barium salt was collected and purified by reprecipitation from its aqueous solution with ethanol. The sample was dried over phosphorus pentoxide *in vacuo:* 72 mg. (36%).

Anal. Calcd. for $C_9H_{11}BaN_2O_9P\cdot 3H_2O$: C, 21.05; H, 3.34; N, 5.46; P, 6.03. Found: C, 20.13; H, 3.41; N, 5.27; P, 5.89.

Attempted Synthesis of Uridine-3′-phosphate by Reaction of X with VI.—To a solution of VI (34 mg.) in 3 ml. of dioxane was added 2′,5′-di-O-trityl-2,3′-cyclouridine (Xb, 10 mg.). The solution was stirred at 37°. The process of the reaction was followed as described above. After the solution had been stirred at the same temperature for 3 days, paper chromatography showed the presence of only the starting materials (Xb and VI) indicating that no reaction had taken place. The same reaction was repeated at 60°, but even after 12 hr. reaction did not occur. 2,3′-Cyclouridine (Xa) in place of Xb was tried as a substrate, the other conditions being kept constant. However, on paper chromatography no indication of the presence of any nucleotidic products in the reaction mixture could be obtained. In each experiment, replacement of the dioxane by dimethylformamide or dimethyl sulfoxide was found to be ineffective in phosphorylation of Xa and Xb.

Azabicyclic Alcohols. III. Stereochemistry of the 7- and 8-Hydroxyindolizidines[1]

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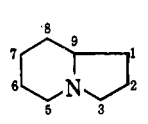
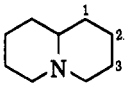
Received January 4, 1965

Each of the 7- and 8-hydroxyindolizidine racemates has been synthesized and characterized. Configurational and conformational assignments have been made on the basis of infrared, n.m.r., g.l.c., pK_a, and chemical evidence. In all cases, the *trans* ring fusion prevails, and no significant fraction (>2%) of the *cis* ring fusion could be detected by infrared methods. In the 8-hydroxy series, intramolecular hydrogen bonding exists between the nitrogen and an axial β-hydroxyl group. The Bohlmann correlation, originally deduced for conformational assignment of the quinolizidine ring fusion, has been shown to be valid for application to the indolizidine system.

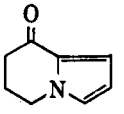
We have investigated the hydroxyindolizidines (*cf.* I) as part of a broader stereochemical study of simple azabicyclic ring systems. In a preceding paper in this series,[2] it was shown that the 1-, 2-, and 3-hydroxyquinolizidines (*cf.* II) exist in a *trans* ring fusion, and the presence of the *cis* fusion could not be detected by infrared methods. The present study constitutes a similar investigation of the 7- and 8-hydroxyindolizidines. In each of these, two epimeric racemates are possible, depending upon the configuration of the hydroxyl group relative to that of the bridgehead (C-9) hydrogen.



indolizidine
I



quinolizidine
II



III

Neither of the 7-hydroxyindolizidines has been reported; a picrate of one of the 8-hydroxy racemates has been described.[3] Alkaloids containing a substituted 8-hydroxyindolizidine ring system recently have been reported.[4] The chemistry of the indolizidine ring system has been reviewed.[5] Its stereochemistry is analogous to that of the better known hydrindane system,[6] except that the ring fusion is not necessarily fixed owing to the possible inversion of the bridgehead nitrogen.

Results

The 7- and 8-ketoindolizidines were reduced by both chemical and catalytic methods to give mixtures (see Tables I and II) of the corresponding hydroxyindolizidine racemates. These epimeric racemates were con-

TABLE I

EPIMERIC RATIOS OF 7-HYDROXYINDOLIZIDINES RESULTING FROM REDUCTIONS OF THE CORRESPONDING KETONE

Catalyst or reducing agent	Medium	Epimer A–B,[a] %
PtO_2	EtOH	24–76
5% Rh–carbon	EtOH	20–80
5% Ru–carbon	EtOH	45–55
10% Pd–carbon	EtOH	16–84
PtO_2	Aq. HCl	23–77
5% Rh–carbon	Aq. HCl	23–77
5% Ru–carbon	Aq. HCl	38–62
10% Pd–carbon	Aq. HCl	28–72[b]
Na–EtOH	Benzene	4–96
K–EtOH	Benzene	2–98
$NaBH_4$	H_2O	6–94
$LiAlH_4$	Ether	8–92

[a] Determined by g.l.c. analysis. [b] Results reproducible only within ±5%.

TABLE II

EPIMERIC RATIOS OF 8-HYDROXYINDOLIZIDINES RESULTING FROM REDUCTIONS OF THE CORRESPONDING KETONE

Catalyst or reducing agent	Medium	Epimer A–B, %
PtO_2	EtOH	60–40
5% Rh–carbon	EtOH	80–20
5% Ru–carbon	EtOH	82–18
10% Pd–carbon	EtOH	8–92
PtO_2	Aq. HCl	49–51
5% Rh–carbon	Aq. HCl	79–21
5% Ru–carbon	Aq. HCl	82–18
10% Pd–carbon	Aq. HCl	31–69
Na–EtOH	Benzene	27–73
Na–*n*-BuOH	Benzene	22–78
K–EtOH	Benzene	20–80
$NaBH_4$	H_2O	23–77
$LiAlH_4$	Ether	23–77

(1) Presented in part at the 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964.

(2) H. S. Aaron, G. E. Wicks, Jr., and C. P. Rader, *J. Org. Chem.*, **29**, 2248 (1964).

(3) N. J. Leonard, S. Swann, Jr., and J. Figueras, Jr., *J. Am. Chem. Soc.*, **74**, 4620 (1952).

(4) R. Kuhn and I. Loew, *Chem. Ber.*, **95**, 1748 (1962); T. R. Govindachari, B. R. Pai, I. S. Ragade, S. Rajappa, and N. Viswanathan, *Chem. Ind.* (London), 966 (1960).

(5) W. L. Mosby, "Heterocyclic Compounds with Bridgehead Nitrogen," part I, Interscience Publishers, Inc., New York, N. Y., 1961, p. 302.

(6) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 276.

TABLE III

PHYSICAL DATA FOR 7- AND 8-KETO- AND HYDROXYINDOLIZIDINES

Indolizidine compd.	G.l.c. retention time, min.[a]	pK_a[b]	Infrared bands,[c] ν_{max}, cm.$^{-1}$ OH region	Infrared bands,[c] ν_{max}, cm.$^{-1}$ Bohlmann region	N.m.r., carbinol hydrogen[d] τ	N.m.r., carbinol hydrogen[d] Half-width, c.p.s.[e]
7-Keto	4.7	7.70		2797, 2747, 2701		
7-OH, A (VI)	6.4	9.53	3626	2800, 2745	5.98	7.4
7-OH, B (VII)	7.1	8.96	3624	2788, 2751, 2714	6.53	21
8-Keto	4.4	8.40		2784, 2741, 2719		
8-OH, A (IV)	3.0	9.80	3522	2789, 2736	6.32	6.5
8-OH, B (V)	5.7	8.33	3627	2790, 2725	6.75	>20

[a] Measured from air peak on 10 ft. × 0.25 in. column of Carbowax 20 M (15%) on 60:80 Gas-Chrom P at 200° and 120 ml./min. (He). [b] Ionic strength, 0.0050. [c] Dilute carbon tetrachloride solutions in 1-cm. matched quartz cells. [d] Carbon tetrachloride solutions (20%); tetramethylsilane as internal standard. [e] Width of spin–spin multiplet at one-half the maximum absorption.

veniently separated by gas–liquid chromatography (g.l.c.) and designated A and B according to their order of elution from a Carbowax 20 M column. Larger samples of the individual epimers were obtained either by column chromatography or by distillation. The g.l.c., pK_a, and infrared and n.m.r. spectral data obtained for each of these isomers are presented in Table III.

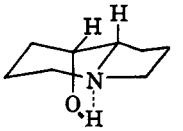
In order to obtain chemical evidence regarding the ring fusion, pyrrolo[1,2-*a*]piperidone-8 (III) was reduced over platinum oxide in aqueous hydrochloric acid to give a 76:24 A–B mixture of the 8-hydroxyindolizidines.

8-Hydroxyindolizidines.—In this series the g.l.c. data (shorter retention time of an alcohol than that of its corresponding ketone) suggest[2] and the infrared data prove that epimer A exists in an intramolecularly bonded N···HO conformation. Infrared spectra taken in dilute (0.007 *M*) carbon tetrachloride solution show a single, concentration-independent, bonded O–H stretching band. No trace of any free O–H stretching absorption band was detected. An examination of Dreiding stereomodels shows that, for intramolecular hydrogen bonding to occur, this epimer must possess an axial hydroxyl group, regardless of the prevailing ring fusion.

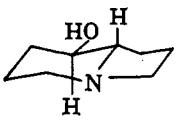
In the case of epimer B, the g.l.c. data imply and the infrared data conclusively demonstrate that this system does not show intramolecular hydrogen bonding. For infrared spectra taken in dilute (0.005 *M*) carbon tetrachloride solution, no trace of any bonded O–H band was detected, and only a free O–H stretching band was observed.

Examination of the stereomodels clearly reveals that the 8-hydroxy epimer capable of intramolecular hydrogen bonding in one ring fusion is incapable of such in the other ring fusion. Therefore, the fact that one of the two 8-hydroxy epimers shows only intramolecularly bonded O–H absorption and the other epimer shows only free O–H absorption establishes that the stereochemistry of the ring fusion is the same within the respective epimeric pair. Further, the possible equilibrium between the *cis* and *trans* ring fusions in this system must lie so far to one side (>98%) as to be undetectable by infrared methods.

That this ring fusion is *trans* may be assigned from an examination of the 2700–2800-cm.$^{-1}$ region of the infrared. According to the Bohlmann correlation,[7] a quinolizidine system will show one or more strong bands in this region, when two or more hydrogens on carbon atoms adjacent to the nitrogen are *trans* diaxial to the unshared nitrogen electron pair. The 8-hydroxyindolizidines satisfy this criterion only when in a *trans* ring fusion. Therefore, the fact that each of these epimers shows these spectral bands permits the configurations and conformations of the 8-hydroxyindolizidines to be assigned as follows.



epimer A; *cis*-8,9-H
IV



epimer B; *trans*-8,9-H
V

The empirical nature of the Bohlmann correlation and the fact that it was originally established for quinolizidine systems, however, prompted us to seek independent evidence for the assignment of the ring fusion in these compounds. Thus, the catalytic hydrogenation of pyrrolo[1,2-*a*]piperidone-8 (III) on platinum oxide in aqueous hydrochloric acid was examined. Here, the 76:24 A–B product ratio obtained compares to a 49:51 ratio obtained (Table II) under the same conditions from the corresponding saturated ketone. Assuming a predominance of all *cis* addition[8] of hydrogen to the unsaturated ketone, one concludes that this increase in the percentage of epimer A represents an increase in that epimer which has the *cis*-8,9-hydrogen configuration. This result establishes the ring fusion in both epimers (IV and V), since only the *trans* fusion is compatible with the presence of intramolecular hydrogen bonding in the *cis*-8,9-H isomer, and the absence of such bonding in its *trans*-8,9-H epimer.

7-Hydroxyindolizidines.—In this system intramolecular hydrogen bonding is not possible for either epimer, with the piperidinol ring in the favored chair conformation. In the absence (*vide infra*) of intramolecular bonding,[9] therefore, one concludes from the alkali metal–ethanol product ratios (Table I) that epimer B is the more stable equatorial alcohol. This conclusion is well supported by results of reductions of unhindered substituted cyclohexanone[10] and piperi-

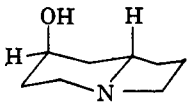
(7) F. Bohlmann, *Chem. Ber.*, **91**, 2157 (1958).

(8) R. P. Linstead, W. E. Doering, S. B. Davis, P. Levine, and R. R. Whetstone, *J. Am. Chem. Soc.*, **64**, 1985 (1942).

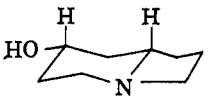
(9) The use of alkali metal–ethanol reduction data for conformational assignment must be used with care in systems which show intramolecular N···HO bonding. Thus it has been shown [M. R. Bell and S. Archer, *ibid.*, **82**, 4642 (1960)] that, under certain conditions, the equilibrium can be shifted in favor of the intramolecularly bonded axial hydroxyl epimer.

(10) D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953); A. V. Kamernitzky and A. A. Akhrem, *Tetrahedron*, **18**, 705 (1962).

done[11,12] systems. The fact that both epimers show the strong Bohlmann infrared spectral bands establishes (in view of the results presented for the 8-hydroxy system) the *trans* ring fusion and allows one to make the following structural assignments. The rela-



epimer A; *trans*-7,9-H
VI



epimer B; *cis*-7,9-H
VII

tive g.l.c. retention times correspond to those which would be expected from these assignments.

Analysis of the infrared spectral data provides a confirmation of these assignments. In carbon tetrachloride solution, both epimers show a sharp O–H stretching band above 3600 cm.$^{-1}$ and a broad intermolecularly bonded O–H band between 3100 and 3500 cm.$^{-1}$. In each case, only the free O–H band was observed below a concentration of 0.007 *M*. Thus, any intramolecular hydrogen bonding (which would arise from a sterically unfavorable boat conformation) could involve only a very small minority (<2%)[13] of the molecules. That epimer A is an axial and epimer B an equatorial alcohol is established by the shapes of the free O–H stretching bands. It has been demonstrated that for a vicinally unsubstituted cyclohexanol or piperidinol in carbon tetrachloride solution, an axial hydroxyl will have a highly symmetrical free O–H band[14] that occurs at a slightly higher frequency[15] than that of its equatorial epimer, which has an unsymmetrical band. These distinctions are apparently due to the relative populations of isomers which correspond to rotational conformations of the hydroxyl group about the C–O bond. Examination of the free O–H bands of the 7-hydroxy epimers clearly demonstrates A to have a symmetrical ($\alpha:\beta$ = 0.94)[16] and B an unsymmetrical ($\alpha:\beta$ = 0.40) band. These results establish the fact that these epimers exist as a distinct axial and equatorial hydroxyl pair. Therefore, the indolizidine ring system must exist in a predominantly *trans* fusion, since a *cis* fusion should allow the hydroxyl of each epimer to exist in a preferred equatorial conformation. This analysis provides additional proof of the validity of the Bohlmann correlation in the indolizidine system.

N.m.r. and pK_a Correlations.—The conformational assignments of the carbinol protons, made on the basis of the criteria that the axial hydrogen isomer will give a broader[17] proton magnetic resonance spin–spin multiplet at a higher field[18] than that of its equatorial counterpart, are in agreement with the above (IV–VII) assignments.

The pK_a data for the 8-hydroxy series show that the intramolecularly bonded axial hydroxyl isomer A is markedly more basic (ΔpK_a = 1.47) than its equatorial epimer, while, in the nonintramolecularly bonded 7-hydroxy series, the axial alcohol A is only slightly more basic (ΔpK_a = 0.57) than its equatorial epimer. These results are in agreement with the above structural assignments, when compared with the pK_a correlations previously noted for the conformationally related hydroxyquinolizidine[2] and 3-tropanol[13] systems.

Ketone Reductions.—The presence of the Bohlmann bands (Table III) in the infrared spectra of the 7- and 8-ketoindolizidines suggests that each of these compounds exists in a predominantly *trans* ring-fused conformation. In the catalytic hydrogenations, presumably each is adsorbed and subsequently reduced in this form. On each of the metal catalysts, the product ratio is altered by only a moderate amount, if at all, when the solvent is changed from ethanol to aqueous acid. Therefore, the "anchor effect" observed in the hydrogenations of the ketoquinolizidines[12] does not appear to be operating in these systems.

It may be noted that, in ethanol solution, ruthenium gives the most and palladium the least of the axial hydroxyl epimer. This result corresponds to that observed in the ketoquinolizidine hydrogenations.

The metal hydride reductions of the 7- and 8-ketoindolizidines resulted in A–B product ratios which were similar to those obtained from the alkali metal–ethanol reductions. This result leads to the conclusion that, as with the ketoquinolizidines, product development control governs the approach of the hydride ion to the carbonyl group.

Experimental

The same procedures and catalyst sources reported for the ketoquinolizidines[12] were used for the various catalytic and chemical reductions of the 7- and 8-ketoindolizidines. The catalytic hydrogenations were all carried out in a rocking Parr hydrogenation apparatus at 3–5 atm. of hydrogen pressure and at room temperature. The methods and instrumentation used for the g.l.c., pK_a, infrared, and n.m.r. measurements were the same as previously described,[2,12] unless otherwise indicated.

Pyrrolo[1,2-*a*]piperidone-8 (III).—This compound was prepared[19] as previously described.[20] The product (b.p. 94° at 0.18 mm.) gave a carbonyl band at 1665 cm.$^{-1}$ (Perkin-Elmer Infracord 237B spectrophotometer) and crystallized on standing, m.p. 32–33° (hexane) (lit.[20] 34°). Its semicarbazone melted at 202–203° (lit.[20] 193°).

Anal. Calcd. for $C_9H_{12}N_4O$: C, 56.26; H, 6.25; N, 29.15. Found: C, 56.0; H, 6.5; N, 28.9.

7-Ketoindolizidine was prepared[19] as previously reported.[21] It distilled at 96–98° (14 mm.), and had $n^{21}D$ 1.4881, carbonyl absorption at 1718 cm.$^{-1}$ (CCl_4 solution). Its **picrate**, prepared in ether and recrystallized from ethanol, had m.p. 210–211° dec. (lit.[21,22] 198–200° dec.).

Anal. Calcd. for $C_{14}H_{16}N_4O_8$: C, 45.66; H, 4.38; N, 15.21. Found: C, 45.7; H, 4.6; N, 15.0.

8-Ketoindolizidine was prepared[19] as previously reported,[3] except that DL-ethyl proline was alkylated with ethyl γ-bromobutyrate[23] rather than with the corresponding nitrile. Isolated by distillation, the amino ketone had b.p. 85–86° (4 mm.), $n^{22.5}D$ 1.4894, and carbonyl absorption at 1723 cm.$^{-1}$ (CCl_4 solution). Its picrate melted at 146.5–147° dec. (lit.[3] 144.5–145°).

(11) A. H. Beckett, N. J. Harper, A. D. J. Balon, and T. H. E. Watts, *Tetrahedron*, **6**, 319 (1959).

(12) C. P. Rader, G. E. Wicks, Jr., R. L. Young, Jr., and H. S. Aaron, *J. Org. Chem.*, **29**, 2252 (1964).

(13) H. S. Aaron and C. P. Rader, *ibid.*, **29**, 3426 (1964).

(14) H. S. Aaron and C. P. Rader, *J. Am. Chem. Soc.*, **85**, 3046 (1963).

(15) A. R. H. Cole, P. R. Jefferies, and G. T. A. Müller, *J. Chem. Soc.*, 1222 (1959).

(16) The degree of symmetry is expressed as he ratio of the segments of the half band width on the high (α) and low (') frequency sides of ν_{max}, as measured from the absorption band recorded on an expanded frequency scale.

(17) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); E. W. Garbisch, Jr., *J. Org. Chem.*, **27**, 4249 (1962), and references cited therein.

(18) J. I. Musher, *J. Chem. Phys.*, **35**, 1159 (1961); E. L. Eliel, M. H. Gianni, T. H. Williams, and J. B. Stothers, *Tetrahedron Letters*, **No. 17**, 741 (1962).

(19) Synthesis was performed by Regis Chemical Co., Chicago, Ill., under a U. S. Army Research and Development Contract.

(20) G. R. Clemo and G. R. Ramage, *J. Chem. Soc.*, 49 (1931).

(21) F. Lions and A. M. Willison, *J. Proc. Roy. Soc. N. S. Wales*, **73**, 240 (1940).

(22) R. T. Holden and R. Raper, *J. Chem. Soc.*, 2545 (1963).

(23) W. Reckhow and D. Tarbell, *J. Am. Chem. Soc.*, **74**, 4960 (1952).

7-Hydroxyindolizidine (Epimer A).—7-Ketoindolizidine (5.0 g.) in 25 ml. of 95% ethanol was hydrogenated over 0.5 g. of 5% ruthenium-on-carbon catalyst. After a 30-min. induction period, the theoretical quantity of hydrogen was rapidly absorbed. Removal of catalyst and solvent gave 4.84 g. of a mixture of epimeric amino alcohols (A–B) in a ratio of 45:55 (g.l.c.). This mixture was dissolved in petroleum ether (b.p. 30–60°) and separated by chromatography on neutral alumina (600 g., Woelm activity grade IV). Ether was used as the eluent. The first 1.36 g. of amino alcohol emerging from the column was pure A with succeeding fractions containing increasing amounts of B. Epimer A gave m.p. 99–100°.

Anal. Calcd. for $C_8H_{15}NO$: C, 68.04; H, 10.71. Found: C, 68.1; H, 10.7.

The **picrate of A** was prepared in ether. Upon recrystallization from ether–methanol it gave m.p. 193° dec.

Anal. Calcd. for $C_{14}H_{18}N_4O_8$: C, 45.44; H, 4.90. Found: C, 45.4; H, 4.9.

7-Hydroxyindolizidine (Epimer B).—7-Ketoindolizidine (2.0 g.) was reduced with potassium–ethanol in benzene according to a previously reported procedure.[12] The crude reduction mixture gave an A–B ratio of 4:96 (g.l.c.) with a small amount (about 3%) of an unknown higher boiling material. Vacuum distillation gave 1.3 g. of product, which upon sitting at 3° formed a white solid, m.p. 47–49.5°. Two recrystallizations from petroleum ether did not change this melting point. G.l.c. analysis revealed the product to contain only epimers A and B in a ratio of 4:96, respectively.

The picrate of B was prepared in ether and recrystallized (ethyl acetate–ether) to give m.p. 164–166°.

Anal. Calcd. for $C_{14}H_{18}N_4O_8$: C, 45.44; H, 4.90. Found: C, 45.4; H, 5.0.

8-Hydroxyindolizidine (Epimer A).—8-Ketoindolizidine (5.0 g.) was dissolved in absolute ethanol and reduced over 0.5 g. of 5% ruthenium-on-carbon catalyst. After a theoretical absorption of hydrogen, both catalyst and solvent were removed, leaving a crude reduction mixture of 85:15 A–B ratio (g.l.c.). Vacuum distillation gave an estimated 3.5 g. in four cuts of comparable size. Cut 1 contained >99.5% pure epimer A, a mobile liquid, b.p. 66–67° (3.8 mm.), $n^{25}D$ 1.4931. Cut 2 contained A of >98% epimeric purity (g.l.c.).

Anal. Calcd. for $C_8H_{15}NO$: C, 68.04; H, 10.71. Found: C, 68.1; H, 10.8.

The **picrate of A** was prepared in ether and gave m.p. 145–146° (ethyl acetate–ether).

Anal. Calcd. for $C_{14}H_{18}N_4O_8$: C, 45.44; H, 4.90; N, 15.13. Found: C, 45.7; H, 5.0; N, 15.0.

8-Hydroxyindolizidine (Epimer B).—8-Ketoindolizidine (5.0 g.) in 25 ml. of absolute ethanol was reduced over 0.7 g. of 10% palladium-on-carbon catalyst. Removal of solvent and catalyst gave a crude reduction mixture with a 29:71 A–B ratio.[24] Vacuum distillation separated the mixture into four cuts, total of 3.4 g., of which cuts 3 (1.37 g.) and 4 (0.52 g.) contained B in 95 and 98% epimeric purities, respectively. Epimer B (cut 4) was a viscous liquid, b.p. 85° (3 mm.), $n^{25}D$ 1.5039.

The **picrate of B** was prepared in ether and gave m.p. 174–176° (lit.[3] 175–176°, isolated from what is now known to have been about a 23:77 A–B mixture) which was unchanged by further recrystallizations from ethyl acetate.

Anal. Calcd. for $C_{14}H_{18}N_4O_8$: C, 45.44; H, 4.90. Found: C, 45.2; H, 4.6.

(24) The discrepancy between this A–B ratio and that given in Table II is likely due to the difference in catalyst–substrate ratio. The stereochemistry of palladium-on-carbon reductions is known to be sensitive to this ratio. See R. L. Augustine, *J. Org. Chem.*, **28**, 152 (1963).

An Approach to the Synthesis of 8a-Azoniaacridine Salts[1]

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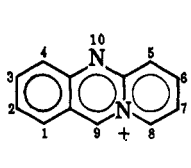
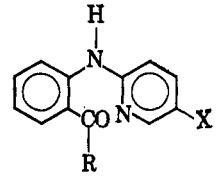
The addition of excess phenyl- or methyllithium to 2-(2-carboxyanilino)pyridine yields not the expected ketones, but instead tertiary alcohols which may be cyclodehydrated to 6,11-dihydro-11-azaacridizinium derivatives. 2′-Aminoacetophenone and, to a more limited extent, -benzophenone undergo condensation with 2-bromopyridines and 2-chloroquinolines. With one exception, the new condensation products appear to be the pseudo-bases of 8a-azoniaacridine derivatives.

Although the 1-azaquinolizinium ion is known,[2] neither of its fully aromatic linear benzologs has been reported. The present communication describes experiments directed toward the synthesis of one of these, the 8a-azoniaacridine[3] (or pyrido[2,1-*b*]quinazolin-10-ium) system (I).

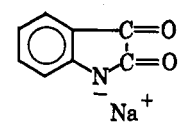


I

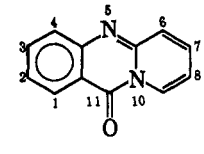


II

The best approach to the new aromatic system (I) appeared to be the synthesis and cyclization of a 2-anilinopyridine (II) with an acyl, aroyl, or formyl group at the *ortho* position of the phenyl ring. The sodio derivative (III) of isatin, which can be alkylated[4] with methyl iodide, could not be made to react with 2-bromopyridine. Likewise the attempt to prepare an anilinopyridine from 2-aminobenzonitrile by reaction with 2-bromopyridine failed under basic or neutral (sealed tube) conditions. The condensation of ethyl anthranilate (or the free acid) with 2-chloro- or 2-bromopyridine is known to yield 11H-pyrido[2,1-*b*]-quinazolin-11-one (IV), and alkaline hydrolysis of IV, followed by acidification, is known to yield 2-(2-carboxyanilino)pyridine (II, R = OH, X = H).[5] It was found that treatment of the acid II with excess



III



IV

(1) This research project was supported by U. S. Public Health Research Grants (H-2170) from the National Heart Institute and (CA-05509) from the National Cancer Institute.

(2) A. N. Nesmeyanov, M. I. Rybinskaya, and N. K. Belskii, *Dokl. Akad. Nauk SSSR*, **113**, 343 (1957); *Chem. Abstr.*, **51**, 14712 (1957).

(3) Nomenclature as recommended by Commission on the Nomenclature of Organic Chemistry of the International Union of Pure and Applied Chemistry (IUPAC 1957 Rules); *J. Am. Chem. Soc.*, **82**, 5545, 5572 (1960).

(4) G. Heller, *Ber.*, **40**, 1294 (1907).

(5) S. Carboni, *Atti Soc. toscana sci. nat. Pisa, Proc. Verbali Mem.*, **62A**, 261 (1955); *Chem. Abstr.*, **50**, 16767 (1956).