The Chemistry of 7-Aminoindoline and Certain Pyrrolo- and Pyrido[1,2,3-*de*]quinoxalines

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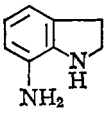
The synthesis of 7-aminoindoline (I) was accomplished by the hydrolysis of 1-acetyl-7-aminoindoline. Reactions designed to form 2-substituted 4,5-dihydropyrrolo[1,2,3-*cd*]benzimidazoles from I and carboxylic acid type reagents yielded 7-(N-substituted)aminoindolines. Certain aromatic or heterocyclic benzoin-type reagents condensed with I to form the desired 2,3-disubstituted 5,6-dihydro-3H-pyrrolo[1,2,3-*de*]quinoxalines (VII). No characterizable products were obtained when aliphatic α-hydroxy ketones were treated with I. Benzil, when condensed with I, formed the corresponding 5,6-dehydro analog of VII. Diethyl oxalate, when condensed with I, formed the 2-hydroxy-3-keto derivative of VII. Certain 2,3-disubstituted 6,7-dihydro-3H,5H-pyrido[1,2,3-*de*]quinoxalines (XV) were also prepared and examined as the next higher homologs of VII. Data establishing the structures of the ring systems are given. A major chromophore in these systems is discussed in terms of the electronic absorption spectra.

As an extension of earlier work[1,2] involving fused tetrahydroquinolines, an investigation of the synthesis of fused indolines was begun. It was, therefore, necessary to prepare 7-aminoindoline (I) as a starting material for the reactions involved.



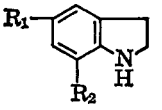
I

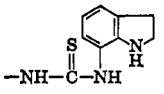
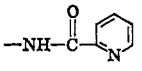
Gall, *et al.*,[3] prepared 1-acetyl-7-aminoindoline by starting with 1-acetylindoline which was subsequently brominated, nitrated, and hydrogenated. The structure of the product was later confirmed by Holland.[4] Gall's procedure was employed in this work, and the 1-acetyl-7-aminoindoline thus obtained was then hydrolyzed in refluxing, aqueous hydrochloric acid solution. The product, 7-aminoindoline (I), separated as a crystalline, characterizable monohydrate when the acidic solution was neutralized with aqueous ammonia. When the hydrate was dried and vacuum distilled, the anhydrous 7-aminoindoline (I) was obtained as a colorless oil. The product was further characterized as the dihydrochloride salt and as the picrate (Table I). The base, when exposed to the atmosphere, re-formed the crystalline monohydrate and simultaneously became very dark. It was therefore stored under a nitrogen atmosphere in a freezer.

For comparison, 5-aminoindoline (II) was prepared by hydrogenating 5-nitroindoline,[3] and the product was characterized as the dihydrochloride salt (Table I).

TABLE I

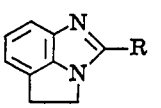
INDOLINES



Compd.	R_1	R_2	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
I[a]	H	NH_2	225–230 dec.	$C_8H_{10}N_2 \cdot 2HCl$	46.39	46.80	5.84	5.82	13.53	13.66
II[b]	NH_2	H	261–262 dec.	$C_8H_{10}N_2 \cdot 2HCl$	46.39	46.31	5.84	5.77	13.53	13.78
IV[c,d]	H	NHCHO	192 dec.	$C_9H_{10}N_2O \cdot HCl$	54.41	54.17	5.58	5.49	14.10	14.00
V	H	NHCN	90.0–91.5	$C_9H_9N_3$	67.91	67.75	5.70	5.66	26.40	26.09
VI[e]	H		223	$C_{17}H_{18}N_4S$	65.81	65.68	5.84	5.72	18.05	17.98
XIII	H		162.0–162.5	$C_{14}H_{13}N_3O$	70.28	70.35	5.48	5.43	17.56	17.42

[a] Melting point and analyses taken on the dihydrochloride salt. Free base is an oil, b.p. 150–152° (6–7 mm.), $n^{23}D$ 1.6340; monohydrate m.p. 60.5–62.0°; picrate m.p. 198° dec. [b] Melting point and analyses taken on the dihydrochloride salt. [c] Lit.[4] m.p. 126–127° for the base. [d] Melting point and analyses taken on the hydrochloride salt. [e] Lit.[4] m.p. 216–217°.

Several reactions were run in attempts to form 2-substituted 4,5-dihydropyrrolo[1,2,3-*cd*]benzimidazoles (III) from 7-aminoindoline (I) and formic acid, carbon



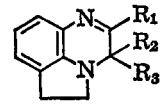
III

disulfide, phosgene, or cyanogen bromide. In no case was the desired compound isolated. No characteriz-

(1) A. Richardson, Jr., and E. D. Amstutz, *J. Org. Chem.*, **25**, 1138 (1960).
(2) A. Richardson, Jr., *ibid.*, **28**, 2581 (1963).
(3) W. G. Gall, B. D. Astill, and V. Boekelheide, *ibid.*, **20**, 1538 (1955).
(4) D. G. Holland, Ph.D. Thesis, Lehigh University, 1962; *Dissertation Abstr.*, **24**, 515 (1963).

TABLE II

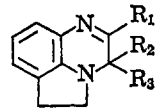
PYRROLO[1,2,3-*de*]QUINOXALINES



Compd.	R_1	R_2	R_3	M.p., °C.	Yield, %	Method[a]	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
VIII	C_6H_5	C_6H_5	H	150–152	21	A	$C_{22}H_{18}N_2$	85.13	85.24	5.84	5.69	9.03	9.13
IX[b]	*p*-$CH_3OC_6H_4$	*p*-$CH_3OC_6H_4$	H	158.5–160.0	52	B	$C_{24}H_{22}N_2O_2$	77.82	78.05	5.99	5.84	7.56	7.61
X	2-Furyl	2-Furyl	H	107–109	0.2	B	$C_{18}H_{14}N_2O_2$	74.47	74.08	4.86	5.02	9.65	9.42
XI	*p*-$C_2H_5C_6H_4$	*p*-$C_2H_5C_6H_4$	H	*c*	*c*	A	$C_{26}H_{26}N_2$	*c*					
XII	OH	=O	..	303–305	19	C	$C_{10}H_8N_2O_2$	63.82	63.68	4.28	4.12	14.89	15.20
XIV[d]	C_6H_5	C_6H_5	H	151.5–153.0	9	D	$C_{22}H_{16}N_2$	85.68	85.71	5.23	5.12	9.09	9.19

[a] Refer to the Experimental section. [b] Picrate, dark brown, m.p. 146.5–148.0°. [c] Obtained as an impure oil. Identified by ultraviolet and visible spectroscopy. [d] This compound contains a 5,6-double bond.

able product was obtained when 7-aminoindoline (I) and phosgene were refluxed in benzene and acetic acid; however, by refluxing I with formic acid, the N-(7-indolinyl)formamide (IV) was formed. In addition, 7-aminoindoline (I) and cyanogen bromide yielded 7-indolinecarbamonitrile (V) while 7-aminoindoline (I) and carbon disulfide formed 1,3-bis(7-indolinyl)-2-thiourea (VI). Compounds IV and VI, although obtained independently, appeared to be the same as those described by Holland.[4] These indoline derivatives are listed in Table I. Since reactions designed to form a five-membered ring (III) with the nitrogen atoms of 7-aminoindoline were unsuccessful, one may conclude that 7-aminoindoline (I) is unlike 8-amino-1,2,3,4-tetrahydroquinoline[1,2] or *o*-phenylenediamine in its ability to form cyclized products with carboxylic acid type reagents. Further attempts to synthesize the pyrrolo[1,2,3-*cd*]benzimidazoles were not made; instead, syntheses of the pyrrolo[1,2,3-*de*]quinoxalines (VII) were initiated (Table II).



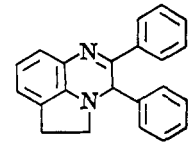
VII

When 7-aminoindoline (I) and benzoin were heated together, a considerable evolution of water occurred and the desired 5,6-dihydro-2,3-diphenyl-3H-pyrrolo-[1,2,3-*de*]quinoxaline (VIII) was isolated in 21% yield. A 52% yield of the corresponding 2,3-bis(*p*-methoxyphenyl) analog IX was obtained when 7-aminoindoline (I) and *p*-anisoin were azeotropically refluxed in toluene with a trace of *p*-toluenesulfonic acid. Under similar conditions, α-furoin and I formed the 2,3-bis(2-furyl) analog X but no characterizable product was obtained when *p*-toluoin or 4,4′-diethylbenzoin (XVI) were similarly refluxed with 7-aminoindoline (I). When 4,4′-diethylbenzoin (XVI) was fused with 7-aminoindoline (I), however, a very small amount of oily material was isolated which, by characterization *via* ultraviolet and visible spectroscopy, appeared to be the desired 2,3-bis(*p*-ethylphenyl) analog XI. The condensation of 7-aminoindoline (I) and diethyl oxalate in refluxing toluene formed 5,6-dihydro-2-hydroxy-3H-pyrrolo[1,2,3-*de*]quinoxaline-3-one (XII)[5a] in 19% yield.

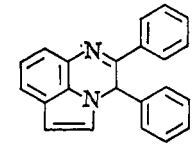
Attempts to condense 7-aminoindoline (I) with acetoin or butyroin were unsuccessful. When purified α-pyridoin was treated with 7-aminoindoline (I), the only product isolated was N-(7-indolinyl)picolinamide (XIII, Table I). Buehler, *et al.*,[5c] demonstrated that α-pyridoin is cleaved to picolinamide with sodamide in liquid ammonia, and to methyl picolinate with methanolic potassium hydroxide. The formation of XIII may have been the result of a similar cleavage of α-pyridoin with 7-aminoindoline.

The condensation of benzil with 7-aminoindoline (I) in refluxing toluene, aided by a catalytic amount of *p*-toluenesulfonic acid, produced 2,3-diphenyl-3H-pyrrolo[1,2,3-*de*]quinoxaline (XIV) in 9% yield.

Compounds VIII and XIV exhibited similar electronic absorption spectra, indicating a similar chromophore; however, the spectrum of XIV was shifted hypsochromically.



VIII



XIV

The infrared spectrum of VIII exhibited a methylene CH stretch doublet[6] at 3.48 and 3.42 μ as well as a methylene CH deformation band[6] at 6.95 μ. These bands were also present in the spectra of IX, X, and XII, but they were not present in the spectrum of XIV. Both VIII and XIV analyzed correctly for the assigned structures which were further confirmed by n.m.r. analysis.[7]

Both compounds exhibited a multiplicity of peaks in the 7-p.p.m. region which were attributable to 13 aromatic protons. The dihydro derivative VIII exhibited a broad peak at 2.80 p.p.m. attributable to four aliphatic-type indoline protons,[8] while the spectrum of XIV exhibited no aliphatic proton peaks. The spectrum of XIV did, however, exhibit two doublets, one centering at 6.38 p.p.m. and the other centering at 6.96 p.p.m. These doublets were assigned to the α- and β-indole protons,[9,10] respectively. The 5,6-double bond in XIV was thus confirmed.

(5) (a) A determination of the relative proportions of the amide and imidol tautomers which may be present in XII and XIX has not been made; however, Cheeseman[5b] has indicated that hydroxyquinoxalines are predominantly in the amide form in solution. By analogy, XII and XIX may also exist in the amide form in solution. (b) G. W. H. Cheeseman, *J. Chem. Soc.*, 108 (1958). (c) C. A. Buehler, J. W. Addleburg, and D. M. Glenn, *J. Org. Chem.*, **20**, 1350 (1955).

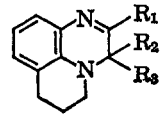
(6) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958.

(7) N.m.r. spectra were taken on $CDCl_3$ solutions with the Varian A-60. Chemical shifts reported here, δ, are given in parts per million relative to tetramethylsilane.

(8) F. A. L. Anet and J. M. Muchowski, *Chem. Ind.* (London), 81 (1963).

TABLE III

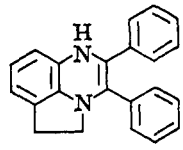
PYRIDO[1,2,3-*de*]QUINOXALINES



Compd.	R_1	R_2	R_3	M.p., °C.	Yield, %	Method[a]	Formula	—Carbon, %— Calcd.	Found	—Hydrogen, %— Calcd.	Found	—Nitrogen, %— Calcd.	Found
XVII	*p*-$C_2H_5C_6H_4$	*p*-$C_2H_5C_6H_4$	H	136–138	23	B	$C_{27}H_{28}N_2$	85.22	84.93	7.42	7.15	7.36	7.43
XVIII	*p*-$CH_3C_6H_4$	*p*-$CH_3C_6H_4$	H	130–131	34	A	$C_{25}H_{24}N_2$	85.19	85.48	6.86	7.06	7.95	7.77
XIX	OH	=O	..	258–261[b]	16	E	$C_{11}H_{10}N_2O_2$	65.33	65.44	4.98	4.86	13.86	13.90
XX	C_6H_5	C_6H_5	H	148.0–148.5	*c*	*c*	$C_{23}H_{20}N_2$	*c*					
XXI	*p*-$CH_3OC_6H_4$	*p*-$CH_3OC_6H_4$	H	148–149	*c*	*c*	$C_{25}H_{24}N_2O_2$	*c*					

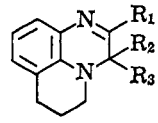
[a] Refer to the Experimental section. [b] Lit.[1] m.p. 258–260°. [c] Sample used was that described in ref. 1.

Both compounds also exhibited singlets which have been assigned to the benzyl proton at the 3-position, that for VIII appearing at 5.54 p.p.m. and that for XIV appearing at 6.59 p.p.m. The n.m.r. spectra of VIII and XIV remained unchanged after deuteriochloroform solutions of the compounds were shaken with sodium deuterioxide–deuterium oxide. Exchangeable protons were therefore not present in either compound; thus, the isomeric 1H-pyrrolo[1,2,3-*de*]quinoxaline (*i.e.*, VIIIa) was ruled out in each case.



VIIIa

Several derivatives of 6,7-dihydro-3H,5H-pyrido-[1,2,3-*de*]quinoxaline (XV, Table III) were examined as the next higher homologs of VII. The condensa-



XV

tion of 4,4′-diethylbenzoin (XVI) with 8-amino-1,2,3,4-tetrahydroquinoline[1] was successful, and the desired 6,7-dihydro-2,3-bis(*p*-ethylphenyl)-3H,5H-pyrido[1,2,3-*de*]quinoxaline (XVII) was obtained in 23% yield. This compound was a bright yellow, fluorescent material which was highly soluble in most organic solvents, including petroleum ether. Under similar conditions *p*-toluoin and 8-amino-1,2,3,4-tetrahydroquinoline formed the corresponding 2,3-bis(*p*-tolyl) derivative XVIII in 34% yield. Furthermore, by treating 8-amino-1,2,3,4-tetrahydroquinoline with ethyl oxalyl chloride in toluene, the 2-hydroxy-3-keto derivative XIX[5a] was formed in 16% yield.

Discussion of the Electronic Absorption Spectra

The electronic absorption spectra of the pyrrolo- (VII) and pyrido[1,2,3-*de*]quinoxalines (XV) are illustrated in a general manner in Figure 1, while values for the maxima are listed in Table IV. In both series

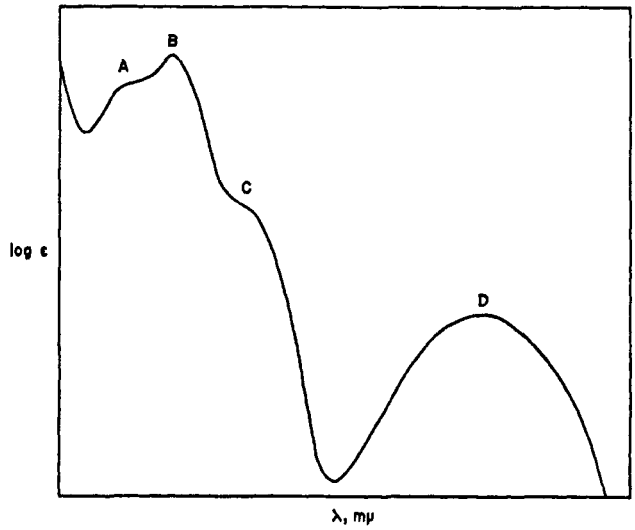


Figure 1.—General electronic absorption spectrum of the pyrrolo[1,2,3-*de*]quinoxalines (VII) and the pyrido[1,2,3-*de*]-quinoxalines (XV) in methanol (see Table IV).

TABLE IV

ELECTRONIC ABSORPTION MAXIMA OF PYRROLO[1,2,3-*de*]-QUINOXALINES AND PYRIDO[1,2,3-*de*]QUINOXALINES[a]

Compd.	λ_{max}, mμ (log ε)[b] A[c]	B	C[d]	D
VIII	258(4.26)	276(4.34)	318(3.83)	428(3.55)
IX	258(4.19)	284(4.36)	322(4.14)	419(3.68)
X	250(4.03)	279(4.15)	318(4.18)	425(3.70)
XI[e]	—	270(4.50)	318(3.94)	422(3.50)
XIV	—	262(4.24)	—	377(3.97)
XVII	258(4.24)	278(4.35)	318(3.84)	420(3.58)
XVIII	254(4.29)	278(4.42)	320(3.97)	420(3.69)
XX	250(4.26)	276(4.36)	318(3.81)	427(3.62)
XXI	—	282(4.43)	320(4.09)	413(3.75)

[a] Refer to Figure 1. [b] A dash indicates that such a maximum does not appear in the spectrum. [c] These data represent the approximate midpoint of an inflection. [d] This band is an inflection in the spectra of VIII, IX, and XI, and a true peak in the spectra of X, XVII, XVIII, XX, and XXI. [e] The log ε values were estimated by comparing the spectrum of impure XI with the spectra of VIII, IX, XVII, XVIII, XX, and XXI.

of compounds, a hypsochromic shift of the longest wave length band (band D, Figure 1) occurs as the substituents on the 2,3-diaryl groups are changed from hydrogen to alkyl to methoxy. This is also the order of increasing electron repulsion of such substituents according to Hammett's σ values[11] or Taft's σ_R values.[12] The latter are a measure of the resonance

(9) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectra Catalog," Vol. 1, Varian Associates, Palo Alto, Calif., 1962.

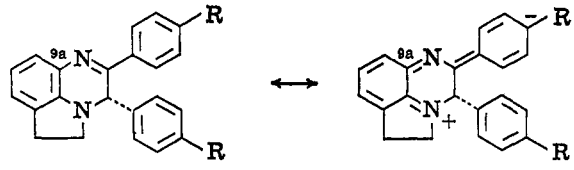
(10) L. A. Cohen, J. W. Daly, H. Kny, and B. Witkop, *J. Am. Chem. Soc.*, **82**, 2184 (1960).

(11) D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958).

(12) R. W. Taft, Jr., *J. Am. Chem. Soc.*, **79**, 1045 (1957).

contribution to the over-all electron-repelling nature of a benzene substituent and they have been found to be more useful[13,14] in correlating the shifts in electronic absorption spectra with the nature of the substituent.

Since models show that the 2-aryl group in VII and XV can become coplanar (and therefore conjugate) with the rest of the molecule, and since the electron-repelling substituents on the aryl groups cause hypsochromic shifts in the spectra of the compounds examined, it is reasonable to conclude that the electron-repelling substituents are operating in opposition to the main chromophores in these systems. One may also consider XXIIa to be representative of one of the major chromophores in the pyrrolo[1,2,3-*de*]quinoxalines and that a similar chromophoric system exists in the homologous pyrido[1,2,3-*de*]quinoxalines.



XXII XXIIa

Note, furthermore, that the contribution of a chromophore such as XXIIa to the hybrid will be lessened by situations which decrease the electron density at the carbon designated as 9a. In XIV, the 9a-position is analogous to the 7-position in indole at which the π-electron density is less than at most of the other positions in the indole molecule.[15] It, therefore, appears reasonable to assume that in XIV the electron density at 9a is diminished (as compared with the dihydro derivative, VIII) by the indole-type conjugation between the five-membered ring and the fused benzene ring. The involvement of the lone pair of electrons on the indole nitrogen results in a diminished interaction of those electrons with the pyrroloquinoxaline system, and therefore a hypsochromic shift of the spectrum occurs.

Experimental

All melting points were taken with a calibrated Thomas–Hoover melting point apparatus. The ultraviolet and visible spectra were taken on methanolic solutions with a Cary ultraviolet spectrophotometer. The infrared spectra were taken using potassium bromide disks except for XVI, whose spectrum was determined on the neat oil in a sodium chloride cell. A Perkin-Elmer Model 21 infrared spectrophotometer was used in obtaining the infrared spectra. Yields, in most cases, correspond to the quantity of analytically pure material obtained.

Benzoin (Matheson), α-furoin (Eastman), α-pyridoin (Aldrich), and benzil (Matheson) were commercially available. The *p*-anisoin, now commercially available, was originally prepared according to the method of Schacklett and Smith.[16] The *p*-toluoin and 4,4′-diethylbenzoin intermediates were prepared by the procedure describing the synthesis of XVI.

7-Aminoindoline (I).—A solution of 60.5 g. (0.235 mole) of 1-acetyl-7-aminoindoline hydrobromide[3] in 250 ml. of 4 *N* hydrochloric acid was refluxed for 0.5 hr. The solution was cooled and brought to pH 8 with concentrated aqueous ammonia. The solid which separated was extracted with ether, dried over magnesium sulfate, and recrystallized from ether–petroleum ether (b.p. 75–90°) at −20°. The product, which analyzed as a monohydrate, melted at 60.5–62.0°.

Anal. Calcd. for $C_8H_{10}N_2 \cdot H_2O$: C, 63.13; H, 7.95; N, 18.41. Found: C, 62.97; H, 7.55; N, 18.19.

The hydrate was dissolved in ether and dried over magnesium sulfate in a nitrogen atmosphere. The mixture was then filtered and distilled. The product was a colorless oil, b.p. 150–152° (6–7 mm.), $n^{28}D$ 1.6340, weighing 23.8 g. (76%): $\lambda_{max}^{CH_3OH}$ 246 mμ (sh, log ϵ 3.80) and 295 mμ (log ϵ 3.39). This material darkened rapidly in air; therefore, it was stored under nitrogen in a freezer. The dihydrochloride salt decomposed over the range 225–230° after recrystallization from ethanol: $\lambda_{max}^{CH_3OH}$ 241 mμ (log ϵ 4.05) and 286 mμ (log ϵ 3.33).

Anal. Calcd. for $C_8H_{10}N_2 \cdot 2HCl$: C, 46.39; H, 5.84; N, 13.53. Found: C, 46.80; H, 5.82; N, 13.66.

The picrate, melting at 198° dec., formed as golden yellow needles from ethanol.

Anal. Calcd. for $C_8H_{10}N_2 \cdot C_6H_3N_3O_7$: C, 46.29; H, 3.61; N, 19.28. Found: C, 46.32; H, 3.57; N, 19.06.

5-Aminoindoline (II).—A solution of 2.9 g. (0.018 mole) of 5-nitroindoline[3] in 75 ml. of ethanol was hydrogenated at 2 atm. pressure over 1 g. of 10% Pd–C catalyst. The mixture was filtered and treated with alcoholic HCl. The solid which separated was recrystallized from dimethylformamide–ether and dried. The dihydrochloride salt weighed 2.1 g. (56%, Table I): $\lambda_{max}^{CH_3OH}$ 246 mμ (log ϵ 3.93) and 300 mμ (log ϵ 3.32).

N-(7-Indolinyl)formamide (IV).—A solution of 5.0 g. (0.037 mole) of 7-aminoindoline (I) in 50 ml. of formic acid was refluxed for 2 days. It was cooled, poured onto ice, and made slightly alkaline with concentrated aqueous ammonia. The oil which separated was extracted with ether and dried over magnesium sulfate. After filtration of the solution and evaporation of the solvent, the product remained as an oil, $n^{24}D$ 1.6032 (picrate, m.p. 154–155°), which produced a red-brown color with aqueous ferric chloride solution. The base was converted to the hydrochloride salt (1.0 g., 14%) and characterized as such (Table I). A cold nitrous acid solution of the product, when added to an alkaline solution of β-naphthol, yielded no coupling product, thus indicating the absence of a primary amino group on the molecule.[17]

7-Indolinecarbamonitrile (V).—A 7.5-g. (0.055-mole) sample of 7-aminoindoline (I) was slurried in 75 ml. of warm water under nitrogen. The mixture was stirred and treated with cyanogen bromide in small portions. The reaction mixture was stirred for a total of 3 hr. and filtered. The solid which separated was washed with water and then slurried with 10% aqueous sodium hydroxide solution. The residue was taken up in ethanol and treated with an equal volume of ether. A solid separated which melted at 222° dec. but its elemental analyses fit none of the expected structures.

Anal. Found: C, 64.17; H, 5.55; N, 26.77.

The ethanol–ether mother liquor yielded another solid when cooled to −20°. This material, after recrystallization from ethanol, weighed 0.4 g. (5%, Table I). The infrared spectrum of this material exhibited a nitrile band at 4.55 μ. Treatment of the product first with nitrous acid and subsequently with alkaline β-naphthol solution produced no coupling product, thus indicating the absence of a primary aromatic amine.[17]

1,3-Bis(7-indolinyl)-2-thiourea (VI).—A solution of 5.1 g. (0.033 mole) of 7-aminoindoline monohydrate (I) and 2.5 g. (0.033 mole) of carbon disulfide in 50 ml. of ethanol was refluxed for 17 hr. and allowed to cool. The product which separated was recrystallized twice from dimethylformamide–water. After drying, the colorless crystals weighed 0.3 g. (10%, Table I).

N-(7-Indolinyl)picolinamide (XIII).—A mixture of 3.0 g. (0.022 mole) of 7-aminoindoline (I) and 4.8 g. (0.022 mole) of previously recrystallized α-pyridoin (Aldrich) was heated at 225 ± 5° for 15 min. during which time water appeared to evolve. The dark melt was cooled to 35° and taken up in warm ethanol. Upon cooling, pale yellow needles separated which, after a second recrystallization from ethanol, weighed 0.4 g. (8%, Table I).

A strong carbonyl band appeared at 6.02 μ in the infrared spectrum of this compound. The product formed a picrate which

(13) H. H. Jaffé and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1962, pp. 258–259.

(14) C. N. R. Rao, *Chem. Ind.* (London), 1239 (1957).

(15) G. M. Badger, "The Chemistry of Heterocyclic Compounds," Academic Press Inc., New York, N. Y., 1961, pp. 15, 16.

(16) C. D. Schacklett and H. A. Smith, *J. Am. Chem. Soc.*, **75**, 2654 (1953).

(17) The 1-acyl-8-amino-1,2,3,4-tetrahydroquinolines, when diazotized, couple with alkaline β-naphthol, while no coupling occurs when 8-acylamino-1,2,3,4-tetrahydroquinolines or 1-acyl-8-acylamino-1,2,3,4-tetrahydroquinolines are employed.[1] By analogy, this test should therefore be valid when applied to the substituted 7-aminoindolines.

melted at 183–184°, and a nitrous acid solution of XIII did not react with alkaline β-naphthol solution; thus, an amine function other than primary aromatic was indicated.[17] None of the desired 5,6-dihydro-3H-2,3-bis(2-pyridyl)pyrrolo[1,2,3-*de*]quinoxaline was isolated.

4,4′-Diethylbenzoin (XVI).—A mixture of 55.0 g. (0.244 mole) of *p*-ethylbenzaldehyde,[18] 7.8 g. (0.12 mole) of potassium cyanide, 75 g. of ethanol, and 75 g. of water was refluxed. A small amount of ethanol was subsequently added to effect the complete solution of all of the reactants. After 2 hr. at reflux temperature, the solution was cooled. Two volumes of water was added and the oily layer which separated was extracted with ether. The ethereal solution was shaken with aqueous sodium bisulfite solution, dried over magnesium sulfate, filtered, and evaporated *in vacuo*. Of the 17.7 g. of oily residue which remained, 11.7 g. was distilled *in vacuo*. The product obtained boiled at 180–185° (0.2–0.5 mm.), $n^{21}D$ 1.5725, and weighed 9.6 g. (26% based upon an extrapolation back to the original 17.7 g.).

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.41; H, 7.34.

A strong carbonyl band appeared at 5.98 μ in the infrared spectrum of the product.

Pyrrolo- and Pyrido[1,2,3-*de*]quinoxalines (Tables II and III). General Procedures Are Illustrated by Methods A and B.

Method A.—Equimolar amounts of the diamine[19] and the appropriate benzoin were mixed and heated to 150–190° for 0.5 hr. during which time effervescence occurred. The melt was cooled and taken up in warm ethanol. With continued standing, the product crystallized from the ethanolic solution. Recrystallizations were performed as necessary.

Method B.—Equimolar quantities of the diamine and the appropriate benzoin were dissolved in a weight of toluene of about ten times that of the diamine. A trace of *p*-toluenesulfonic acid was added and the solution was refluxed. The water which evolved was collected in a Dean–Stark trap by azeotropic distillation. After the theoretical amount of water had collected or after water ceased to evolve, the reaction mixture was cooled, filtered, and diluted with 3 vol. of petroleum ether (b.p. 75–90°). The material which separated was recrystallized from ethanol as required.

Method C. 5,6-Dihydro-2-hydroxy-3H-pyrrolo[1,2,3-*de*]quinoxaline-3-one (XII).[5a]—A solution of 5.0 g. (0.037 mole) of 7-aminoindoline (I) and 5.5 g. (0.037 mole) of diethyl oxalate (U. S. I.[20]) in 100 ml. of toluene was refluxed for 1 hr. during which time a solid separated. The reaction mixture was cooled and filtered, and the solid was recrystallized once from dimethylformamide–ether and twice from ethanol. The product weighed 1.3 g. (19%, Table II): $\lambda_{max}^{CH_3OH}$ 235 mμ (log ε 3.98), 242 (3.92), 262 (3.71), 272 (3.71), 314 (3.99), 322 (3.95), and 340 (sh, 3.59).

Method D. 2,3-Diphenyl-3H-pyrrolo[1,2,3-*de*]quinoxaline (XIV).—A solution of 5.0 g. (0.037 mole) of 7-aminoindoline (I), 7.8 g. (0.037 mole) of benzil (Matheson Coleman and Bell), and a trace of *p*-toluenesulfonic acid in 150 ml. of toluene was treated according to method B. The gummy residue which remained after treatment of the cooled reaction mixture with petroleum ether (b.p. 75–90°) was extracted with ether. The ether-insoluble residue was recrystallized three times from ethanol and dried. The product weighed 1.0 g. (9%) and melted at 151.5–153.0°. A mixture melting point with VIII was depressed considerably (Table II).

The structure of this product was further confirmed by ultraviolet, visible, infrared, and n.m.r. spectroscopy as described in the text.

Method E. 6,7-Dihydro-2-hydroxy-3H,5H-pyrido[1,2,3-*de*]quinoxaline-3-one (XIX).[5a]—A solution of 5.0 g. (0.034 mole) of 8-amino-1,2,3,4-tetrahydroquinoline[1] in 50 ml. of benzene was stirred and treated dropwise with a solution of 4.6 g. (0.034 mole) of ethyl oxalyl chloride (Eastman) in 25 ml. of benzene. The slurry which formed was stirred for 1 hr. and filtered. The solid was washed with benzene and dried. It was slurried with aqueous sodium bicarbonate solution, and then made more alkaline with 10% aqueous sodium hydroxide solution The solid residue was filtered, washed with water, and recrystallized twice from ethanol. The product weighed 1.1 g. (16%, Table III): $\lambda_{max}^{CH_3OH}$ 236 mμ (log ε 3.98), 242 (3.93), 261 (3.73), 270 (3.69), 312 (3.97), 325 (3.91), and 340 (sh 3.55).

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(18) M. H. Klouwen and H. Boelens, *Rec. trav. chim.*, **79**, 1022 (1960).
(19) 7-Aminoindoline (I) or 8-amino-1,2,3,4-tetrahydroquinoline (ref. 1).
(20) U. S. Industrial Chemicals Co.

The Configurations of the 2,3-Epoxides of Some Diels–Alder Adducts of 1,4-Benzoquinones

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Alkaline epoxidation of the Diels–Alder adducts from cyclic dienes and *p*-benzoquinones yields the appropriate 2,3-epoxides. The epoxides may differ stereochemically from the Diels–Alder adducts. They react with various mercaptans to give 2-thioether enediones. The configurations of these compounds were established to be *endo* by the use of n.m.r. spectroscopy. The epoxide ring was assigned the *exo* configuration. It was found that peracetic acid converts the 2,3-epoxides to 2,3,6,7-diepoxides. Permanganate oxidation of 5,8-methano-4a,5,6,7,8,8a-hexahydro-1,4-naphthoquinone 2,3-epoxide gave cyclopentane-1,3-dicarboxylic acid. Representative enediones were photochemically isomerized to their corresponding cage diketones.

The reaction of equimolar quantities of cyclopentadiene and *p*-benzoquinone at room temperature in numerous solvents gives a homogeneous product in high yield.[1–3] The product was identified as 5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (**1**),[1,2] and assigned the *cis-endo* configuration.[3] This designation was based on the postulated lower enthalpy of activation for *endo* addition. The assignment preceded the formulation of the Alder rule of "maximum accumulation of unsaturation."[4] Attempts to prepare the isomeric *exo* material by chemical means

(1) W. Albrecht, *Ann.*, **348**, 31 (1906).
(2) O. Diels and K. Alder, *ibid.*, **460**, 98 (1928).
(3) A. Wasserman, *J. Chem. Soc.*, 1511 (1935). see also A. Wasserman, *ibid.*, 828 (1935); 432 (1936); 612 (1942); *Trans. Faraday Soc.*, **34**, 128 (1938); **35**, 841 (1939). R. B. Woodward and H. Baer, *J. Am. Chem. Soc.*, **66**, 645 (1944).
(4) K. Alder and G. Stein, *Angew. Chem.*, **50**, 514 (1937).