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Absorption Spectra of Heterocyclic Compounds. II. Amino-Derivatives of Pyridine, Quinoline and Isoquinoline

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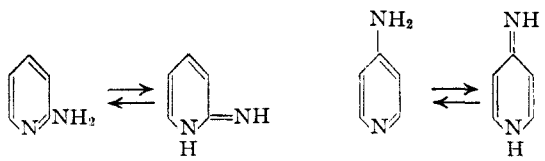
There seems to be little doubt that the simple benzenoid type of hydrocarbon is closely related in characteristics to the heterocyclic compounds containing one nitrogen atom in a six-membered ring. This phase of the concept of isosterism has been supported by considerable evidence, among which may be cited some physico-chemical data[2,3] as well as purely chemical studies. It is unfortunate that, heretofore, there have been very few data to indicate the extent of the similarities between derivatives of certain aromatic nuclei and their nitrogenous isosteres.[4,5]

The present contribution has been planned to examine the ultraviolet absorption spectra of many of the simple amino derivatives of pyridine, quinoline and isoquinoline, and to compare with them the corresponding aromatic types, aniline and the naphthylamines. As will be seen, some of the amino derivatives do not show similarity to the aromatic types, even as we have already shown[4] in the instance of the hydroxy compounds.

I. Aminopyridines.—Of the three aminopyridines, the 2- and 4-substituted compounds (I and II) can undergo a tautomerism of the imine-enamine or vinylogous type. 3-Aminopyridine, on the other hand, shows no such possibility, and therefore will be discussed first.



I

II

The basicity of 3-aminopyridine[6,7] is greater than of either pyridine or aniline (its pK_a is 6.6, compared with 5.36 for pyridine and 4.66 for aniline). This, together with the fact that a stable dihydrochloride can be formed,[8] indicates that both nitrogen atoms are basic in character. When an acid solution of 3-aminopyridine is treated with nitrites, diazotization proceeds in a normal manner and the diazonium salt will undergo the usual reactions of such a compound.[8-14] These chemical properties indicate that the amino group in the 3-position of the pyridine ring is not noticeably influenced by the double bond between the cyclic nitrogen and its adjacent carbon atom. Thus, the compound shows much of the general reactivity of a primary aromatic amine.[15-18] There is, however, a difference in the behavior of nitraminobenzene and 3-nitraminopyridine. While the former is unstable and easily rearranges into *o*- and *p*-nitraniline when treated with sulfuric acid,[19] the latter is stable to the acid to 60°.[20] Hydrogenation of 3-aminopyridine with platinum catalyst[21] proceeded normally to 3-aminopiperidine. These data are summarized in Table I.

TABLE I

COMPARISON OF AMINOPYRIDINES

Reaction	2- and 4-isomers	3-Isomer
pK_a (H_2O)	2-NH_2: 7.2; 4-NH_2: 9.1[6,7]	6.6[6,7]
Diazotization	2-NH_2: Abnormal[10,31,32,33] 4-NH_2: Very difficult[34,35]	Normal[8-13]
Behavior of nitramines with H_2SO_4[19]	Rearrange easily[20]	Stable to 60°[20]
Hydrogenation over Pt catalyst	Incomplete; abnormal products[21,44,45]	Complete, normal[21]
Reaction with RX followed by Ag_2O	N-R-2 (or 4)-pyridoneimide[36-40]	
Action of CH_3I on Na derivative	2-$NHCH_3$-deriv.[36,37,39] N-CH_3-4-pyridoneimide[40]	
Hydrochloride	Mono-[27,28]	Di-[8]
Haloketones or aldehydes, picryl chloride	2-NH_2-: pyrimidazoles, related types[41-43]	

The ultraviolet absorption spectra of 3-aminopyridine are shown in Fig. 1.[22] It is to be noted that its spectrum in a basic medium is very similar to that of aniline in water which shows[23] maxima at λ 230 mμ (ε = 8000) and λ280 (ε = 1250), and does not resemble the pyridine spectrum.[4] As

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(2) (a) Pauling and Sherman, *J. Chem. Phys.*, **1**, 606 (1933); (b) Wrinch, *Science*, **92**, 79 (1940).

(3) Schomaker and Pauling, THIS JOURNAL, **61**, 1769 (1939).

(4) Ewing and Steck, *ibid.*, **68**, 2181 (1946).

(5) (a) Fox and Martin, *J. Chem. Soc.*, 318 (1939); (b) Willis, *Trans. Faraday Soc.*, **43**, 97 (1947).

(6) Albert and Goldacre, *Nature*, **153**, 468 (1944).

(7) Tropsch, *Monatsh.*, **35**, 777 (1914).

(8) Pollak, *ibid.*, **16**, 56 (1895).

(9) Mohr, *Ber.*, **31**, 2495 (1898).

(10) Camps, *Arch. Pharm.*, **240**, 345 (1902).

(11) Friedl, *Ber.*, **45**, 428 (1912).

(12) Räth, *Ann.*, **486**, 95 (1931).

(13) McClelland and Wilson, *J. Chem. Soc.*, 1497 (1932).

(14) Cripa, Long and de Martin, *Gazz. chim. ital.*, **64**, 83 (1934).

(15) Meyer and Jacobson, "Lehrbuch der organ. Chemie," Bd. 2, Tl. 3, de Gruyter, Berlin, 1920, p. 836.

(16) Maier-Bode and Altpeter, "Das Pyridin und seine Derivate," Knapp, Halle, 1934, p. 91.

(17) Bergstrom, *Chem. Rev.*, **35**, 135 (1944).

(18) Morton, "The Chemistry of Heterocyclic Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1946, p. 208.

(19) Holleman, Hartogs and van der Linden, *Ber.*, **44**, 724 (1911).

(20) Chichibabin and Kirssanov, *ibid.*, **60B**, 2433 (1927).

(21) Nienburg, *ibid.*, **70B**, 635 (1937).

(22) The spectra of the aminopyridines have been reported by (a) Spiers and Wibaut, *Rec. trav. chim.*, **56**, 573 (1937), and (b) Ashley, Buchanan and Easson, *J. Chem. Soc.*, 60 (1947). Neither of these reports, however, is sufficiently detailed for present purposes.

(23) Kumler and Strait, THIS JOURNAL, **65**, 2349 (1943).

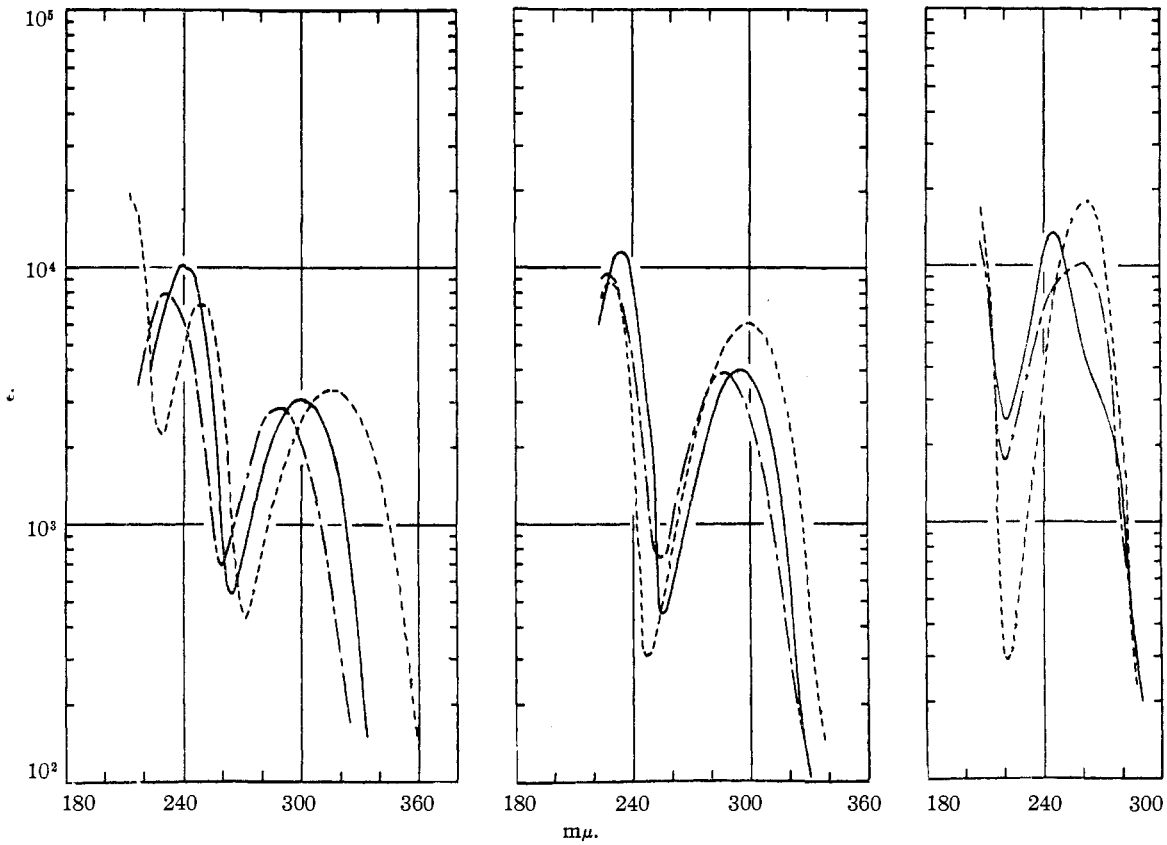


Fig. 1.—3-Aminopyridine. Fig. 2.—2-Aminopyridine. Fig. 3.—4-Aminopyridine.

Solvents: —, 95% ethanol; - - -, 0.01 *N* hydrochloric acid; —·—, 0.01 *N* sodium hydroxide.

the hydrogen ion content of the solution is increased to *p*H 2, both maxima are shifted toward longer wave lengths. This may be taken to indicate that the first proton is taken up by the ring nitrogen atom rather than by the substituent group, for, were this order to be reversed, the spectrum in acid solution would revert to that of pyridine, just as the aniline curve[23] is altered to resemble closely that of benzene. This is in agreement with conclusions in the literature concerning amino derivatives of quinoline[24] (and acridine[25]) which will be discussed presently.

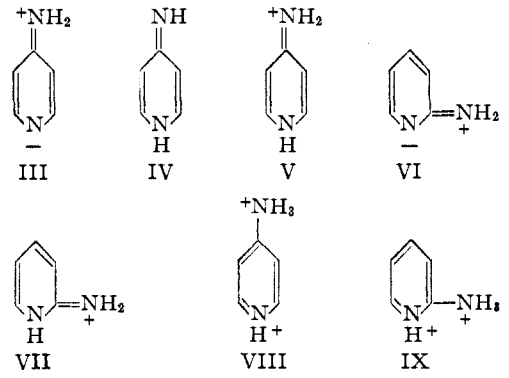
The possibility of the iminopyridine dihydride formulas for the 2- and 4-aminopyridines first occurred to Marckwald many years ago.[15,26] These isomers have been found to resemble each other and to differ from 3-aminopyridine in many respects. They form only monohydrochlorides,[16,27,28] although their dissociation constants show them to be somewhat stronger bases than the 3-isomer (pK_a 7.2 and 9.1, respectively).[6,7] A corresponding difference has been observed in the reaction with N^4-acetylsulfanilyl chloride in several media.[29,30] Although the 3-substituted compound diazotizes normally, the other isomers do not behave in a like manner. Attempts to diazotize 2-aminopyridine by any of the usual procedures have failed to give the expected products.[10,31,32] Diazotization in dilute acids yielded only 2-pyridone, while the use of concentrated acids led to the 2-halopyridines. A diazotate was obtained[31] by treating the sodio derivative with amyl nitrite in ether solution. The sodium pyridine-2-diazotate was found to couple with several phenols and amines in alcoholic solution and to give 2-iodopyridine with potassium iodide solution as well as to show other typical diazo reactions.[31,33] Similarly, difficulties were experienced in attempts to diazotize 4-aminopyridine. It was possible to obtain a diazonium salt under especially rigorous conditions[34,35] and this substance underwent normal coupling reactions.

The potential tautomerism of the 2- and 4-aminopyridines, as compared with the 3-isomer, is

(24) Irvin and Irvin, THIS JOURNAL, **69**, 1091 (1947).
(25) Craig and Short, *J. Chem. Soc.*, 419 (1945).
(26) Sidgwick, Taylor and Baker, "Organic Chemistry of Nitrogen," Clarendon Press, Oxford, 1937, p. 529.
(27) Marckwald, *Ber.*, **27**, 1321 (1894).
(28) Meyer, *Monatsh.*, **15**, 175 (1894).
(29) Winterbottom, THIS JOURNAL, **66**, 836 (1944).
(30) Shepherd, *J. Org. Chem.*, **12**, 277 (1947).
(31) Chichibabin and Ryasanzhev, *J. Russ. Phys. Chem. Soc.*, **47**, 1571 (1915).
(32) Craig, THIS JOURNAL, **56**, 231 (1934).
(33) Chichibabin, *J. Russ. Phys.-Chem. Soc.*, **50**, 512 (1918).
(34) Witt, *Ber.*, **42**, 2953 (1909).
(35) Koenigs, Kinne and Weiss, *ibid.*, **57**, 1172 (1924).

indicated by the above data, but the following evidence even more strongly demonstrates that these compounds behave as imino-pyridine dihydrides. When 2-aminopyridine was caused to react with an alkyl halide and then treated with silver oxide, an N-alkyl-2-pyridone-imide resulted.[36-38] The latter showed several reactions, as loss of ammonia to yield N-alkyl-2-pyridone, indicating it to have an imide structure.[37] The treatment of sodio-2-aminopyridine with methyl iodide, however, gave 2-methylaminopyridine, which did not nitrosate.[36,39] A closely related situation applies to the 4-isomer, but 4-methylaminopyridine could be prepared only by the thermal decomposition of 4-methylaminopyridine-2,6-dicarboxylic acid.[40] The 2- and 4-isomers have been found to form the corresponding nitraminopyridines, as does the 3-amino compound, but differ from the latter in that they rearrange.[20] Further interesting aspects in the chemistry of 2-aminopyridine resulting from the imino character are its reactions with haloketones or aldehydes,[41,42] with picryl chloride,[43] and its behavior on reduction.[21,44,45]

Leis and Curran[46] have reported the dipole moments of pyridine and several 4-substituted derivatives, including 4-aminopyridine, in dioxane solutions. They point out that the moment of 4-aminopyridine is significantly greater than that calculated by combining the observed values for pyridine and aniline. This enhancement they consider to indicate a strong contribution of a polar form with the structure III. They also point out that a form such as IV would have a very low moment, and hence is apparently ruled out as present in any appreciable amount in dioxane solution. This is concordant with the observed high basicity of 4-aminopyridine,[6] for a substance with structure III would have a high tendency to combine with a proton to give the cation V.



The absorption spectra of the 2- and 4-aminopyridines are shown in Figs. 2 and 3, respectively. Both are in essential agreement with the data of Ashley, Buchanan and Easson,[22b] who examined aqueous solutions of the hydrochlorides. The bathochromic shift in acid solution which was seen in the case of the 3-isomer does not occur, although the absorption is somewhat more intense at low *p*H than high. This is in agreement with structure III for 4-isomer and the analogous form VI for the 2-isomer, since structures III and V and also VI and VII should be almost indistinguishable from the standpoint of ultraviolet absorption. In concentrated acid solution, as has been shown by Ashley, Buchanan and Easson,[22b] a second proton is accepted, producing the forms VIII and IX, and the spectra revert to that of pyridine.

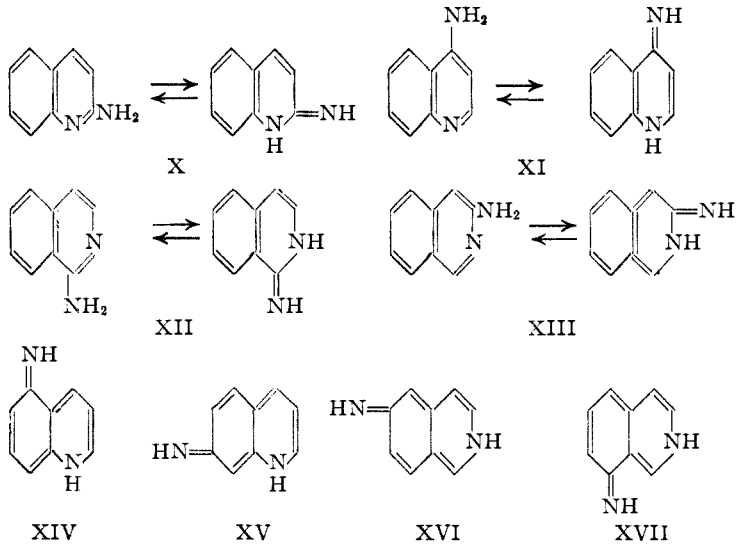
II. Aminoquinolines and Isoquinolines.—Four members of these series can be written in such a manner as to indicate imine-enamine tautomerism occurring in the pyridine ring, namely, the 2- and 4-aminoquinolines (X and XI) and the 1- and 3-aminoisoquinolines (XII and XIII).[47] In addition, the 5- and 7-aminoquinolines (XIV and XV) and 6- and 8-aminoisoquinolines (XVI and XVII) show a formal possibility of similar tautomerism involving the benzenoid ring. No data are available on isomers XIII, XVI and XVII.

The basicities of the aminoquinolines have been investigated by Albert and Goldacre,[6] who found the compounds to fall into three classes. One class contains the 2- and 4-isomers, which are much stronger bases than is quinoline. The second class is made up of the 3-, 5- and 6-isomers, the basicities of which are only slightly greater than that of quinoline. The 7-amino isomer was found to be intermediate between these two groups. A third class consists only of the 8-isomer which is considerably less basic than quinoline, and approximately equal in this respect to α-naphthylamine.[48] The authors show that such an exaltation of basic properties in the 2- and 4-isomers is readily explicable in terms of resonance involving a quinonoid structure as one form.[6,24]

(36) Chichibabin, Konovalova and Konovalova, *J. Russ. Phys.-Chem. Soc.*, **53**, 193 (1921).
(37) Chichibabin, Konovalova and Konovalova, *Ber.*, **54**, 814 (1921).
(38) Reindel, *ibid.*, **57**, 1381 (1924).
(39) Chichibabin and Knunyants, *ibid.*, **61**, 2215 (1928).
(40) Chichibabin and Ossetrova, *ibid.*, **58**, 1708 (1925).
(41) Chichibabin, *ibid.*, **59**, 2048 (1926).
(42) Chichibabin and Plashenkova, *ibid.*, **64**, 2842 (1931).
(43) Morgan and Stewart, *J. Chem. Soc.*, 1292 (1938).
(44) Orthner, *Ann.*, **456**, 246 (1927).
(45) Grave, THIS JOURNAL, **46**, 1462 (1924).
(46) Leis and Curran, *ibid.*, **67**, 79 (1945).

(47) Longuet-Higgins and Coulson, *Trans. Faraday Soc.*, **43**, 87 (1947), have discussed various heterocyclic compounds, including quinoline and isoquinoline, employing the method of orbitals. They show strikingly low values for calculated electron densities at the 2- and 4-positions in quinoline and the 1-position in isoquinoline, while at the 3-position in isoquinoline the density is of the same order as for the carbon atoms of the benzoid ring. Thus one might expect by analogy that 3-aminoisoquinoline (XIII) would show properties resembling more closely the bz-amino derivatives than the tautomeric forms. By a similar analogy, 6-aminoisoquinoline (XVI) may be expected to show a somewhat greater contribution of an imine form than 5-aminoquinoline (XIV).

(48) The pK_a values for α- and β-naphthylamines are, respectively, 4.00 and 4.30, both at 25°, as calculated from the dissociation constants given by Hodgman, "Handbook of Chemistry and Physics," Chemical Rubber Publishing Co., Cleveland, Ohio, 27th edition, 1943, p. 1353. Hodgman does not indicate his authority for these constants.



X XI XII XIII XIV XV XVI XVII

The 3-, 5-, 6-, 7- and 8-aminoquinolines have all been diazotized in the normal manner, though with varying ease, and each diazonium salt has been found to show the normal reactions of the type. For example, they all will couple with pyridine,[49] and, with the possible exception of the 7-isomer, which has not been reported, they, or their simple derivatives, will all undergo the Sandmeyer reaction.[50-58] It should be pointed out, however, that Fieser and Hershberg[51] obtained only tar under the conditions of this reaction, using 8-aminoquinoline, and that Hargreaves, Marshall and Wharton[59] found similar results with the 6-isomer. In addition, the 3-, 7- and 8-quinolinediazonium salts or simple derivatives have been shown to couple normally with the naphthols.[60-62] Other satisfactory reactions of these quinolinediazonium salts are described in the literature.[63-68] Coupling reactions of these aminoquinolines with benzenediazonium chloride have been studied in detail,[69,70] and the various positional isomers obtained have been used as evidence of an Erlenmeyer static-bonding structure for quinoline. It has been observed also that 7-amino-2-chloro-4-methylquinoline can be deazotized to 2-chloro-4-methylquinoline by treatment with hydrazine hydrochloride.[71] The Skraup reaction has been found to proceed satisfactorily in the cases of the 5- and 6-aminoquinolines to give the corresponding phenanthrolines.[66,72-74] Heating the 7-aminoquinoline to 200° with concentrated hydrochloric acid has been found to give the corresponding hydroxy compound.[57]

The absorption spectra of 3-, 5-, 6-, 7- and 8-aminoquinolines, 6-dimethylaminoquinoline, and 4- and 5-aminoisoquinolines are presented in Figs. 4 to 11. As we have pointed out previously,[4] quinoline and isoquinoline show bathochromic shifts in acid solution (*p*H about 2) due to the addition of a proton to the heterocyclic nitrogen atom which permits a strengthening of the resonance contributions of certain quinonoid forms. Aromatic amines, on the other hand, show a strong hypsochromic effect upon acidification, as has been shown in the case of aniline (*vide supra*, and ref. 23). The fact that this effect also occurs in the cases of the two naphthylamines is shown in Figs. 12 and 13, which give the spectra of these two compounds in neutral and acid solutions, together with that of an alcoholic solution of naphthalene, taken from the work of Clar and Lombardi.[75,76] It is significant also that similar results are obtained with the N-dimethyl derivatives of both naphthylamines (Figs. 14 and 15).

In the aminoquinolines both bathochromic and hypsochromic tendencies must exist, and a shift of absorption in acid solution relative to basic or neutral will be either toward longer wave lengths, as in quinoline, or toward shorter, as in naphthylamine, according to which effect is stronger. As pointed out by Craig and Short[25] in the case of the aminoacridines, the spectrum will be shifted toward longer wave lengths if the first proton to be accepted goes to the ring nitrogen, but toward shorter wave lengths if the substituent amino group is neutralized first. In the curves presented herewith it will be seen that in every case there is a bathochromic shift in acid solution (*p*H 2), indicating, as expected from analogy with the aminoacridines, that the ring nitrogen accepts the first

(49) Coates, Cook, Heilbron, Hey, Lambert and Lewis, *J. Chem. Soc.*, 401 (1943).
(50) Freydl, *Monatsh.*, **8**, 383 (1887).
(51) Fieser and Hershberg, THIS JOURNAL, **62**, 1640 (1940).
(52) Colonna, *Boll. sci. facolta chim. ind. Bologna*, 107 (1941).
(53) Howitz, Fraenkel and Schroeder, *Ann.*, **396**, 54 (1913).
(54) Junghanns, *J. prakt. Chem.*, [2] **48**, 260 (1893).
(55) Claus and Setzer, *ibid.*, [2] **53**, 406 (1896).
(56) Claus and Ammelburg, *ibid.*, [2] **51**, 421 (1895).
(57) Kochańska and Bobranski, *Ber.*, **69**, 1807 (1936).
(58) Claus and Grau, *J. prakt. Chem.*, [2] **48**, 167 (1893).
(59) Hargreaves, Marshall and Wharton, *J. Am. Pharm. Assoc.*, **28**, 140 (1939)
(60) Mills and Watson, *J. Chem. Soc.*, **97**, 741 (1910).
(61) Alber, *J. prakt. Chem.*, [2] **71**, 47 (1905).
(62) Seka, *Monatsh.*, **45**, 287 (1925).
(63) Bargellini and Berlingozzi, *Gazz. chim. ital.*, **53**, 3 (1923).
(64) Bargellini and Settinj, *ibid.*, **53**, 601 (1923).
(65) Bargellini and Napolitano, *ibid.*, **53**, 369 (1923).
(66) Noelting and Trautmann, *Ber.*, **23**, 3674, 3683 (1890).
(67) Meigen, *J. prakt. Chem.*, [2] **73**, 249 (1906).
(68) Byvanck, *Ber.*, **31**, 2147 (1898).
(69) Renshaw, Friedman and Gajewski, THIS JOURNAL, **61**, 3322 (1939).
(70) Jacobs and Heidelberger, *ibid.*, **42**, 2278 (1920).
(71) Besthorn and Byvanck, *Ber.*, **31**, 799 (1898).
(72) Skraup, *Monatsh.*, **5**, 532 (1884).
(73) Haworth and Sykes, *J. Chem. Soc.*, 311 (1944).
(74) Kaufmann and Radosevic, *Ber.*, **42**, 2613 (1909).
(75) Clar and Lombardi, *ibid.*, **65**, 1411 (1932).
(76) Our curves for the naphthylamines in alcohol are in substantial agreement with those of (a) Hunter, Qureishy and Samuel, *J. Chem. Soc.*, 1576 (1936), and of (b) Hodgson and Hathway, *Trans. Faraday Soc.*, **41**, 117 (1945). These authors did not report the spectra of acid solutions.

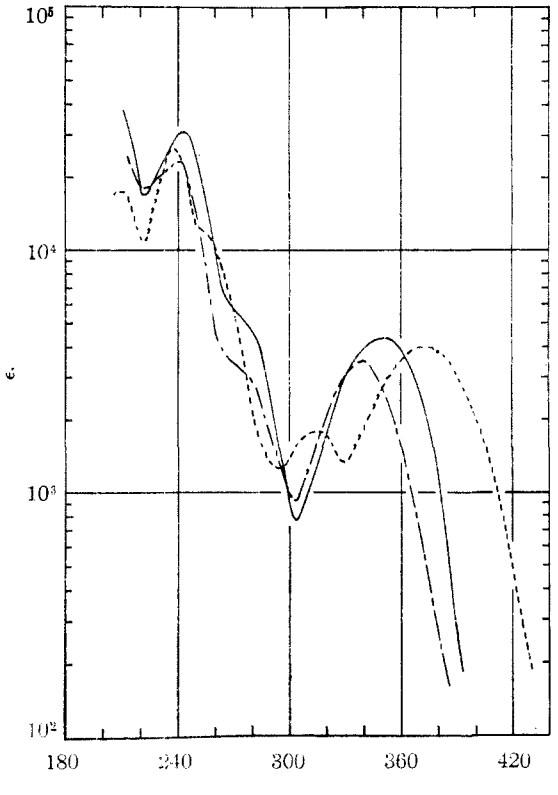


Fig. 4.—3-Aminoquinoline.

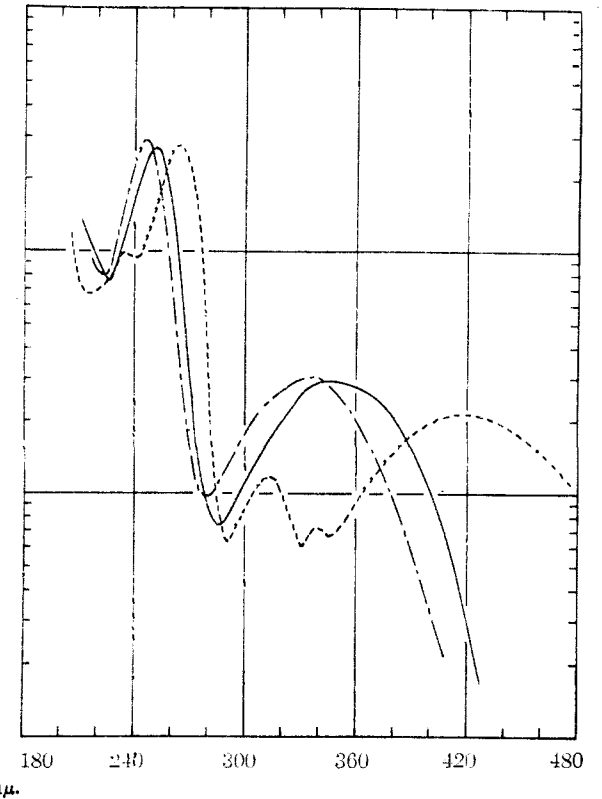


Fig. 5.—5-Aminoquinoline.

Solvents: as indicated above.

proton. This has been shown to be the case for 7-chloro-4-aminoquinoline by Irvin and Irvin[24] both by spectrophotometric measurements and by a potentiometric method.

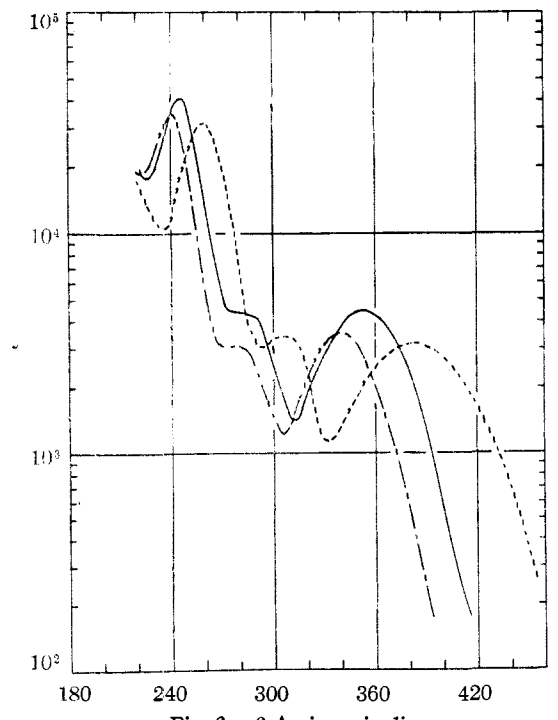


Fig. 6.—6-Aminoquinoline.

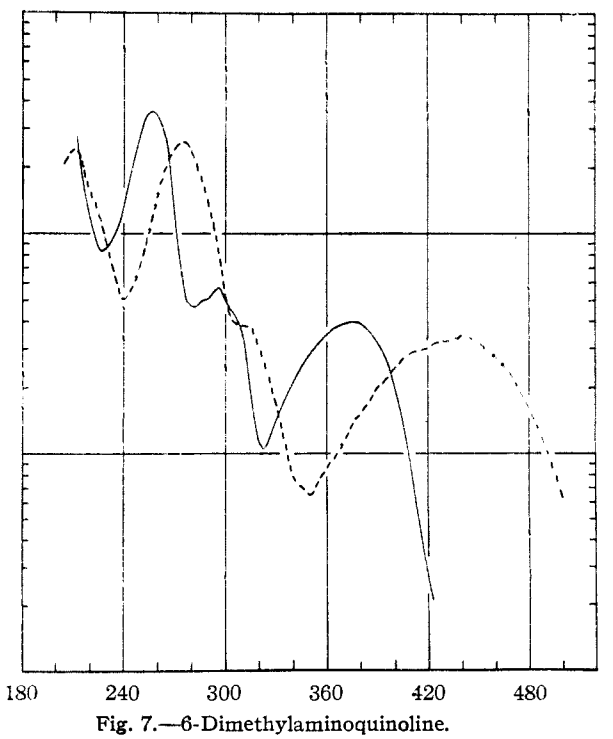


Fig. 7.—6-Dimethylaminoquinoline.

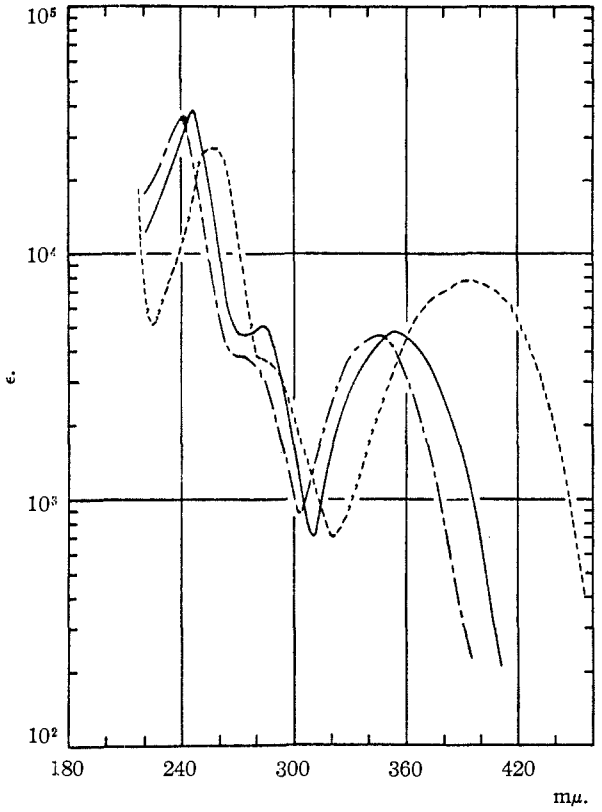


Fig. 8.—7-Aminoquinoline.

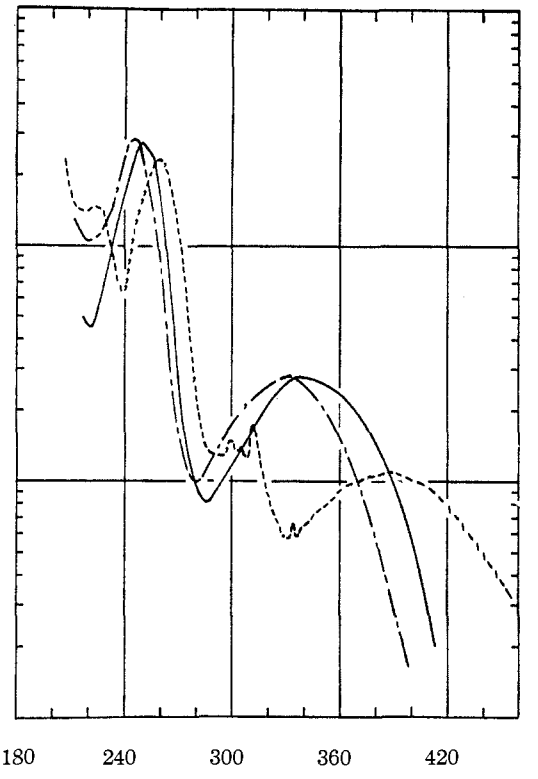


Fig. 9.—8-Aminoquinoline.

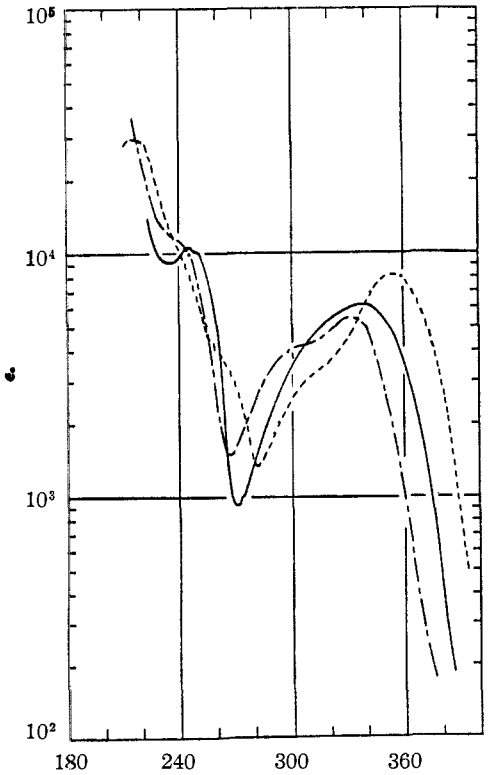


Fig. 10.—4-Aminoisoquinoline.

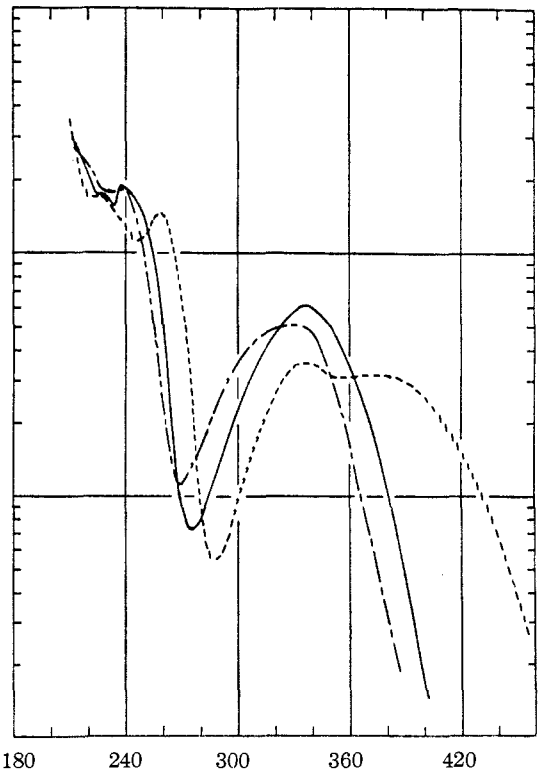


Fig. 11.—5-Aminoisoquinoline.

Solvents: as indicated above.

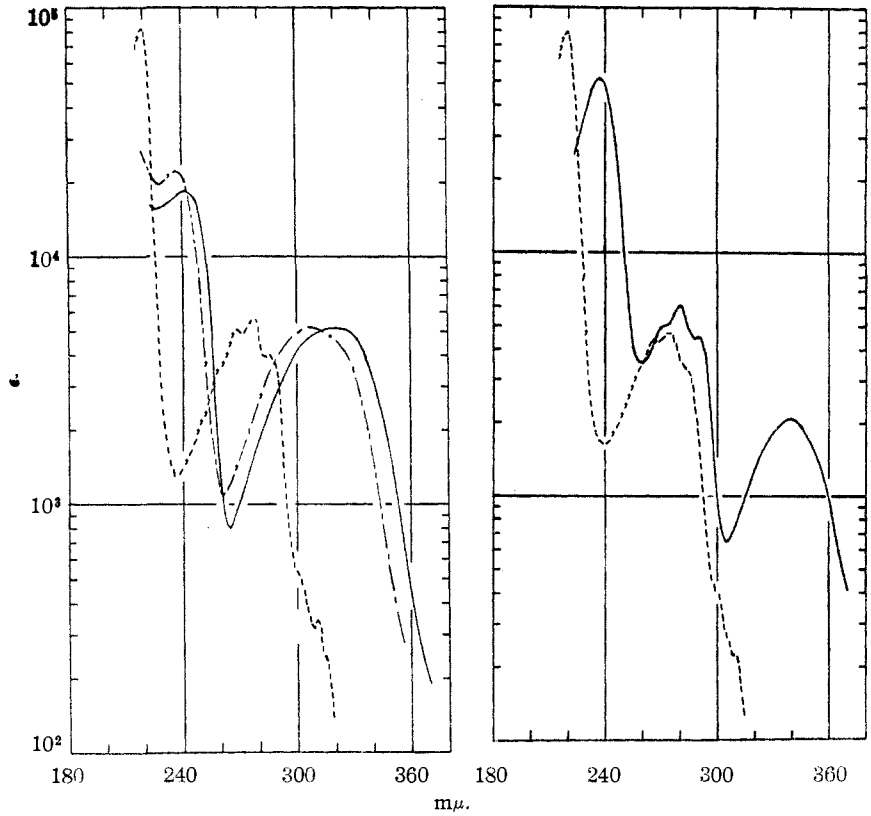


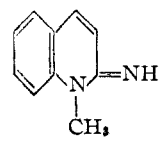
Fig. 12.—α-Naphthylamine.

Fig. 13.—β-Naphthylamine.

In the case of 8-aminoquinoline (Fig. 9), the long-wave absorption is markedly less intense than for any of the other isomers. Albert and Goldacre[6] have pointed out that the difference of this isomer from the so-called "normal" isomers with respect to basicity may be due to hydrogen bonding between the two nitrogen atoms or perhaps to steric hindrance to the approach of an hydronium ion to the ring nitrogen. These effects presumably account for the difference in spectral behavior as well.

The spectra of 6-dimethylaminoquinoline have been included (Fig. 7) to show that the same considerations apply as to the parent amine, though there is more difference in this case than between the naphthylamines and their dimethyl derivatives.

The chemical properties of the 2- and 4-aminoquinolines have frequently been found to contrast with those of the other isomers considered above. This is indicated in Table II. 2-Aminoquinoline was diazotized for the first time by Heilbron and his co-workers[49] in 1943; they used amyl nitrite and sodium ethylate to obtain the sodium diazotate, which would not, however, react with pyridine. The same authors found that the 4-isomer failed to undergo normal diazotization under a wide variety of conditions, including the use of amyl nitrite and ethereal nitrosyl chloride. However, diazo reactions have been reported for 4-aminoquinoline.[77-79] Benzenediazonium chloride has been shown to give a diazoamino derivative with 2-aminoquinoline, but not with the 4-isomer[69]; 2,4-diaminoquinoline gave the 4-amino-2-diazoamino derivative. 4-Aminoquinoline has been shown to undergo both Skraup and Döbner–von Miller reactions,[80] while no such behavior has been reported with the 2-isomer. When 2-aminoquinoline was treated with concentrated or dilute alkali, 2-quinolone resulted.[81] Treatment with methyl iodide gave the N-methyl imide (XVIII),



XVIII

which upon further treatment with sodium hydroxide gave N-methyl-2-quinolone.[82] Picryl chloride has been found to react with 2-aminoquinoline in such manner as to indicate an imino structure for the latter.[43] Nitration with fuming nitric and sulfuric acids gave the nitramino compounds with both the 2- and 4-aminoquinolines.[83]

(77) Claus and Howitz, *J. prakt. Chem.*, [2] **50**, 237 (1894).
(78) Claus and Frobenius, *ibid.*, [2] **56**, 194 (1897).
(79) Wenzel, *Monatsh.*, **15**, 457 (1894).
(80) Marckwald, *Ann.*, **279**, 18 (1894).
(81) Claus and Schaller, *J. prakt. Chem.*, [2] **56**, 206 (1897).
(82) Roser, *Ann.*, **282**, 381 (1894).
(83) Chichibabin, Witkovski and Lapshin, *Ber.*, **58**, 803 (1925).

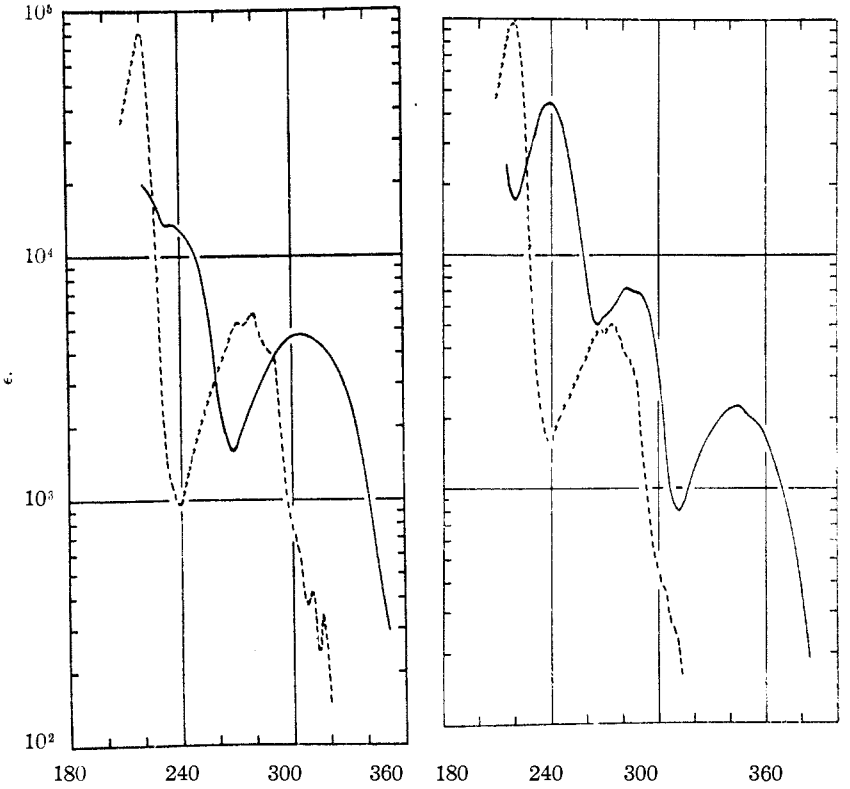


Fig. 14.—Dimethyl-α-naphthylamine. Fig. 15.—Dimethyl-β-naphthylamine.

Solvents: as indicated above.

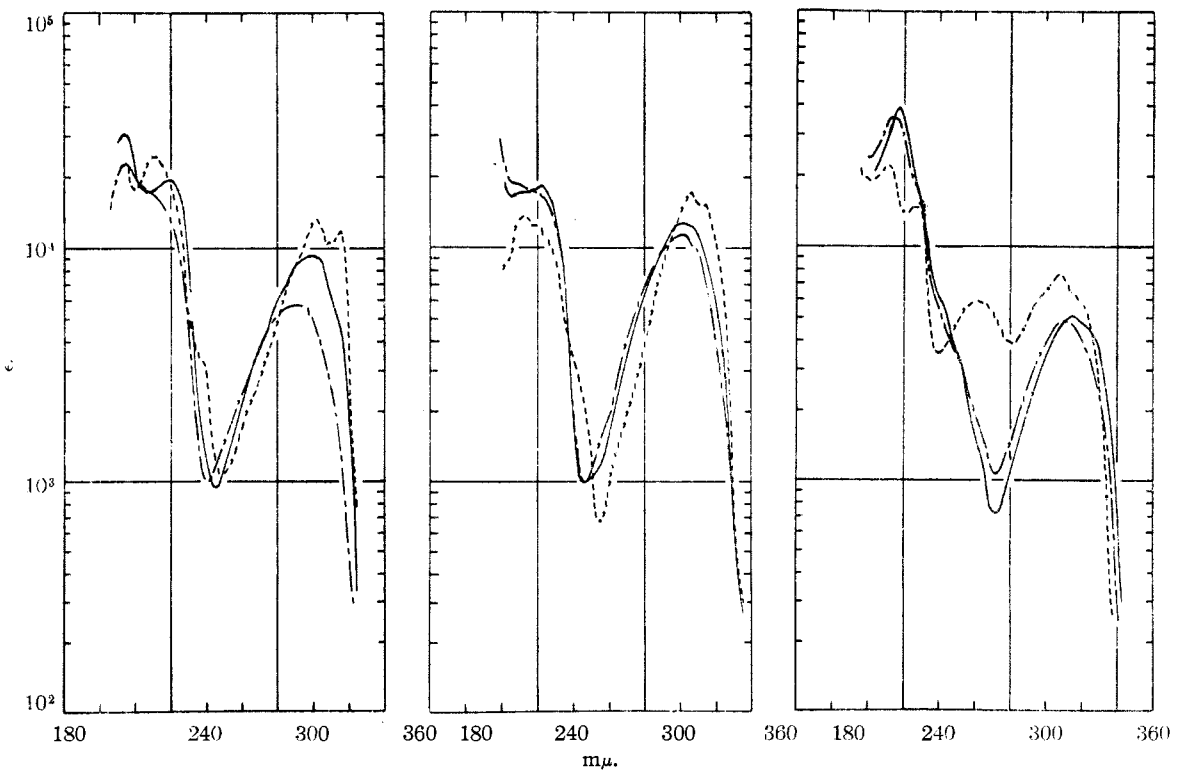


Fig. 16.—4-Aminoquinoline. Fig. 17.—4-Dimethylaminoquinoline. Fig. 18.—2-Aminoquinoline.

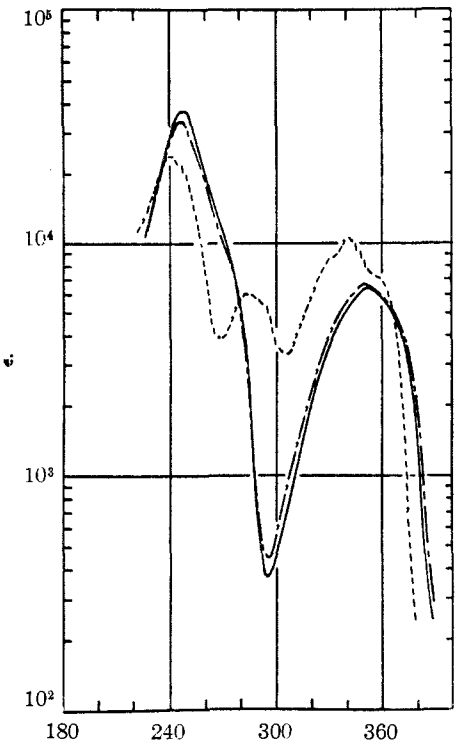


Fig. 19.—2-Dimethylaminoquinoline.

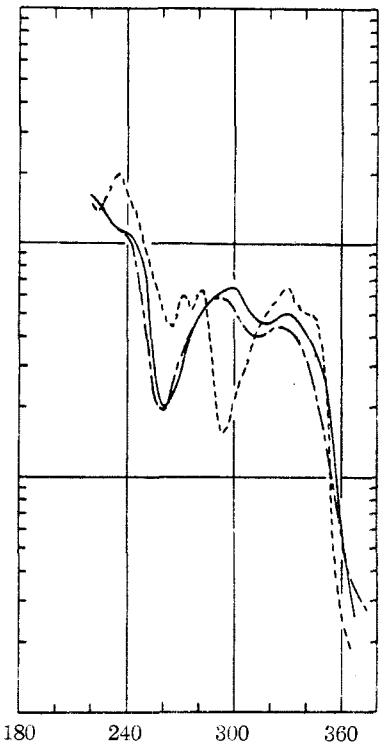


Fig. 20.—1-Aminoisoquinoline.

Solvents: as indicated above.

The spectra of 4-aminoquinoline and of its N-dimethyl derivative are given in Figs. 16 and 17. They show little resemblance to those of the isomers already considered. The absorption in acid solution is somewhat greater than in neutral or basic medium, but not shifted appreciably toward longer wave lengths. The close resemblance between the spectra of the free amine and its dimethyl derivative is particularly significant. This shows again that in dilute acid solution only one proton is taken up and that by the ring nitrogen rather than by the substituent group. Similar considerations apply to the 2-isomer and its N-dimethyl derivative (Figs. 18 and 19) and to 1-aminoisoquinoline (Fig. 20).

TABLE II

COMPARISON OF AMINOQUINOLINES

Reaction	2- and 4-isomers	3-, 5-, 6-, 7- and 8-isomers
pK_a (H_2O)[6]	2-NH_2..7.34	3-NH_2..4.95; 5-NH_2..5.51
	4-NH_2..8.46	6-NH_2..5.62; 7-NH_2..6.65
		8-NH_2..3.93
Diazotization	2-NH_2..Abnormal[49,69]	3-NH_2..Normal[49,52,60,63,64,69]
	4-NH_2..Mostly abnormal[49,69,77-79]	5-NH_2..Normal[a,49-51,53,66,69,70,80]
		6-NH_2..Normal[49,58,67,69] (but note ref. 59)
		7-NH_2..Normal[49,61,65,69,71]
		8-NH_2..Normal[49,53,55,62,69] (but note ref. 70)
Skraup and related syntheses	4-NH_2..Rare[80]	5-NH_2..Normal[66,72]
		6-NH_2..Normal[73]
Reaction with CH_3I then alkali	2-NH_2..N-methyl-2-quinolone imide[81]	

[a] Frisch and Bogert, *J. Org. Chem.*, **9**, 338 (1944).

Experimental Part

Absorption Spectra.—The technique of determining, calculating and plotting the spectra is the same as previously described,[4] and the solvents used are also the same.

The **2-aminopyridine** and **6-aminoquinoline** used were commercial samples which had been purified to constant melting point.

3-Aminopyridine was prepared by the Hoffman degradation of nicotinamide,[10] sublimed and recrystallized from hexane, m. p. 64.5–65°.

4-Aminopyridine was obtained by the reaction of 4-pyridylpyridinium dichloride[84] with ammonium hydroxide at 160°.[85] The compound was crystallized from benzene-octane, m. p. 157–158°. In view of the observation of Spiers and Wibaut,[22a] the absorption spectra of the compound were determined soon after its preparation.

2-Aminoquinoline was prepared by the amination of quinoline with sodamide[86] and crystallized from toluene, m. p. 130.5–131°.

2-Dimethylaminoquinoline was obtained by the reaction of dimethylamine with 2-chloroquinoline,[87] crystallized from hexane, m. p. 71°.

3-Aminoquinoline was obtained from quinoline through the 3-bromo compound[88] by reaction with cuprammonium sulfate–ammonia.[89] The compound, after crystallization from hexane or dilute methanol, melted at 83.5–84°.

(84) Goldsmith, Thesis, Pennsylvania State College, 1942, p. 95.

(85) Koenigs and Greiner, *Ber.*, **64**, 1049 (1931).

(86) Shreve, Riechers, Rubenkoenig and Goodman, *Ind. Eng. Chem.*, **32**, 177 (1940).

(87) Gilman, Crounse, Massie, Benkeser and Spatz, THIS JOURNAL, **67**, 2107 (1945).

(88) Edinger, *J. prakt. Chem.*, [2] **54**, 358 (1896).

(89) Kuhn and Westphal, *Ber.*, **73**, 1107 (1940).

4-Aminoquinoline was formed when 4-chloroquinoline (from 4-quinolinol[90] by reaction with phosphorus oxychloride) was dissolved in phenol and treated with ammonia at about 170°.[91-93] After crystallization from benzene, the melting point was 155–155.5°.

The **5- and 8-aminoquinolines** were obtained by the reduction over Raney nickel in alcohol[94] of the mixed nitro compounds resulting from the nitration of quinoline.[51] The 5-amino compound was crystallized from alcohol, m. p. 110–111°; the 8-isomer melted at 65–66° after crystallization from octane.

7-Aminoquinoline was obtained through a Skraup reaction[95,96] followed by reduction[94]; the anhydrous form[97] was obtained, after crystallization from water, by thorough drying, m. p. 94–94.5°.

4-Dimethylaminoquinoline was prepared from 4-chloroquinoline in a manner similar to that used for the 2-isomer; it was isolated as the monohydrochloride, needles from alcohol–ether, m. p. 214.5–215°.

Anal. Calcd. for $C_{11}H_{12}N_2 \cdot HCl$: Cl, 17.10; N, 13.48. Found: Cl, 16.93; N, 13.45, 13.60.

6-Dimethylaminoquinoline was formed by a Skraup synthesis[95,96]; the compound oxidized very readily in the air, hence was recrystallized from pentane under dry nitrogen, pale yellow warts, m. p. 52–53°. This compound was used immediately, for it turned black within a day or two.

1-Aminoisoquinoline was formed by the amination of isoquinoline with sodamide,[4,86] and crystallized from water as white needles, m. p. 123–123.5°.

4-Aminoisoquinoline was obtained by bromination of isoquinoline and then reaction of the 4-bromo compound with cuprammonium sulfate–ammonia.[98] It crystallized from benzene, creamy white needles of m. p. 109–109.5°.

5-Aminoisoquinoline was prepared by catalytic reduction of the nitro compound in alcohol with palladium–charcoal.[99] The base recrystallized well from chloroform–hexane in the form of yellowish leaflets, m. p. 129.5–130°.

Dimethyl-α-naphthylamine was available commercially; it was redistilled immediately before use.

Dimethyl-β-naphthylamine was prepared essentially as described by Hodgson and Crook,[100] modified slightly on the basis of earlier work on the α-isomer.[101] The resublimed sample melted 46.5–47°.

Acknowledgments.—The authors are pleased to express their appreciation to Mrs. N. P. Gorman for preparative assistance and to Mrs. C. M. Grant and Mr. M. Priznar for aid in the spectrophotometric studies. The development of the present contribution was materially aided by discussions with Dr. F. C. Nachod. Dr. C. J. Cavallito was kind enough to furnish several intermediates used in this work. The analytical staff of the Institute, under the direction of Mr. M. E. Auerbach, carried out requisite analyses.

Summary

1. The ultraviolet absorption spectra have been determined for all of the isomeric amino derivatives of pyridine and quinoline and also for several aminoisoquinolines.

2. Spectrophotometric evidence is in essential agreement with other physical and chemical data in the assignment of an imine structure to the amino pyridines, quinolines and isoquinolines where the substituent is in the α- or γ-position relative to the ring nitrogen. The other isomers exhibit the characteristics of the naphthylamines, the amino group being aromatic in character.

(90) Cavallito and Haskell, THIS JOURNAL, **66**, 1166 (1944).
(91) Andersag, Breitner and Jung, U. S. Patent 2,233,970; *Chem. Abs.*, **35**, 3771 (1941).
(92) Steck, Hallock and Holland, THIS JOURNAL, **68**, 129 (1946).
(93) Elderfield, Gensler, Birstein, Kreysa, Maynard and Galbreath, *ibid.*, **68**, 1250 (1946).
(94) Winterbottom, *ibid.*, **62**, 160 (1940).
(95) Knueppel, *Ber.*, **29**, 706 (1896).
(96) Manske, Leger and Gallagher, *Can. J. Research*, **B19**, 318 (1941).
(97) Hamer, *J. Chem. Soc.*, **119**, 1436 (1921).
(98) Craig and Cass, THIS JOURNAL, **64**, 783 (1942).
(99) Misani and Bogert, *J. Org. Chem.*, **10**, 358 (1945); LeFèvre and LeFèvre, *J. Chem. Soc.*, 1475 (1935).
(100) Hodgson and Crook, *ibid.*, 1502 (1936).
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RENSSELAER, NEW YORK RECEIVED NOVEMBER 3, 1947

[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

Absorption Spectra of Heterocyclic Compounds. III. Some Benzimidazole Derivatives

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Introduction

Interest in the absorption spectra of 2-dialkylaminomethylbenzimidazoles was aroused by the description of two compounds of this type as colored substances.[2,3] There was little reason to expect that the replacement of a methyl by a dialkylaminomethyl group would result in a bathochromic effect. In our hands, none of the compounds of either the 2-methyl or the 2-dialkylaminomethyl benzimidazole type were obtained in colored form when pure, but, nonetheless, the absorption spectra were studied. Matters relating to 2-dialkylaminomethylbenzimidazoles led to investigation of the spectral characteristics of two 2-aminobenzimidazoles.

Imidazoles have long been considered as cyclic amidines (*cf.* ref. 4) and are the most basic of the imide-containing azoles.[5-7] Because imidazole derivatives occupy a position of importance in matters relative to the constitution of heterocycles as well as in biochemistry, their physical proper-

(1) Present address: Department of Chemistry, Union College, Schenectady 8, New York.
(2) Bloom and Day, *J. Org. Chem.*, **4**, 14 (1939).
(3) Roeder and Day, *ibid.*, **6**, 25 (1941).
(4) Bamberger, *Ann.*, **273**, 300 (1893).
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(6) Schwarzenbach and Lutz, *Helv. Chim. Acta*, **23**, 1162 (1940).
(7) Wheland, The Theory of Resonance, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 180.