylbenzimidazole. For 4,5-diphenylimidazole the experimentally determined slope is 0.11. The probable error in the measured slopes is 0.02. Equation 2 was used to calculate $pK°_h$ for use in Equation 1 in every instance. The effect of ionic strength on the pK_h of imidazole and the mono-C-phenylimidazoles was not determined by experiment, and their $pK°_h$ was calculated using 0.10 for m and the reported pK_h values. The pK_h values for 4,5-diphenylimidazole, not previously reported, were obtained in the same manner as that described for the other arylimidazoles. The probable error in the $pK°_a$ values of this work is 0.04 pK units except for the $pK°_a$ of imidazole where the probable error is 0.06 pK units.

The negative logarithm of the thermodynamic acidity constant of the cations, $pK°_{a+}$, is given by the equation

$$pK°_{a+} = pH + \log c_{RH_2^+}/c_{RH} + \log \gamma_{RH_2^+}\gamma_{H_2O}/\gamma_{RH} \qquad (3)$$

The concentrations of the cation, $c_{RH_2^+}$, and of the nonion, c_{RH}, were determined spectrophotometrically.[3] The neutral. molecule's spectrum was measured in a 0.02*M* National Bureau of Standards pH 9.18 borax buffer. The aqueous solutions were acidified with hydrochloric acid to appropriate pH's for the equilibrium absorbancy measurements and the spectrum of the cation. The pH was measured with a Beckman Model G pH meter equipped with glass and calomel electrodes. The pH meter was calibrated with a 0.025*M* National Bureau of Standards pH 6.86 phosphate buffer at 25° ± 0.2. The reported $pK°_{a+}$ values are averages from measurements at three different pH's, and the $pK°_{a+}$ obtained at each pH is in turn the average from measurements at five or more wave lengths. The probable error is 0.03 pK units. We have neglected the activity coefficient term in Equation 3, since the total ionic strength of the solutions used in our equilibrium measurements was less than 10^{-4} g. ions/l.

Spectral data. All spectral measurements were made with a Model DU Beckman spectrophotometer. One-centimeter cells were used in every case except for 4,5-diphenylimidazole where 10-cm. cells were used. The temperature in the cell compartment was maintained at 25° ± 0.2 with Beckman thermospacers. Readings were corrected for any differences in the absorbancies of the two cells when filled with water.

Preparation of compounds. 4,5-Diphenylimidazole was prepared according to Davidson, *et al.*[4]; the other compounds were prepared as indicated in our earlier reports.[1,2]

RESULTS AND DISCUSSION

In Table I are given the thermodynamic acidity constants of the neutral molecules and their cations. To facilitate comparison between the two series of constants, a graph of $pK°_{a+}$ as abscissa and $pK°_a$ as ordinate, with a reference line of unit slope drawn arbitrarily through imidazole, is shown in Fig. 1.

---

(1) H. Walba and R. W. Isensee, *J. Am. Chem. Soc.*, **77**, 5488 (1955).

(2) H. Walba and R. W. Isensee, *J. Org. Chem.*, 21, 702 (1956).

(3) W. Stentstrom and N. Goldsmith, *J. Phys. Chem.*, 30, 1683 (1926).

(4) D. Davidson, M. Weiss, and M. Jelling, *J. Org. Chem.*, **2**, 319 (1937).

TABLE I

THERMODYNAMIC ACIDITY CONSTANTS AT 25°

Compound	pK°_a	pK°_{a+}
Imidazole	14.52	7.05[a]
2-Phenylimidazole	13.32	6.48
4(or 5)-Phenylimidazole	13.42	6.10
2,4(or 2,5)-Diphenylimidazole	12.53	5.64
4,5-Diphenylimidazole	12.80	5.90
Benzimidazole	12.78	5.55[b]
2-Phenylbenzimidazole	11.91	5.23

[a] A pK°_{a+} of 7.05 was selected for consistency and is based on a comparison of our values for the cations of the mono C-phenylimidazoles with those of Kirby and Neuberger.[5] These investigators obtained values of 6.95 for imidazole, 6.39 for 2-phenylimidazole, and 6.00 for 4(or 5)-phenylimidazole. [b] Davies, *et al.*[6] obtained for pK°_{a+} the values 5.44 by one technique and 5.52 by another. Schwarzenbach and Lutz[7] report 5.532 for pK°_{a+}.

The data tabulated and graphed show substitution of a phenyl for a vinyl group to yield benzimidazole, of one or more phenyl groups for C-hydrogens to yield C-phenylimidazoles,[8] or of a combination of phenylations to yield 2-phenylbenzimidazole is, in every case and for both the series, acid strengthening. Further we note that protonation diminishes to varying degrees the acid strengthening role of the phenyl group.

We first consider the special case involving the replacement of a vinyl group in imidazole by a phenyl group to give benzimidazole. The structural change, in this instance, results in benzimidazole being 1.74 pK units stronger as an acid than imidazole and its cation being 1.50 pK units stronger than the imidazolium ion. The acid strengthening effect may be attributed to the three π electrons of the nitrogens in benzimidazole and its ions being more extensively delocalized than in imidazole and its ions. The result of the greater delocalization in all of the benzimidazole species is to decrease the electron density on the nitrogen atoms and hence stabilize the less protonated species. We find the formal charge concept is useful in so far as picturing the electron density change. Extending Wheland's[9] formula for formal charge, F.C., to π electron systems, we obtain

$$\text{F.C.} = Z - (k\sigma/2) - (k\pi/n) - p \qquad (5)$$

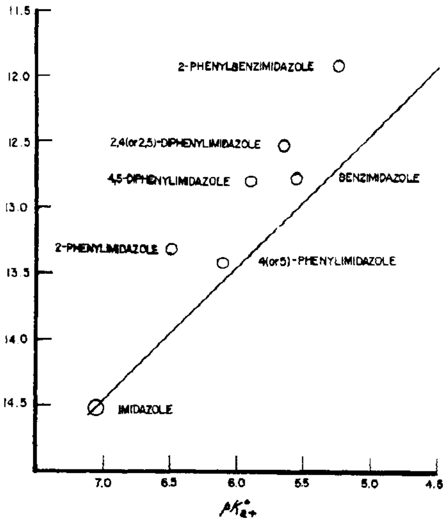
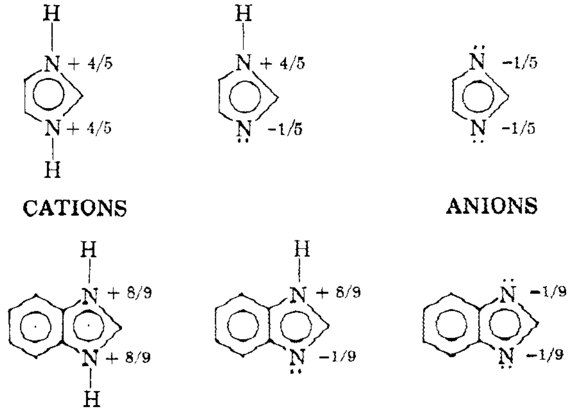


Fig. 1. The effect of phenylation on the acidity constants of imidazole and some arylimidazoles. A reference line of unit slope has been drawn through the coordinates of imidazole

where Z is the kernel charge or the number of valence electrons, $k\sigma$ is the number of *sigma* electrons shared with other atoms, $k\pi$ is the total number of π electrons in the molecular orbital (six for imidazole and ten for benzimidazole), n is the number of atoms encompassed by the π electron system (five for imidazole and nine for benzimidazole) and p is the number of unshared or lone electrons. Using Equation 5 we obtain the formal charges on nitrogen shown in the following formulas for imidazole, benzimidazole, and their ions. Admittedly these representations are crude approximations, since Equation 5 wrongly implies equal sharing of both σ and π electrons by atoms of different electronegativities; the structures do, however, effectively illustrate and, as expected, are consistent with the above-mentioned electron density change on the nitrogen atoms.



We next note that in the 2-phenyl derivatives there is a diminution of the acid strengthening role of the 2-phenyl group on protonation. This effect manifests itself whether imidazole, 4(or 5)-phenylimidazole or benzimidazole is chosen as the reference compound. In the neutral molecule series overlap of the phenyl group with the imidazole or benzimidazole moiety favors a stabilization of the anion.[1] Thus, in this series, the polar inductive

---

[5] A. H. M. Kirby and A. Neuberger, *Biochem. J.*, **32**, 1146 (1938).

[6] M. T. Davies, P. Mamalis, V. Petrow, and B. Sturgeon, *J. Pharm. Pharmacol.*, **3**, 420 (1951).

[7] G. Schwarzenbach and K. Lutz, *Helv. Chim. Acta*, **23**, 1162 (1940).

[8] Lophine, a logical member of the series, was too insoluble to allow its acidity constants to be measured in water.

[9] G. W. Wheland, *Resonance in Organic Chemistry*, J. Wiley and Sons, Inc., New York, 1955, p. 22.

effect and the delocalization effect of the 2-phenyl substituent are acting in the same direction. In the cation series, on the other hand, it is consistent with observation, that overlap of the 2-phenyl group with the imidazole or benzimidazole moiety results in the polar inductive and the resonance effect acting in opposite directions. In the cation, delocalization of the 2-phenyl group appears to favor an increase in the electron density at the point of dissociation accompanied by a stabilizing spreading out of the positive charge. It may also be that the polar inductive effect of the 2-phenyl group is not as effective in the cation series as in the neutral molecule series because the electrons associated with the nitrogen atoms are held more tightly in the cation than they are in the anion. This suggestion is related to the saturation effect.[10]

In both the neutral molecule and the cation dissociation equilibria the 4(or 5)-phenyl group parallels in direction the role of the 2-phenyl group. Variations in magnitude result in 2-phenylimidazole being a stronger acid and a stronger base (a weaker cationic acid) than 4(or 5)-phenylimidazole.

For 2,4(or 2,5)-diphenylimidazole small negative deviations from additivity of the phenyl groups are observed: 0.3 *p*K unit for the neutral molecule dissociation and 0.1 *p*K unit for the cation dissociation. For 4,5-diphenylimidazole, where the phenyl groups are on adjacent carbons and thereby restricted from assuming the coplanar conformation necessary for a maximum delocalization effect, we find larger negative deviations from additivity of the 4(or 5)-phenyl groups: 0.5 *p*K unit in the neutral molecule dissociation and 0.9 *p*K unit in the cation dissociation.

In the neutral molecule dissociation we expect the delocalization effect to be acid strengthening and therefore steric inhibition of resonance should decrease the effectiveness of the phenyl groups. The negative deviation from additivity is 0.2 *p*K unit greater in the 4,5-diphenylimidazole neutral molecule dissociation than in the corresponding sterically uninhibited 2,4(or 2,5)-diphenylimidazole dissociation. The difference is quite small but in the anticipated direction. In the cation dissociation we expect the delocalization effect to be acid weakening and, therefore, steric inhibition of resonance should increase the effectiveness of the phenyl groups. However, since we find that the negative deviation from additivity is greater by 0.8 *p*K unit in the 4,5-diphenylimidazole than in the sterically uninhibited 2,4(or 2,5)-diphenylimidazole cation dissociation, acid strengthening steric inhibition of resonance is not evidenced. A possible explanation for the masking of the steric inhibition of resonance is that the main tautomer of 4(or 5)-phenylimidazole is 4-phenylimidazole. Were this the case, the second phenyl entering the 5 position would be expected by its polar inductive effect to be more acid strengthening than the first phenyl in the neutral molecule dissociation and less acid strengthening in the cation dissociation. Thus in the neutral molecule dissociation of 4,5-diphenylimidazole the greater polar inductive effect of the second phenyl would counteract the expected acid weakening steric inhibition of resonance and in the cation dissociation the lesser polar inductive effect of the second phenyl would counteract the anticipated but not manifested acid strengthening steric inhibition of resonance.

Acknowledgment. We wish to acknowledge the support of the National Science Foundation and the Research Corporation. We are indebted to Michael Barfield for determining the effect of ionic strength on the hydrolysis constant of 2,4(or 2,5)-diphenylimidazole.

SAN DIEGO, CALIF.

---

[10] G. E. K. Branch and M. Calvin, *The Theory of Organic Chemistry*, Prentice-Hall, New York, 1941, pp. 205, 218.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF WITWATERSRAND]

A New Synthesis of 2-Aryl-3-acetyl-4-hydroxyquinolines Using Polyphosphoric Acid

B. STASKUN

Received September 29, 1960

β-Amino-α-(*N*-arylimidoyl) crotonates are converted into 2-aryl-3-acetyl-4-hydroxyquinolines on treatment with polyphosphoric acid at 170°. The infrared spectra of the compounds and other evidence is presented in support of their formulation.

A general and unambiguous synthesis of the 2-aryl-3-acetyl-4-hydroxyquinolines (II) has until now not been available and these substances are relatively unknown and inaccessible. The preparative methods of Shah *et al.*, which involve the condensation of imidoyl chlorides (I) with ethyl sodioacetoacetate[1,2] and of arylamines with ethyl benzoylacetoacetate[3] respectively, have been found[4,5] not