priate acid chloride. The mixture was cooled, solvents evaporated almost to dryness *in vacuo;* water added and the gum triturated and washed with excess water yielding the desired compound in the form of its hydrochloride. Conversion of the crude salt to the free base was accomplished by slurrying in methanol solution for 10 minutes with an equal weight of silver carbonate. After filtration from silver salts and evaporation of the methanol the ester was crystallized from one of the solvents listed in B.

(F) The dimethylamino ester was prepared by reductive alkylation as illustrated by the preparation of methyl 18-O-(4-dimethylaminobenzoyl)-reserpate: Methyl 18-O-(4-aminobenzoyl)-reserpate (2.8 g., 0.005 mole) was dissolved in 200 ml. of methanol plus 4 ml. of 37% formaldehyde and subjected to reduction over 2 g. of 10% palladium-on-charcoal for two days until approximately the theoretical uptake of hydrogen was observed. The catalyst was removed by filtration and the solution evaporated *in vacuo* leaving the product as a pale yellow foam which was crystallized from ethanol–water; yield 0.35 g. (12%). (The nitro compound may be used instead of the corresponding amino ester.)

(G) Methyl 18-O-(4-aminobenzoyl)-reserpate (1 g., 0.0019 mole) was refluxed with 0.3 ml. (0.0027 mole) of phenyl isocyanate in 50 ml. of methylene chloride for 6 hours. The solution was evaporated *in vacuo* and the product recrystallized from acetone; yield 0.65 g. (52%).

(H) As an example of this preparation methyl 18-O-(3,5-dimethoxy-4-hydroxybenzoyl)-reserpate (2 g., 0.0034 mole) was refluxed for 2 hours in 50 ml. of methylene chloride with 0.4 ml. (0.0036 mole) of phenyl isocyanate. The reaction mixture was filtered to clarify and the filtrate evaporated *in vacuo*. The product was crystallized from acetone; yield 0.9 g. (37%).

(I) This preparation is illustrated by the reaction of methyl reserpate (4 g., 0.0097 mole) with 1.2 g. (0.01 mole) of phenyl isocyanate in refluxing methylene chloride (100 ml.). After one hour the mixture was filtered, the filtrate evaporated *in vacuo* and the product crystallized from acetone; yield 1.3 g. (24%).

(J) Methyl 18-O-(3,4,5-trimethoxycinnamoyl)-reserpate (5 g., 0.0079 mole) isolated from *Rauwolfia vomitoria* was hydrogenated at atmospheric pressure and room temperature in 300 ml. of methanol over 1 g. of 10% palladium-on-charcoal until the theoretical amount of hydrogen was absorbed during 16 hours. The solution was filtered from catalyst, evaporated *in vacuo* and the residue recrystallized from ethyl acetate–ether; yield 4.3 g. (85%) of methyl 18-O-[3-(3,4,5-trimethoxyphenyl)-propionyl]-reserpate.

(K) Hydrogenation of methyl 18-O-(3,4,5-trimethoxycinnamoyl)-reserpate (5 g., 0.0079 mole) in 300 ml. of methanol containing 5 drops of acetic acid over 1 g. of platinum oxide at room temperature and atmospheric pressure proceeded with the expected uptake of hydrogen during 4 hours. Removal of the catalyst by filtration and washing with methylene chloride and partial evaporation of the solvent *in vacuo* yielded 4.5 g. (90%) of crystalline methyl 18-O-[3-(3,4,5-trimethoxyphenyl)-propionyl]-isoreserpate.

Under the same conditions reserpine was approximately 20% converted to 3-isoreserpine.

(L) Methyl reserpate (3 g., 0.0072 mole) in 60 ml. of chloroform containing 1.27 g. (0.0068 mole) of antipyrene was treated with 0.48 ml. (0.68 g., 0.007 mole) of phosgene in 5 ml. of toluene at −10°. After standing overnight at room temperature the mixture was filtered and the filtrate cooled to 0° and treated with excess gaseous NH_3. The ammonium chloride was filtered, the solution washed with water, dried over K_2CO_3 and evaporated *in vacuo*. The brown gum was crystallized from ethanol; yield 0.2 g. (6%).

(M) The preparation of acid esters of methyl reserpate is illustrated by the preparation of the maleic acid ester: To a solution of 4.14 g. (0.01 mole) of methyl reserpate in 300 ml. of methylene chloride was added 0.02 mole of maleic anhydride and after 3 days at 25° the solution was evaporated to dryness *in vacuo*. Upon addition of 25 ml. of acetone and chilling the product crystallized and was recrystallized from acetone; yield 2.0 g. (39%).

(N) **N,N-Dimethylglycine Ester of Methyl Reserpate.**—A solution of 4.14 g. (0.01 mole) of methyl reserpate and 1.57 g. (0.010 mole) of the acid chloride–hydrochloride of N,N-dimethylglycine in 100 ml. of methylene chloride was stored in the dark for 7 days at 25°. The reaction mixture was then poured onto a column of 80 g. of alumina (Woelm, Activity III, basic). The crude ester collected in the first 200 ml. of methylene chloride eluate was recrystallized from methylene chloride–benzene giving 0.27 g. (5%) of product.

(O) **N-Benzoylglycine Ester of Methyl Reserpate.**—Methyl reserpate (4.14 g., 0.010 mole) and hippuryl chloride (2.2 g., 0.11 mole) were dissolved in 80 ml. of methylene chloride and stored in the dark at 25° for 18 days. At this time the concentration of ester, which was followed daily by paper chromatographic assay of aliquot portions of the reaction mixture, had reached a maximum and began to decrease. The mixture was now poured onto a column of 100 g. of alumina (Woelm, Activity III, basic) and eluted with 1000 ml. of methylene chloride. Concentration of the eluate and recrystallization of the residue from methylene chloride–methanol gave 0.73 g. (13%) of pure product.

SUMMIT, N. J.

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, CIBA PHARMACEUTICAL PRODUCTS, INC.]

The Alkaloids of *Tabernanthe iboga*. Part VIII[1]

BY M. F. BARTLETT, D. F. DICKEL, R. C. MAXFIELD, L. E. PASZEK AND A. F. SMITH

RECEIVED OCTOBER 23, 1958

Iboluteine and iboluteine lactam were reduced and the dihydro compounds rearranged to yield the new indoles IX (or XII) and XIII.

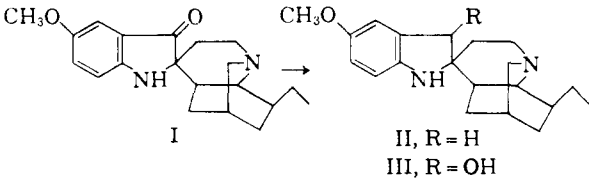
In the course of our detailed study of the alkaloids of *Tabernanthe iboga* the reactions of iboluteine (I) were further investigated.

Goutarel, Janot, Mathys and Prelog[2] reported that ibogaine was obtained on reduction of iboluteine with lithium aluminum hydride.[3] This reaction has now been repeated but no ibogaine could be detected in the reaction mixture. The major product was dihydrodeoxyiboluteine (II) which was isolated in 85% yield. Dihydroiboluteine (III) was detected by paper chromatography as a minor component in the crude reaction product. Reduction of iboluteine with sodium borohydride gave a mixture of two diastereoisomers, dihydroiboluteine A (m.p. 150°) and dihydroiboluteine B (m.p. 184°), having typical dihydroindole ultraviolet absorption spectra and OH and NH absorption in the infrared. The molecular rotation differences between the two compounds and their common reduction product,

(1) Part VII, L. H. Werner and S. Ricca, Jr., THIS JOURNAL, **80**, 2733 (1958).

(2) R. Goutarel, M.-M. Janot, F. Mathys and V. Prelog, *Helv. Chim. Acta*, **39**, 742 (1956).

(3) However, Goutarel stated in his thesis that iboluteine was reduced to dihydrodeoxyiboluteine with lithium aluminum hydride but identified the product only by its ultraviolet absorption spectrum; R. Goutarel, These doc. sci. Paris, 1954.



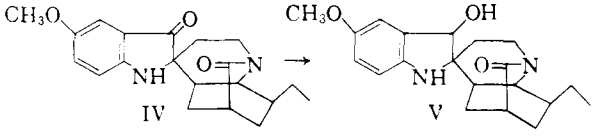
I II, R = H III, R = OH

dihydrodeoxyiboluteine (II) are of the same magnitude and are opposite in sign confirming their formulation as diastereoisomers (Table I). Treatment of either dihydroiboluteine A or B with lithium aluminum hydride resulted in the hydrogenolysis of the hydroxyl group giving dihydrodeoxyiboluteine (II) as the sole product.

TABLE I

	$[\alpha]_D$	M_D	Δ(OH)
Dihydroiboluteine A	+28°	+ 92	+154
Dihydroiboluteine B	−63	−207	−145
Dihydrodeoxyiboluteine	−20	− 62	

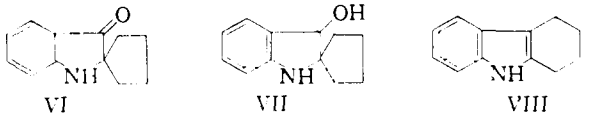
Iboluteine lactam[4] (IV) was also reduced to its dihydro derivative V with sodium borohydride. In contrast to dihydroiboluteine this reduction product was found to be very unstable and could not be crystallized. A crystalline picrate was ob-



IV V

tained from this product; however the ultraviolet absorption spectrum is that of an indole rather than a dihydroindole. When the picrate mother liquors were decomposed on alumina a new indole lactam $C_{20}H_{24}N_2O_2$ was obtained. This compound was also obtained directly from the crude reduction product in good yield by rearrangement in dilute acid.

Similar reactions of indoles and dihydroindoles have been studied, particularly by Witkop in the reduction of spiro-[cyclopentane-1,2′-pseudoindoxyl] (VI) to a mixture of spiro-[cyclopentane-1,2′-dihydroindoxyl] (VII) and spiro-[cyclopentane-1,2′-dihydroindole] (VII, H instead of OH) and the acid-catalyzed rearrangement of VII to 1,2,3,4-tetrahydrocarbazol (VIII).[5] He also suggested that



VI VII VIII

isoquinamine could be converted to cinchonamine through the same reaction sequence,[6] although in a later publication it was reported that another product was found.[7] The conversion of fluorocurine and norfluorocurine to mavacurine and normavacurine, respectively, published by Bickel, Giesbrecht, Kebrle, Schmid and Karrer may be cited as an example of this reaction scheme.[8]

(4) M. F. Bartlett, D. F. Dickel and W. I. Taylor, THIS JOURNAL, **80**, 126 (1958).

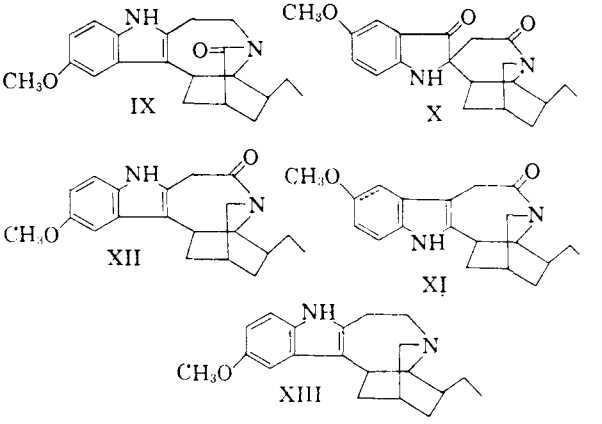
(5) B. Witkop, *ibid.*, **72**, 614 (1950).

(6) B. Witkop, *ibid.*, **72**, 2311 (1950).

(7) B. Witkop, *Bull. soc. chim. France*, 423 (1954).

(8) H. Bickel, E. Giesbrecht, J. Kebrle, H. Schmid and P. Karrer, *Helv. Chim. Acta*, **37**, 553 (1954).

Distinct differences between the new lactam and ibogaine lactam were noted in the infrared absorption, R_f values, mixed melting point and optical rotation. The ultraviolet absorption is identical with that of ibogaine lactam, and since the structure of ibogaine lactam has been established unequivocally,[4] the most probable structure of the new lactam is IX. However, the structure X for iboluteine lactam has not been rigidly excluded which brings two additional formulas XI and XII under consideration. Structure XI is ruled out because this compound would yield ibogaine on reduction with lithium aluminum hydride. Actually a new indole (XIII) was isolated from this reduction.



IX X XII XI XIII

The compound could not be induced to crystallize but was characterized as its crystalline picrate which although not identical to ibogaine picrate had marked similarities in the infrared absorption.

The acid-catalyzed rearrangement of dihydroiboluteine proceeded more slowly than the rearrangement of the corresponding lactam and yielded a mixture of XIII and ibogaine. Although the mixture was not separated the identity of the compounds was apparent from paper chromatography and infrared absorption. In the ibogamine series the complete sequence of reactions was not carried out because dihydrodemethoxyiboluteine failed to rearrange under the conditions used.

Acknowledgment.—The authors express appreciation to Dr. W. I. Taylor for helpful discussions, to Mr. Louis Dorfman and his staff for the analytical and spectral data and Mr. B. Korzun for the paper chromatography.

Experimental

Melting points are uncorrected. Whatman No. 1 paper impregnated with formamide was used for the paper chromatography in the systems: benzene–cyclohexane–pyridine and chloroform. The optical rotations were measured in chloroform.

Dihydroiboluteine B.—Iboluteine (1 g.) was dissolved in a solution of 0.18 g. of sodium methoxide in 50 ml. of methanol. To this solution 1 g. of sodium borohydride was added and the reaction allowed to proceed at room temperature for 3 hours. The course of the reaction was followed by changes in the ultraviolet absorption. Aliquots (0.1 ml.) were acidified with acetic acid, diluted to 1 ml. and the absorption maxima determined. The 224 and 416 mμ maxima of the starting material were no longer apparent after two hours while the 242 and 315 mμ absorption of the product reached maximum intensity after 2.5 hours.

Glacial acetic acid (5.0 ml.) was added to the reaction mixture, the solvent removed by evaporation *in vacuo*, and the residue extracted four times with methylene chloride.

The methylene chloride extract was washed with water, dried over anhydrous sodium sulfate and the solvent evaporated giving 0.74 g. of an amorphous product. Crystallization from a mixture of 40 ml. of hexane and 15 ml. of benzene yielded clusters of long needles, m.p. 179–184°. For analysis the material was recrystallized three times from benzene, m.p. 184–186°, $[\alpha]^{26}D$ −63°; λ_{max}^{MeOH} 243–244 mμ (9,000), 315–319 mμ (2,810), shld. 320–321 mμ (2,690). The infrared absorption showed the presence of both −OH and −NH groups. Carbonyl absorption was not present.

Anal. Calcd. for $C_{20}H_{28}N_2O_2$: C, 73.13; H, 8.59; N, 8.53. Found: C, 73.13; H, 8.44; N, 8.30.

Dihydroiboluteine A.—The mother liquor material (1 g.) from a preparation similar to that described above was chromatographed on neutral alumina (Act. III). Elution with 200 ml. of benzene followed by 40 ml. of methylene chloride–benzene (1:1) gave 0.26 g. of colored impurities. A total of 250 ml. of methylene chloride afforded 0.61 g. of crude dihydroiboluteine A. Crystallization from hexane–benzene gave 0.34 g. of crystals melting at 150°. For analysis a small sample was sublimed in high vacuum at 128°, m.p. 150–152°, $[\alpha]^{25}D$ +28°; λ_{max}^{MeOH} 242–244 mμ (8,860), 314–316 mμ (2,640), shld. 322 mμ (2,490). The infrared absorption showed both −OH and −NH groups. The presence of bands at 1,340 and 957 cm.$^{-1}$ distinguish this compound from the previous isomer.

Anal. Calcd. for $C_{20}H_{28}N_2O_2$: C, 73.13; H, 8.59; N, 8.53. Found: C, 73.69; H, 8.46; N, 8.67.

Continued elution of the alumina column with methylene chloride containing 1% methanol yielded additional dihydroiboluteine B which after crystallization from hexane–benzene melted at 175–180°.

Dihydrodeoxyiboluteine.—(a) A slurry of 2 g. of dihydroiboluteine B (m.p. 180–184°) in 100 ml. of anhydrous ether was added to a solution of 2 g. of lithium aluminum hydride in 50 ml. of ether. The reaction mixture was stirred at room temperature for 0.5 hour and then refluxed for 2 hours. Excess lithium aluminum hydride was decomposed by the slow addition of water and the product extracted with methylene chloride. The extract was washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent left 1.5 g. of an oily residue which crystallized from methanol, m.p. 55–65°. Repeated sublimation in high vacuum raised the melting point to 79–81°, $[\alpha]^{26}D$ −20; λ_{max}^{MeOH} 241 (12,080), 310 mμ (4,160).

Anal. Calcd. for $C_{20}H_{28}N_2O$: C, 76.88; H, 9.03; N, 8.97. Found: C, 76.62; H, 8.89; N, 8.92.

Reduction of dihydroiboluteine A (0.04 g.) under similar conditions gave a product having the identical ultraviolet absorption and the same R_f value on paper chromatography as dihydrodeoxyiboluteine.

(b) Iboluteine (0.50 g.) was added to a solution of lithium aluminum hydride (0.50 g.) in ether (50 ml.) by means of a soxhlet. After refluxing for two hours, excess water and methylene chloride were added and the solution was filtered. The filtrate was extracted with dilute sulfuric acid. The acidic extract was made basic with sodium hydroxide and extracted with methylene chloride. After drying with sodium sulfate the solution was evaporated to dryness.

The residue (0.48 g.) was chromatographed on a column of activity III basic alumina 22 × 90 mm. Dihydrodeoxyiboluteine (0.42 g.) was eluted with benzene which after crystallization from ether–hexane melted at 78–79°.

Dihydroiboluteine Lactam.—Iboluteine lactam (0.66 g.) was added to a solution of 2.00 g. of sodium borohydride and 0.50 g. of sodium hydroxide in 65 ml. of 85% aqueous methanol. The solution was stirred overnight at room temperature. The solvent was partly removed *in vacuo*, diluted with water and extracted with methylene chloride. After drying with sodium sulfate the solvent was removed under reduced pressure leaving a residue of 0.68 g., λ_{max}^{EtOH} 242 and 317 mμ.

Rearrangement of Dihydroiboluteine Lactam.—(a) Crude dihydroiboluteine lactam (0.68 g.) was dissolved in 30 ml. of 95% ethanol and 3 ml. of 2 *N* sulfuric acid and the solution refluxed for 20 minutes. The change in the ultraviolet absorption showed that the dihydroindole was completely converted to an indole. The solution was partially evaporated, then diluted with water and extracted with methylene chloride. After drying with sodium sulfate the methylene chloride extract was evaporated to dryness. The residue (0.68 g.) was crystallized from methanol–ether yielding 0.40 g. of crystals, m.p. 215–218°. For analysis a sample was recrystallized from methanol–ether and acetone and dried at 78° *in vacuo*, m.p. 223–224°, mixed melting point with ibogaine lactam (m.p. 217–218°) 165–170°, $[\alpha]D$ −154°; λ_{max}^{EtOH} 221–224 mμ (26,200) and 282–285 mμ (7,800); plateau 293–297 mμ (7,400); shld. 309 mμ (4,200); λ_{min} 250–252 mμ (2,000).

Anal. Calcd. for $C_{20}H_{24}N_2O_2$: C, 74.04; H, 7.46; N, 8.64. Found: C, 73.79; H, 7.53; N, 8.34.

(b) Crude dihydroiboluteine lactam (0.10 g.) in ethanol and picric acid in ethanol were mixed and boiled to a small volume. After cooling, 40 g. of a reddish-black picrate was obtained, m.p. 131–133°. After recrystallization from ethanol a low yield of the picrate was recovered, m.p. 141–142°; λ_{max}^{EtOH} 296–297 mμ (9,830), 357–360 mμ (15,800), plateaus 217–222 mμ (40,140) and 285–287 mμ (9,460), shld. 307 mμ (8,300) and 357–360 mμ (15,800); λ_{min} 264–266 (7,700) and 316 mμ (6,320).

Anal. Calcd. for $C_{26}H_{27}N_5O_9$: C, 56.41; H, 4.92. Found: C, 56.81; H, 5.22.

The mother liquors from the picrate formation were washed through a column of basic alumina with methylene chloride. The eluate recrystallized from acetone melted at 222–223°. This was identical in all respects to the indole lactam obtained by procedure (a).

Lithium Aluminum Hydride Reduction of the Indole-lactam IX (or **XII**).—The indole-lactam IX (0.15 g.) was refluxed with lithium aluminum hydride (0.20 g.) in tetrahydrofuran (25 ml.) for 8 hours. Water (1 ml.) was added and the mixture was filtered and the residue washed with ethanol. The combined filtrate was evaporated to dryness and the residue dissolved in methylene chloride and extracted with dilute sulfuric acid. The acidic extract was made alkaline with sodium hydroxide, extracted with methylene chloride and after drying evaporated to dryness leaving a residue of 0.13 g. The residue was dissolved in 1 ml. of ethanol and added to 0.12 g. of picric acid in 3 ml. of ethanol. The precipitate was redissolved by heating and allowed to crystallize slowly yielding 0.20 g. of picrate, m.p. 201–202°. The melting point remained constant on recrystallizing from ethanol. For analysis a sample was dried at 78° *in vacuo*; λ_{max}^{EtOH} 274–277 (8,600), 296 (8,400) and 356–361 mμ (15,300), shld. 304–308 (7,600) and 402 mμ (10,500); λ_{max}^{EtOH} 263–267 (8,400), 287–289 (8,300) and 316 mμ (6,000).

Anal. Calcd. for $C_{26}H_{29}N_5O_8$: C, 57.88; H, 5.42; N, 12.98. Found: C, 57.66; H, 5.36; N, 12.98.

A sample of the picrate (0.09 g.) was dissolved in 1:1 acetone–methanol and passed through a column of Amberlite CG 400 (Cl) 15 × 150 mm. The recovered hydrochloride, eluted with methanol and pure by paper chromatography could not be induced to crystallize. A sample of the glass was dried at 100° for 1 hour for analysis, $[\alpha]D$ +10 ±6°.

Anal. Calcd. for $C_{22}H_{28}N_2O \cdot HCl \cdot {}^2/_3H_2O$: C, 66.91; H, 7.97. Found: C, 66.97; H, 8.11.

Rearrangement of Dihydroiboluteine.—(a) Dihydroiboluteine A (0.100 g.) was added to 100 ml. of 0.01 *N* sulfuric acid and refluxed for 7 hours. The compound dissolved slowly in the boiling acid. The ultraviolet absorption was determined on an aliquot of this solution: max. at 222, 276, 294 mμ and min. at 257 and 288 mμ. To the cooled acid solution 1 equivalent of picric acid (0.070 g.) in 10 ml. of water was added slowly. The precipitate (0.087 g.) melted with gradual decomposition over the range of 125–135°. Although paper chromatography of the picrate showed one alkaloidal spot it appeared to be a mixture of ibogaine and the indole XIII from the fluorescent color; leading edge blue-green, trailing edge orange. A comparison of its infrared absorption spectrum with that of ibogaine picrate and the picrate of XIII bears this out.

(b) Dihydroiboluteine B (0.50 g.) was treated in a similar manner and yielded a picrate melting with gradual decomposition from 122–130°. The infrared absorption and paper chromatographic behavior were the same as that of the picrate described above. Attempts to separate either the picrates or the free bases were not successful.

Dihydrodemethoxyiboluteine.—Demethoxyiboluteine (1.28 g.) in aqueous methanol (50 ml.), sodium borohydride (1.28 g.) and a trace of sodium hydroxide were stirred at 0° for 3 hours. Sodium borohydride (0.20 g.) was again added and

the solution stirred at room temperature overnight. The solution was concentrated under reduced pressure, diluted with water and extracted with methylene chloride. The extract was dried with sodium sulfate and concentrated to dryness. The residue (0.80 g.) was recrystallized from benzene and sublimed for analysis, m.p. 188–189°, $[\alpha]_D$ −87.3°; λ_{max}^{EtOH} 246 (8,400) and 303 mμ (2,100), shld. 312 mμ (1,900); λ_{min} 224 (2,900) and 271 mμ (590).

Anal. Calcd. for $C_{19}H_{26}N_2O$: C, 76.47; H, 8.78; N, 9.39. Found: C, 76.76; H, 8.78; N, 9.50.

SUMMIT, N. J.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS, THE STATE UNIVERSITY]

A Comparison of the Structure and Reactivity of Pyridine and Pyridine-1-oxide

BY RODERICK A. BARNES

RECEIVED OCTOBER 23, 1958

The electron distribution and atom localization energies of pyridine and pyridine-1-oxide have been calculated by the molecular orbital method using a consistent set of parameters for both molecules. The results have been compared with the available experimental data and satisfactory agreement is observed if the resonance integral of the oxygen–nitrogen bond of pyridine-1-oxide is approximately 0.75β.

The resonance or valence-bond method for approximating the true electron distribution works very well for aromatic systems containing no heteroatoms. However, in heterocycles such as pyridine-1-oxide this method may be of doubtful value even for a *qualitative* description. For example, from contributing structures I and II it could be assumed that pyridine-1-oxide has a small negative charge at carbon two because of the somewhat

I II

greater stability[1] of structure II; but, whether the contributions of the two structures are really sufficiently different to produce a finite charge at this position could not be predicted with any degree of confidence.

The failure of the valence-bond procedure for *quantitative* descriptions of heterocycles results from the fact that there is no generally acceptable method for determining exactly the contribution of charged structures such as I and II.[2]

In contrast, the simple molecular orbital method, although subject to some limitations[3] affords a convenient procedure for calculating the charge distribution and relative reactivity of heterocyclic molecules. The main difficulty is in deciding on the correct parameters to be used in the calculations. The ideal situation, in which one set of parameters would serve for a quantitatively accurate description of all heterocycles, is quite unlikely to be operative, but the definition of a set of parameters which give a good qualitative description of a wide variety of heterocycles may be realizable.

The purpose of this paper is to compare the reactivity and electron distribution of pyridine and pyridine-1-oxide, as calculated using a consistent set of parameters for both molecules with the available experimental data. Many of the earlier calculations for systems containing nitrogen atoms assumed that the coulomb integral of nitrogen was represented by $\alpha_N = \alpha_C + 2\beta$, but in this work the suggestion of Coulson[4] that $\alpha_N = \alpha_C + {}^1/_2\beta$ has been followed. Recent calculations by Brown[5] have demonstrated that for attack of the phenyl radical on the pyridine nucleus, only the parameters used here, $\alpha_N = \alpha_C + {}^1/_2\beta$ and $\beta_{CN} = \beta$, produced calculated reactivities which agree with the experimentally observed rate factors.[6] Other calculations for pyridine[7] and pyridine-1-oxide[8] have been made using rather different values for the coulomb integral of nitrogen.

Because there was little basis for choosing a value for the resonance integral of the nitrogen–oxygen bond (β_{NO}), the calculations for pyridine-1-oxide were repeated using three different values covering the range in which the true value is almost certainly located. The charge distributions resulting from these calculations are given Fig. 1.

It is apparent that the change in value of β_{NO} has a profound effect on the charge distribution of pyridine-1-oxide. For the lower value of β_{NO}, the charges on the carbons are much as in pyridine, but at the higher values a part of the negative charge on the oxygen atom appears at positions 2 and 4. In principle it should be possible to determine exactly the value of β_{NO} by calculating the dipole moment for various values of β_{NO}, and comparing it with the experimental value. The part of the moment which arises from the π-electrons is readily calculated, but there is difficulty in deciding on the values to be used for the σ-bond moments, which certainly must vary with the charge on the two atoms of the bond. In spite of this uncertainty, these calculations have been made in a man-

(1) The smaller separation of charge and the greater number of bonds in II are the reasons for the prediction of its greater stability.

(2) B. Bak, *Acta Chim. Scand.*, **9**, 1355 (1955), has proposed a formula for determining the contribution of charged and uncharged structures from accurate values for the bond lengths, but this procedure has been tested for only a few examples.

(3) R. D. Brown, *Quart. Revs.*, **6**, 63 (1952).

(4) Coulson, "Valence," Oxford University Press, Amen House, London E. C. 4, 1952, p. 242.

(5) R. D. Brown, *J. Chem. Soc.*, 272 (1956).

(6) The only uncertainty about these calculations is that the coefficient a of the equation $RT \log k_1/k_2 = a(A_2 - A_1)$, which relates rate constants to atom localization energies (A_i), was assumed to be the same for phenyl radicals as for trichloromethyl radicals.

(7) P. Yvan, *Compt. rend.*, **229**, 622 (1949), used $\alpha_N = \alpha_C + \beta$ and $\beta_{CN} = \beta$ but neglected inductive effects.

(8) H. H. Jaffé, THIS JOURNAL, **76**, 3527 (1954), calculated the coulomb integrals $\alpha_N = \alpha_C + 2.004\beta$ and $\alpha_O = \alpha_C + 1.016\beta$ from a relationship he has developed between the coulomb integral and the substituent constants of the Hammett equation; see H. H. Jaffé, *J. Chem. Phys.*, **20**, 279 (1952).