5-Phenyl-2-(3-quinolylmethyl)hydantoic acid. The reaction of the 3-(3-quinolyl)alanine with phenyl isocyanate was carried on as described for 4-(3-quinolyl)alanine.[5] The resulting hydantoic acid melted at 219–222° after recrystallization from ethanol.

Anal. Calcd. for $C_{19}H_{17}O_3N_3$: C, 68.04; H, 5.11; N, 12.53. Found: C, 68.02; H, 5.12; N, 12.59.

3-Phenyl-5-(3-quinolylmethyl)hydantoin. The hydantoic acid was cyclized by boiling with dilute hydrochloric acid, and precipitated at *p*H 4 to 5. The hydantoin was recrystallized from ethanol to a melting point of 226–227°.

Anal. Calcd. for $C_{19}H_{15}O_2N_3$: C, 71.89; H, 4.81; N, 13.24. Found: C, 71.39; H, 4.39; N, 13.52.

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A Spectral Study of Some Schiff Base Derivatives of *p*-Aminoazobenzene

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Received October 14, 1960

Derivatives of *p*-phenylazoaniline are known carcinogens; *p*-dimethylaminoazobenzenes produce liver tumors in rats.[2,3] In addition as first reported by Kehrman[4] *p*-dimethylaminoazobenzene and its derivatives add protons in acid solutions with a resulting change in their spectra. In the case of the addition of the first proton to these molecules some argument exists in the literature as to its position. Cilento,[5] Badger,[6] Sawicki,[7] and Rogers[8] conclude that addition results in a tautomeric mixture while Klotz[9] and McGuire[10] conclude that the first proton adds exclusively to the amino nitrogen. Prior to the study of their carcinogenic activity a spectral study of the compounds listed in Table I in solutions of varying acid strengths was initiated.

The first and second acid dissociation constants were determined by the method of Rogers[8] with the exception that the buffer solutions used were made up to a constant ionic strength, μ, of 0.1.

$$pK_1 = pH - \log \frac{\epsilon_{BH^+} - \epsilon}{\epsilon - \epsilon_B} - \frac{A\mu^{1/2}}{1 + \mu^{1/2}} \qquad (1)$$

Consequently, the equation due to Herington,[11] was used for the addition of the initial proton. Although a color change from light yellow to intense orange was noted in the case of *N*,*N*′-dibenzal-1,4-diaminobenzene and *N*-(*p*-dimethylaminobenzal)aniline in 50% sulfuric acid solution, it proved impossible to determine the dissociation constants since these Schiff bases hydrolyzed rapidly. This behavior has been previously reported as a general property for Schiff bases.[12] The creditability of the reported measurements can be ascertained by comparison of the results of this work with other investigators in the case of *p*-dimethylaminoazobenzene which has been extensively investigated. The summary appears in Table II.

The results of this study may be summarized by the following statements: (1) The first and second acid dissociation constants for three Schiff base derivatives of *p*-phenylazoaniline have been determined. (2) The visible spectrum of these molecules in mild acid solution displays both the 320 mμ and the 500 mμ absorption peaks which are identical with those observed in the case of the substituted *N*,*N*-dialkyl-*p*-phenylazoanilines. In the case of these last named molecules spectral evidence strongly indicates that the addition of the first proton results in a tautomeric mixture. The evidence for such a decision is (a) *p*,*p*′-Dimethoxyazobenzene in acid solution absorbs only at 520 mμ.[6] Presumably this form would exist only in the azonium form. (b) The trimethyl quaternary ammonium salt of *p*-phenylazoaniline has absorption peaks at 315 mμ and 425 mμ which is quite similar to azobenzene itself, 313 mμ and 418 mμ.[13] (c) *N*,*N*-Dimethyl-2-methyl-4-phenylazoaniline in acid solution has only the absorption peak at 320 mμ. This is reasonable since the methyl group *ortho* to the dimethylamino group prevents this latter group from becoming planar with the ring. The possibility of the quinoid structure is therefore inhibited.[14] The marked spectral similarity between these Schiff bases and the *N*,*N*-dialkyl-*p*-phenylazoanilines in mild acid allows the conclusion that the addition of the first proton to the Schiff bases results in a tautomeric mixture with the 320 mμ peak due to addition at the azomethine nitrogen and the 500 mμ peak due to addition to the azo nitrogen. (3) Whereas Schiff bases are in general easily hydrolyzed in acid solution, the presence of *p*-phenylazo group stabilizes the molecule even in solutions as concentrated as 96% sulfuric acid. (4) Although the information is admittedly only

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TABLE I

SPECTRAL MAXIMA, MOLAR EXTINCTION COEFFICIENTS, AND DISSOCIATION CONSTANTS FOR SOME SCHIFF BASES

Compound	Solvent	λ mμ	ε × 10^{-3}	pK_1	pK_2
N,*N*-Dimethyl-*p*-phenylazoaniline	Ethanol[a]	255	9.55	3.12 ± 0.01	−4.51 ± 0.04
		405	28.3		
	Base[b]	450	32.4		
	Monoprotonated[c]	320	8.28		
		515	37.4		
	Diprotonated[d]	415	25.5		
N-Benzal-*p*-phenylazoaniline	Ethanol	250	9.31	2.71 ± 0.05	−3.97 ± 0.04
		385	25.3		
	Base	380	20.2		
	Monoprotonated	320	16.6		
		495	11.4		
	Diprotonated	415	29.4		
N-(*p*-Dimethylaminobenzal)-*p*-phenylazoaniline	Ethanol	245	13.8	2.62 ± 0.04	−3.91 ± 0.03
		385	30.8		
	Base	355	42.0		
	Monoprotonated	320	14.8		
		495	26.7		
	Diprotonated	415	29.6		
1-Methyl-4-carbostyrilcarboxaldehyde-*p*-phenylazoanil	Ethanol	230	30.4	2.76 ± 0.03	−3.96 ± 0.04
		385	30.0		
	Base	375	24.2		
	Monoprotonated	320	22.2		
		495	14.3		
	Diprotonated	415	35.6		
N,*N*′-Dibenzal-1,4-diaminobenzene	Ethanol	230	17.1		
		270	21.2		
		350	24.8		
N-(*p*-Dimethylaminobenzal)aniline	Ethanol	240	11.4		
		355	31.2		

[a] Solvent dry ethanol, less than 0.05 ml. water per 10 ml. solution as determined by method of Botset.[20] [b] Solvent buffer solution of *p*H 7.08. [c] Solvent 2.10*N* sulfuric acid. [d] Solvent 96% sulfuric acid.

TABLE II

COMPARISON RESULTS FOR *N*,*N*-DIMETHYL-*p*-PHENYLAZOANILINE

Investigator	Media	pK_1	pK_2	λ mμ
Klotz[9]	Water	3.5	−4.37	
Rogers[8]	50% aq. ethanol	2.27	−4.5	
Guntelberg[15]	Water	3.29		
Kohltoff[16]	Aq. ethanol	3.1		
Badger[6]	Aq. ethanol	3.21		320 mild acid
				520 mild acid
This work	Aq. ethanol	3.12	−4.51	415 ethanol
				450 base
				320 mild acid
				515 mild acid
Brode[17]				410 ethanol
				450 neutral aq.
Hantzsch[18]				510 mild acid
Cilento[5]				320 mild acid
				518 mild acid

fragmentary, a study of the infrared spectra of these Schiff bases in carbon tetrachloride indicates that the azomethine stretching frequency disappears in those molecules in which a $(CH_3)_2N-$ group is substituted *para* to the —C═N— group. In those molecules in which a band appears, the assignments are: *N*,*N*′-Dibenzal-1,4-diaminobenzene, 1630 cm.$^{-1}$; *N*-benzal-*p*-phenylazoaniline, 1630 cm.$^{-1}$ which are in accord with the study of seventeen Schiff bases by Claugherty.[19]

EXPERIMENTAL

The compounds used were either purchased or prepared as described in the literature. They were further purified by three recrystallizations from the solvent listed. Agreement of the melting point with that reported in the literature and satisfactory nitrogen analysis formed the criteria for purity.

N,N-Dimethyl-p-phenylazoaniline was recrystallized from 1-propanol; m.p. 116–117° (lit.[21] m.p. 116–117°).

Anal. Calcd. for $C_{14}H_{15}N_3$: N, 18.69. Found: N, 18.69.

N-Benzal-p-phenylazoaniline[22] was recrystallized from 1-propanol; m.p. 130–131° (lit.[22] m.p. 130.5°).

Anal. Calcd. for $C_{19}H_{15}N_3$: N, 14.74. Found: N, 14.41.

N-(p-Dimethylaminobenzal)-p-phenylazoaniline[23] was re-

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crystallized from 1-propanol; m.p. 174–174.5° (lit.[23] m.p. 174°).

Anal. Calcd. for $C_{21}H_{20}N_4$: N, 16.57. Found: N, 16.79.

1-Methyl-4-carbostyrilcarboxaldehyde-p-phenylazoaniline-anil.[24] Attempts to recrystallize the product from either ethanol or propanol resulted in a resin. The product was dissolved in benzene and the solution was poured into a large excess of petroleum ether (b.p.; 60–75°) m.p. 91–99° (lit.[24] m.p. 93–99°).

Anal. Calcd. for $C_{23}H_{18}N_4O$: N, 15.30. Found: N, 15.52.

N,N'-Dienabzal-1,4-diaminobenzene[25] was recrystallized from 1-propanol; m.p. 138-139° (lit.[25] m.p. 139°).

Anal. Calcd. for $C_{20}H_{16}N_2$: N, 9.85. Found: N, 9.78.

N-(p-Dimethylaminobenzal) aniline[26] was recrystallized from ethanol; m.p. 100–100.5° (lit.[26] m.p. 100°).

Anal. Calcd. for $C_{15}H_{16}N_2$: N, 12.50. Found: N, 12.56.

The ultraviolet and visible spectra in ethanol of the molecules in the range 220 to 600 mμ were determined with the Beckmann DU Spectrophotometer using matched silica cells. The cell compartment was thermostated to 24.9 ± 0.2°. In the case of the aqueous ethanol solutions of various acid strengths the spectral range covered was from 300 to 600 mμ. The range of acidities covered was from pH 7 through concentrated sulfuric acid. The pH of the buffer solutions, pH 1 through 7, was determined using the Beckman Model G pH meter. The pH values of the various sulfuric acid solutions were computed using the extended scale of Michaelis and Granick.[27] The infrared spectra of the molecules were determined in CCl_4 solution using the Perkin-Elmer Infracord.

Acknowledgment. The authors wish to thank Mr. Ronald Bowen for the nitrogen analyses of these compounds.

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3-Aminopiperidones. I. The Cyanoethylation of 2-(*N,N*-Diethylamino)-2-phenylacetonitrile and the Synthesis of an Enaminonitrile[1]

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Received August 11, 1960

The cyanoethylation of 2-disubstituted amino-2-phenylacetonitriles has been studied in this laboratory in the interest of developing a synthetic route to appropriate dinitriles which, in turn, could be hydrolyzed and cyclized to yield a series of 3-disubstituted amino-3-phenyl (and substituted phenyl)-2,6-piperidinediones. Studies directed toward the synthesis of this series, as well as of corresponding basically-substituted 2-piperidones, has been undertaken to provide compounds for use in experiments designed to correlate the biological activity of these structurally-modified compounds with the activity of 3-alkyl-3-phenyl (and substituted phenyl)-2,6-piperidinediones (*e.g.*, Doriden[2] and Elipten[3]).

During the course of a part of this investigation, the authors discovered that the product which was isolated from a reaction involving the cyanoethylation of 2-(*N,N*-diethylamino)-2-phenylacetonitrile displayed (as evidenced by its infrared spectrum and elemental analysis) the characteristics of an enaminonitrile. Supportive evidence for the formation of this compound is found in a recent report by Hauser *et al.*[4] concerning the synthesis of enamines from alkyl derivatives of 2-(*N,N*-dimethylamino)-2-phenylacetonitrile. A description of the method involved in the formation of the enaminonitrile (I) and the details of its identification are presented herewith.

The literature does not record previous work on the cyanoethylation of α-aminonitriles. Therefore, the conditions of the reaction, specifically as applied to 2-(*N,N*-diethylamino)-2-phenylacetonitrile (II), were studied with reference to those usually employed in the Michael addition. The reaction in the present instance was accomplished only in the absence of solvent and by using, as a catalyst, benzyltrimethylammonium hydroxide[5] (35% solution in methanol). Furthermore, it was exothermic and a blue color which changed rapidly to brown was observed when the catalyst was added to II. The difficulty experienced in this case, compared to the relative ease with which the cyanoethylation of α-alkylphenylacetonitriles is accomplished, may be attributed to the decrease in acidity of the α-hydrogen due to the electron-donating tendency of the amino nitrogen.

Distillation of the residue obtained after ether extraction of the cyanoethylation reaction mixture yielded a compound which, according to its infrared absorption spectrum, contained a cyano group other than that attached to the α-carbon atom of the starting material. It was possible to make this observation because the characteristic infrared absorption band for CN, noted in the spectrum of 2-phenylacetonitrile (5% solution in carbon tetrachloride) at 2250 cm.$^{-1}$, was "quenched" in 2 - (*N,N*-diethylamino) - 2 - phenylacetonitrile apparently by the diethylamino group. The so-called "quenching" of nitrile absorption intensity has been noted previously in compounds bearing oxygen functions on the same carbon atom as that carrying the CN group.[6] Analysis of the

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(1) This investigation was supported in part by funds provided for biological and medical research by the State of Washington Initiative Measure No. 171.

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