m.p. 176–180° dec. One recrystallization from water gave white needles, m.p. 181–183° dec.

Anal. Calcd. for $C_{16}H_{21}IN_2O$ (384.25): C, 50.01; H, 5.51; I, 33.03; N, 7.30. Found: C, 50.29; H, 5.75; I, 32.01, 32.04, 31.87; N, 7.04.

7-Benzyloxy-2,3-dihydro-1-(N-pyrrolidino)-1H-pyrrolo[1,2-*a*]-indole (XIX).—A mixture of 0.660 g. (2.0 mmoles) of 7-benzyloxy-1-(N-pyrrolidino)-3H-pyrrolo[1,2-*a*]indole (XV) and 66 mg. of platinum oxide in 50 ml. of ethyl acetate was shaken under a hydrogen atmosphere. In 10 min. a pressure drop corresponding to a theoretical uptake of hydrogen was noted; no further pressure drop was noted in the subsequent 45 min. The mixture was filtered, and the filtrate was taken to dryness. The residue was crystallized from ether–petroleum ether (b.p. 60–70°) with the aid of activated charcoal to give, in two crops, 0.432 g. (65%) of crystals, m.p. 98–101°. Two recrystallizations from the same solvent pair gave needles: m.p. 101.0–102.5°; λ_{max} 278, 297 (sh), and 310 (sh) mμ (ε 9300, 5300, and 3330); λ 6.15 and 6.34 μ.

Anal. Calcd. for $C_{22}H_{24}N_2O$ (332.43): C, 79.48; H, 7.28; N, 8.43. Found: C, 79.73; H, 7.59; N, 8.70.

1-(7-Benzyloxy-2,3-dihydro-1H-pyrrolo[1,2-*a*]indol-1-yl)-1-methylpyrrolidinium Iodide (XX).—A solution of 332 mg. (1 mmole) of 7-benzyloxy-2,3-dihydro-1-(N-pyrrolidino)-1H-pyrrolo[1,2-*a*]indole (XIX) and 1 ml. of methyl iodide in 10 ml. of methanol was allowed to stand at room temperature in the dark for 18 hr. The crystals were collected by filtration to give 362 mg. (78%) of crystals, m.p. 166–168°. Two recrystallizations from water gave glistening white plates: m.p. 156–158°; λ_{max} 278 and 306 mμ (ε 10,800 and 4280); λ 6.12, 6.33, and 6.44 μ.

Anal. Calcd. for $C_{23}H_{27}IN_2O$ (474.37): C, 58.35; H, 5.74; I, 26.76; N, 5.91. Found: C, 58.22; H, 6.21; I, 26.82; N, 5.62.

7-Benzyloxy-9H-pyrrolo[1,2-*a*]indole (XXV).—To a solution prepared by the interaction of 118 mg. (3.01 mg.-atoms) of potassium with 25 ml. of *t*-butyl alcohol was added 948 mg. (2.0 mmoles) of 1-(7-benzyloxy-2,3-dihydro-1H-pyrrolo[1,2-*a*]indol-1-yl)-1-methylpyrrolidinium iodide (XX) and 20 ml. of dimethylformamide. The dark solution was heated on the steam bath under a nitrogen atmosphere for 3.5 hr. The cooled solution was distributed between methylene chloride and water; the organic layer was treated with activated carbon, dried, and taken to dryness. The residue was crystallized from petroleum ether to give 254 mg. (49%) of needles, m.p. 132–135°. Two recrystallizations from this solvent gave white needles: m.p. 132–133°; λ_{max} 264 and 301 mμ (ε 19,900 and and 3260); λ 6.21 (w), 6.41, 8.01, 8.14, 14.27, and 14.68 μ; p.m.r.[21] τ 2.70 (phenyl protons), multiplets at approximately 3.09 and 3.18, 3.68 (apparent triplet, C-2 proton), multiplet at 3.96 (C-1 proton), 5.09 (benzylic methylene protons), and 6.35 (broad signal, C-9 methylene protons); p.m.r. (in deuteriodimethyl sulfoxide measured with a Varian HR-100 spectrometer)[18] multiplet at low field (benzylic aromatic protons), multiplet at τ 2.74 (C-3 proton), multiplet at 2.83 (C-8 proton), quartet centered at 3.02 ($J_{5,6}$ = 8 c.p.s., $J_{6,8}$ = 3 c.p.s., C-6 proton), apparent triplet at 3.77 (C-2 proton), multiplet at 3.97 (C-1 proton), sharp singlet at 4.93 (benzylic methylene protons), and a somewhat broader single resonance at 6.28 (C-9 methylene protons). Irradiation at a frequency near this last signal resulted in a sharpening of the multiplets at τ 2.74, 2.83, 3.02, and 3.97; the multiplet at τ 2.83 now appeared as sharp doublet having $J_{6,8}$ = 3 c.p.s., a typical *meta* coupling constant. Irradiation at low field near the C-3 and C-8 proton resonance caused a collapse of the apparent triplet at τ 3.77 into a doublet with $J_{1,2}$ = 2.5 c.p.s. and sharpening of the multiplet at τ 3.97.

Anal. Calcd. for $C_{18}H_{15}NO$ (261.31): C, 82.73; H, 5.79; N, 5.36. Found: C, 82.97; H, 6.25; N, 5.40.

Acknowledgment.—We are indebted to Mr. L. Brancone and his staff for the microanalyses, to Mr. W. Fulmor and his associates for the spectral data, and to Mr. J. Poletto for assistance in certain large-scale preparations. We wish to thank Dr. J. S. Webb for helpful discussions, particularly with respect to p.m.r. spectral interpretations.

The Mitomycin Antibiotics. Synthetic Studies. VII.[1] An Exploration of Pyrrolo[1,2-*a*]indole A-Ring Chemistry Directed toward the Introduction of the Aziridine Function

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An exploration of the chemistry of the interesting pyrrolo[1,2-*a*]indole A-ring is reported. This exploration was directed toward fusion with an aziridine group in order to obtain the complete ring system of the mitomycin antibiotics. Although we were unable to prepare such a fused aziridine, despite utilization of a variety of approaches, syntheses of A-ring systems found in certain of the mitomycin degradation products, such as two isomeric aminohydrins and a diol, were accomplished. A novel bisborane derivative of an oxime was prepared in the course of this investigation, and an unusual ester interchange *via* the enolate anion of a β-keto *t*-butyl ester was discovered.

In the preceding article in this series[1] studies leading to the preparation of 7-methoxymitosene[2] were summarized, and it was noted that this compound lacks only the aziridine ring fused to the pyrrolo[1,2-*a*]indole A-ring to complete the structure of the important antibiotic 7-methoxy-1,2-(N-methylaziridino)mitosene.[3] This article also described preliminary studies in functionalizing the pyrroloindole A-ring in order to set the stage for introduction of the aziridine group. The present article is concerned with further exploration of A-ring chemistry directed toward the synthesis of the fused aziridine ring.

At the outset we anticipated considerable difficulty in closing an aziridine ring onto the A-ring, since the latter is strained relative to cyclopentane.[4] Furthermore, certain unexpected properties of the pyrrolo-[1,2-*a*]indole system such as the propensity of 1H-pyrroloindoles to rearrange to 9H-pyrroloindoles[1,5] suggested additional pitfalls. We therefore conceived a number of approaches to this problem, offering considerable variety in methodology.

(1) Preceding paper in this series: G. R. Allen, Jr., and M. J. Weiss, *J. Org. Chem.*, **30**, 2904 (1965).

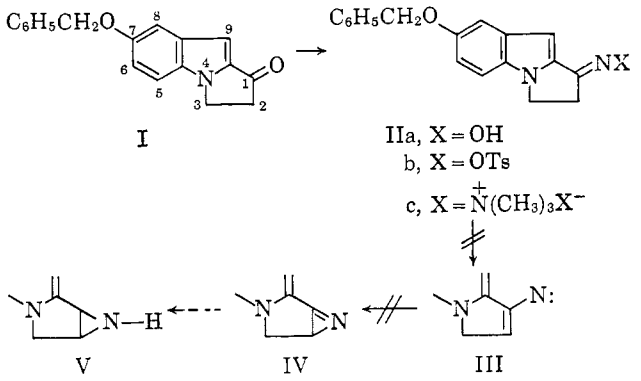
(2) (a) G. R. Allen, Jr., J. F. Poletto, and M. J. Weiss, *J. Am. Chem. Soc.*, **86**, 3877 (1964); (b) *J. Org. Chem.*, **30**, 2897 (1965).

(3) J. B. Patrick, R. P. Williams, W. E. Meyer, W. Fulmor, D. B. Cosulich, R. W. Broschard, and J. S. Webb, *J. Am. Chem. Soc.*, **86**, 1889 (1964).

(4) Preparation of cyclopentanoaziridine has been reported by P. E. Fanta [*J. Chem. Soc.*, 1441 (1957)].

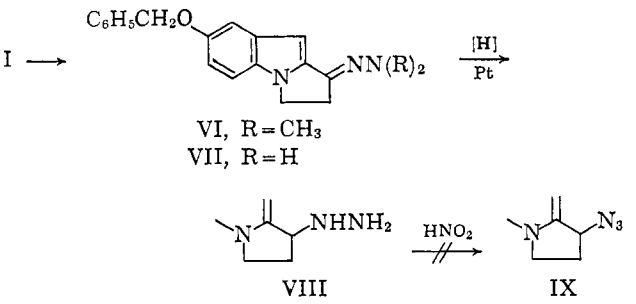
(5) W. A. Remers, *J. Am. Chem. Soc.*, **86**, 4608 (1964).

The most direct potential route to an aziridine from a 1-ketopyrroloindole (*e.g.*, I)[1] involves conversion of the carbonyl to a C=N—X group, wherein X is a good leaving group. With this system the base-induced generation of a nitrene *via* proton removal from the adjacent methylene group[6] was considered possible and, if insertion at C-2 followed, the resulting intermediate (*e.g.*, IV) might be reducible[7] to an aziridine (V). In accord with this reasoning we first attempted the Neber reaction[6,8] utilizing the following procedures based on those of Cram and Hatch,[7] despite the fact that the literature examples[6-8] of this reaction involve oxime tosylates having adjacent *benzylic* hydrogens. However, treatment of IIb with sodium ethoxide in ethanol followed by addition of sodium borohydride afforded only starting material, and treatment with sodium hydride followed by addition of lithium aluminum hydride converted IIb to an unidentified crude oil that lacked the infrared absorption (8.18–8.35 μ) characteristic of the aziridine ring as found in the mitomycins.[3,9]



A closely related approach was based on the interesting finding of Smith and Most[10] that quaternary hydrazones (see IIc) having α hydrogens (not necessarily benzylic) undergo, upon treatment with sodium ethoxide, a rearrangement analogous to the Neber, affording products derived from the intermediate azirine (see IV). Treatment of I with 1,1-dimethylhydrazine proved to be a sluggish reaction, yielding after prolonged reflux a mixture of dimethylhydrazone VI (low yield), starting material, and the aldol condensation product XVI of starting material (see below). Partition chromatography resolved this mixture and the resulting pure dimethylhydrazone was treated with a large excess of methyl iodide, both undiluted and in methanol. Surprisingly, no quaternary salt could be obtained in either case, even on standing for 7 days. In contrast, Smith and Most[10] obtained good yields of the quaternary compounds after 4 days.

We next attempted the preparation of azide IX in the hope that on photolysis it would furnish a nitrene that might insert at C-2 to give directly the desired aziridine. Treatment of I with hydrazine gave the corresponding hydrazone VII. This reaction was facile and uncomplicated by by-products, in contrast to the reaction of I with dimethylhydrazine. Hydrazone VII was reduced catalytically to the corresponding hydrazine VIII, but attempts to convert VIII to azide IX with nitrous acid were unsuccessful.



Having failed to achieve a quick solution to this problem *via* "nitrene" intermediates, we next undertook a more classical approach and directed our investigation toward the preparation of a *trans*-aminohydrin in order to attempt modifications of the Wenker aziridine synthesis.[11] Reduction of the 2-bromo-1-ketopyrroloindole X[1] with sodium borohydride in methanol afforded the corresponding bromohydrin XI.[12] Since the reducing agent in this case is bulky, it was anticipated that hydride addition would occur at the side of X opposite the bromine; hence bromohydrin XI should be *cis*. Evidence for *cis* stereochemistry is provided by formation of ketone I from the pure (chromatographically homogeneous) bromohydrin by treatment with sodium hydroxide in methanol.[12] [In certain experiments XI was converted to the aldol condensation product of I under these conditions. Direct preparation of this aldol condensation product (XVI) from I could be readily effected under these conditions.] Furthermore a shift of -30 cm.$^{-1}$ in the OH stretching frequency in the infrared absorption spectrum of bromohydrin XI relative to that of nonbrominated alcohol XV[1] suggests a hydrogen bond to bromine in XI, affording further support to *cis* stereochemistry.[13]

The n.m.r. spectrum of XI shows $J_{1,2} = 4.5$ c.p.s. This value appears low for *cis* hydrogens, but the pyrrolo[1,2-*a*]indole system might not give coupling constants in conformity with the simpler form of the Karplus equation.[14]

We were unable to obtain an aminohydrin from bromohydrin XI by heating it with ammonia, starting material being the only substance isolated from the reaction mixture. Bromo ketone X also failed to react with ammonia. However, it was possible to prepare in good yield aminohydrin XIII by treating XI with sodium azide followed by catalytic reduction of the resulting hydroxy azide XII. Since the reaction of the highly nucleophilic azide ion with XI is most probably an SN2-type displacement, hydroxy azide XII and aminohydrin XIII are assigned *trans* stereochemistry.

Having thus prepared the requisite *trans*-aminohydrin XIII, we next investigated various methods for the transformation of this compound to an aziridine, which, in principle, required the conversion of the 1-

(6) For a discussion of the probability of the Neber rearrangement proceeding *via* an unsaturated nitrene, see H. O. House and W. F. Berkowitz, *J. Org. Chem.*, **28**, 2271 (1963).

(7) D. J. Cram and M. J. Hatch, *J. Am. Chem. Soc.*, **75**, 33, 39 (1953).

(8) P. W. Neber and A. Friedolsheim, *Ann.*, **449**, 109 (1926).

(9) J. S. Webb, D. B. Cosulich, J. H. Mowat, J. B. Patrick, R. W. Broschard, W. E. Meyer, R. P. Williams, C. F. Wolf, W. Fulmor, C. Pidacks, and J. E. Lancaster, *J. Am. Chem. Soc.*, **84**, 3185, 3187 (1962).

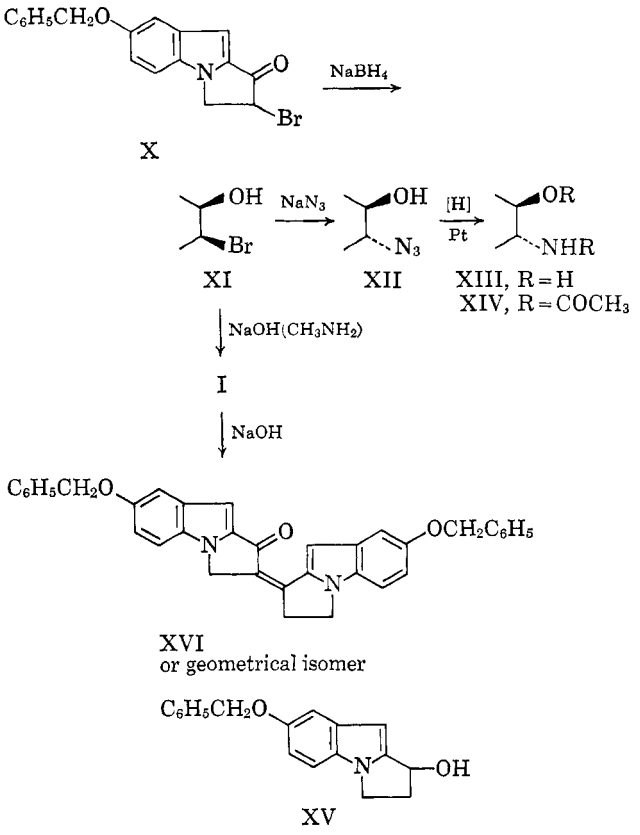
(10) P. A. S. Smith and E. E. Most, Jr., *J. Org. Chem.*, **22**, 358 (1957).

(11) H. Wenker, *J. Am. Chem. Soc.*, **57**, 2328 (1935).

(12) This reaction was first investigated by Allen and Weiss.[1]

(13) See G. P. Mueller and W. F. Johns, *J. Org. Chem.*, **26**, 2403 (1961), for a discussion of assignment of steroidal cyclopentane halohydrin configurations.

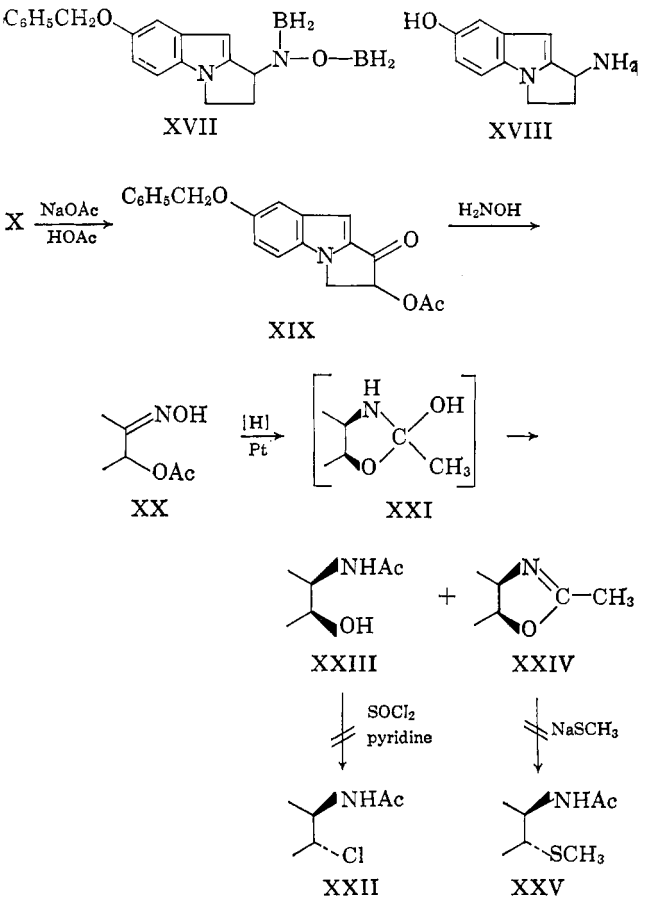
(14) M. Karplus, *J. Am. Chem. Soc.*, **85**, 2870 (1963).



hydroxy function to a suitable leaving group. Treatment of XIII with sulfuric acid or chlorosulfonic acid caused immediate decomposition; hence, as anticipated, the widely used sulfate method[4,11,15] could not be applied to this purpose. Model studies on the tosylation and mesylation of 1-hydroxypyrroloindole XV were discouraging. With the sulfonyl chlorides in pyridine, either starting material or tar was obtained. It was also not possible to effect sulfonylation of the sodium or potassium salts of XV. This failure to obtain a sulfonate ester contrasts with the ease with which XV can be acetylated.[16]

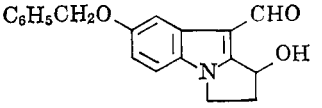
In view of these difficulties we abandoned sulfonate ester formation as a means of activating the 1-hydroxy group of XIII and turned our attention to an interesting possible new method of aziridine formation[18] involving displacement of acetoxy by the anion derived from neighboring *trans*-acetamido. However, treatment of O,N-diacetate XIV with lithium hydride or sodium hydride in tetrahydrofuran was unsuccessful and starting material or the equivalent was recovered in each instance.

Since we were unable to utilize the 2-amino-1-hydroxy compound XIII, we next turned our attention to the preparation of the alternate 1-amino-2-hydroxy system. Treatment of bromo ketone X with sodium acetate afforded 2-acetoxy ketone XIX,[19] oximation of which introduced nitrogen at the 1 position. With oxygen and nitrogen thus present at the proper positions in XX, only reduction of the oximino group was necessary to obtain the desired alternate aminohydrin. Prior to attempting this reduction we undertook a model study with 2-substituted oxime IIa in order to determine the most effective reagent. Surprisingly, oxime IIa proved stable to reduction by lithium aluminum hydride.[20] Similarly, the corresponding methoxime was inert to this reagent. The latter compound is even more striking in its failure to react since the possibility of insoluble salt formation does not exist. Diborane[21] reacted with oxime IIa to give an amorphous solid that showed B–H stretching at 4.15, 4.3, and 4.4 μ in the infrared and gave a fair analysis for O,N-bisborane derivative XVII. Treatment of XVII with alkali regenerated IIa.[22] Successful reduction of the oximino group in IIa was finally achieved by catalytic hydrogenation with palladium. This catalyst also promoted hydrogenolysis



(15) (a) R. C. Elderfield and H. A. Hageman, *J. Org. Chem.*, **14**, 605 (1949); (b) K. N. Campbell, A. H. Sommers, and B. K. Campbell, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1960, p. 148.

(16) A parallel observation was made with 9-formyl derivative i,[17] a compound stable to forcing conditions. This compound readily gave an acetate with acetic anhydride[17]; however, it was recovered unchanged after treatment with tosyl chloride and pyridine at steam bath temperature for 30 hr.



i

(17) W. A. Remers, R. H. Roth, and M. J. Weiss, *J. Am. Chem. Soc.*, **86**, 4612 (1964).

(18) Suggested to us by Professor Marshall Gates.

(19) Prepared by Dr. G. R. Allen, Jr., of these laboratories.

(20) The reduction of oximes to amines by this reagent is well known. See N. G. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, Inc., New York, N. Y., 1956, p. 753.

(21) H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **82**, 681 (1960).

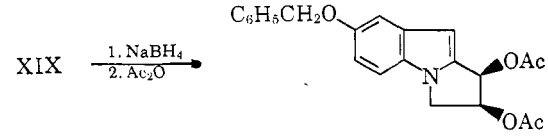
(22) During the course of this work, H. Feuer and B. F. Vincent, Jr. [*ibid.*, **84**, 3772 (1962)], communicated their finding that oximes were converted by diborane to borane derivatives which could be hydrolyzed by alkali to hydroxylamines.

of the benzyl group, affording 7-hydroxy-1-amine XVIII as the isolated product.

With a method for reducing a 1-oximinopyrroloindole to the corresponding amine thus established we returned to the problem of converting acetoxy oxime XX to an amino compound suitable for aziridine formation. For the catalytic reduction of XX, platinum was chosen in order to minimize hydrogenolysis of the benzyl group.[1] This reduction went slowly, but to completion. Resolution of the reaction mixture by fractional crystallization afforded two products, neither of which was the anticipated 1-amino-2-acetoxypyrroloindole. That one product (XXIII) had lost the O-acetyl group but gained an N-acetyl group was established by infrared and n.m.r. evidence. Inasmuch as XXIII apparently is formed by an O → N acyl migration *via* intermediate XXI, we presume it to have the *cis* configuration. The second product showed no carbonyl absorption in the infrared, but n.m.r. indicated a methyl group on a doubly bonded carbon at τ 8.33 (three protons, unsplit). Its ultraviolet spectrum was that of an ordinary pyrroloindole. From these data oxazoline XXIV emerges as the most reasonable structure. Unfortunately, good analytical data could not be obtained for XXIV (contamination with XXIII was indicated by n.m.r. and infrared data).[23]

To utilize either of these substances for an aziridine synthesis it was first necessary to invert one of the centers to obtain *trans* stereochemistry. Drawing on an analogy in cyclohexane chemistry,[24] we treated 1-acetamido-2-ol XXIII with thionyl chloride in pyridine in an attempt to prepare the epimeric 1-acetamido-2-chloropyrroloindole XXII, a compound that should afford an N-acetylaziridine. Unfortunately, these conditions led to tar formation. A method of epimerizing a center in the presumed oxazoline XXIV was sought in the opening of the oxazoline ring by reaction with a good nucleophile such as methyl mercaptide ion.[25] The resulting 1-acetamido-2-methylthiopyrroloindole XXV might then be converted to the N-acetylaziridine *via* a sulfonium salt intermediate.[26] However, treatment of oxazoline XXIV with sodium methyl mercaptide failed to incorporate any sulfur into the molecule.

The experiment just mentioned was the final attempt at aziridine formation. Although this goal was not achieved, the studies described above and those that follow provided considerable insight into the chemistry of the unusual pyrrolo[1,2-*a*]indole system. In addition they led to the synthesis of a number of the A-ring features present in certain of the mitomycin degradation products. For example, acid degradation of mitomycin A produced derivatives that appeared to have both *cis*- and *trans*-2-amino-1-hydroxy functions, as well as the isomeric 1-amino-2-hydroxy function.[9] Furthermore, nitrous acid treatment of the former type gave, in addition to the important 1-keto product, a small amount of 1,2-diol.[27] A pyrrolo[1,2-*a*]indole containing this 1,2-diol feature (as the diacetate) was prepared in the present study by sodium borohydride in methanol reduction of acetoxy ketone XIX followed by treatment of the resulting product with acetic anhydride. The immediate borohydride reduction product was not the expected diol, but appeared to be a boron-containing complex derived from it. It was amorphous and did not give combustion analyses consistent with any simple structure. Alkaline hydrolytic conditions did not affect this substance. However, acetic anhydride and sodium acetate at steam-bath temperature converted it in good yield to 1,2-diol diacetate XXVI. This diacetate is considered to have *cis* stereochemistry because of the stability of the complex and by analogy to the borohydride reduction of the corresponding bromo ketone X described above.



XXVI

Finally, we wish to describe additional experiments directed toward formation of 2-amino-1-hydroxypyrroloindoles. These experiments involved 1-hydroxy- and 1-ketopyrroloindoles substituted at the 2 position with carboxyl and related functions and were aimed at the introduction of nitrogen at C-2 by Curtius or Hofmann rearrangement or by decarboxylative nitrosation. The first route explored envisioned reduction of β-keto ester XXVIII[1] to the corresponding β-hydroxy ester, followed by conversion to β-hydroxy acid hydrazide XXXI and Curtius rearrangement. Entry into this route from β-keto ester XXVIII proved infeasible when no conditions for the reduction of this compound could be devised. Reduction with sodium borohydride in methanol or lithium borohydride in tetrahydrofuran failed. In view of our subsequent success in effecting borohydride reduction of the corresponding β-ketoamide and β-ketonitrile (see below), we presume that the inability of β-keto ester XXVIII to undergo reduction is related to a more complete conversion of XXVIII to enolate anion. It was also not possible to effect low-pressure catalytic (Pt) reduction of the ketonic carbonyl of XXVIII. However, preparation of β-hydroxy acid hydrazide XXXI was accomplished in the following manner. Condensation of ethyl 5-benzyloxy-2-indolecarboxylate XXVII with acrylamide by the previously described method[2] gave β-ketoamide XXIX. This β-ketoamide system, in contrast to the corresponding β-keto ester system, was susceptible to reduction with lithium borohydride in tetrahydrofuran and β-hydroxyamide XXX was obtained in good yield.[28] Treatment of XXX with excess hy-

(23) O → N acyl migration during catalytic hydrogenation, with isolation of an oxazoline, was reported for a steroid D-ring by F. Winternitz and C. R. Engel at the 2nd International Symposium on the Chemistry of Natural Products, Prague, 1962; Abstracts of the Meeting, p. 130.

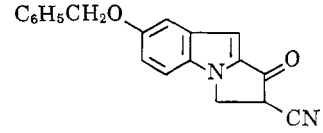
(24) W. S. Johnson and E. N. Schubert, *J. Am. Chem. Soc.*, **72**, 2187 (1950).

(25) This reaction also has precedent in cyclohexane systems. For examples, see T. Taguchi and M. Kojima, *ibid.*, **78**, 1464 (1956); M. Svoboda, J. Sicher, J. Farkas, and M. Pankova, *Collection Czech. Chem. Commun.*, **20**, 1426 (1955).

(26) Method of T. Taguchi and M. Kojima, *J. Am. Chem. Soc.*, **81**, 4318 (1959).

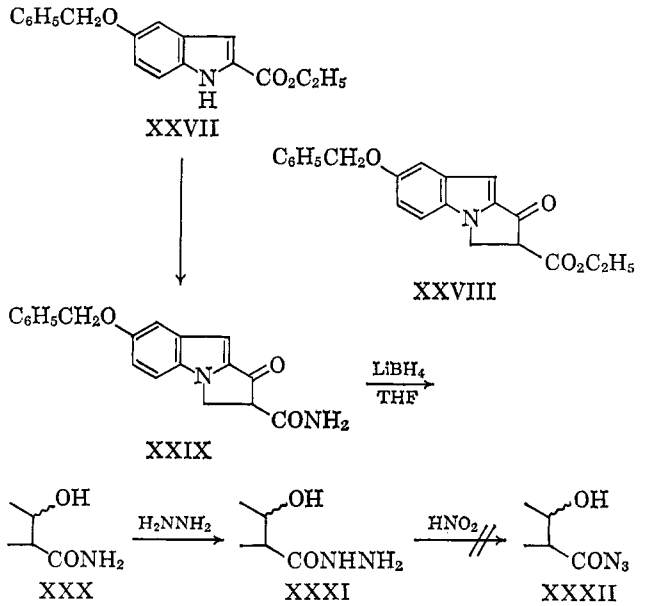
(27) Private communication from Dr. J. S. Webb and colleagues.

(28) β-Ketonitrile ii, formed by condensation of XXVII with acrylonitrile, also underwent reduction with lithium borohydride in tetrahydrofuran. The resulting β-hydroxynitrile appeared to be a mixture of *cis* and *trans* isomers in approximately equal amounts (see Experimental).

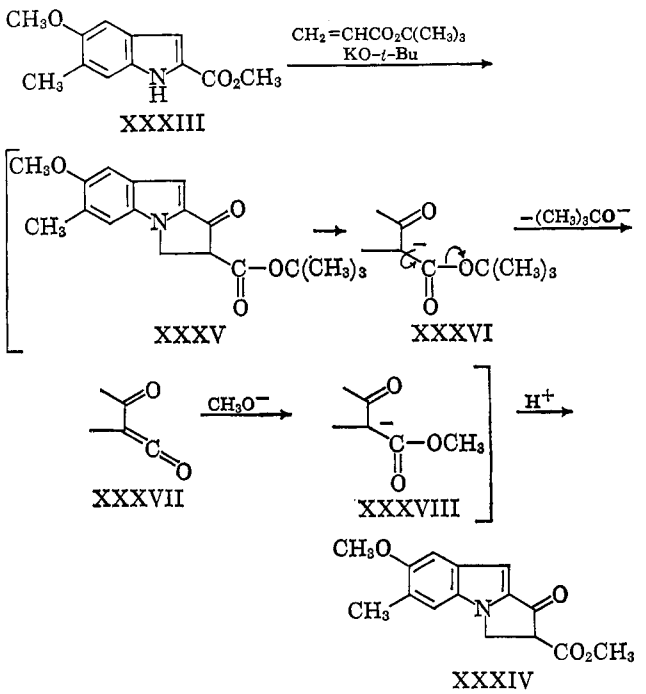


ii

drazine hydrate furnished hydrazide XXXI. Several attempts to prepare hydroxy azide XXXII by nitrous acid treatment of XXXI failed and only starting material could be recovered in each case. Furthermore, no trace of the desired thermal decomposition product of XXXII, the isocyanate that would be formed by Curtius rearrangement, was observed when a benzene extract of the nitrosating solution was heated. Several attempts at Hofmann rearrangement of β-ketoamide XXIX and β-hydroxyamide XXX also were unsuccessful.



The last route tried for aminohydrin preparation was based on the principle that nitrosation of mono α-substituted β-keto acids proceeds with decarboxylation, affording the α-nitroso ketones.[29,30] For this approach we utilized the available methyl ester XXXIV[2] since, in principle, hydrolysis to a β-keto acid from a methyl ester should be easier than from an ethyl ester. Nevertheless, XXXIV proved resistant to hydrolysis by sodium hydroxide,[31] the enolate anion formed being unreactive under mild conditions toward negatively charged hydroxide. Weaker bases such as carbonate and bicarbonate also failed to saponify XXXIV. We sought to circumvent this difficulty by preparing β-keto *t*-butyl ester XXXV, a compound that should be readily hydrolyzed by acid. Thus, methyl 5-methoxy-6-methyl-2-indolecarboxylate (XXXIII)[2] was treated with *t*-butyl acrylate and potassium *t*-butoxide in benzene. Surprisingly, the β-keto ester isolated from this condensation was not the anticipated *t*-butyl ester XXXV, but rather the corresponding *methyl* ester XXXIV. This remarkable ester interchange with a *t*-butyl ester can be explained by invoking ketene intermediate XXXVII which might result by elimination of *t*-butoxide anion from the enolate anion XXXVI of the initially formed β-keto *t*-butyl ester. Methoxide addition to this ketene



would afford the enolate anion XXXVIII of the observed β-keto methyl ester.[32]

Experimental

General.—Melting points were determined on a hot-stage microscope and are corrected. Ultraviolet spectra were determined in methanol (unless otherwise specified) using a Cary recording spectrophotometer. Infrared spectra were determined in potassium bromide disks on a Perkin-Elmer spectrophotometer (Model 21). N.m.r. were determined in hexadeuteriodimethyl sulfoxide, with deuterium oxide added in exchange experiments, on a Varian A-60 spectrometer with tetramethylsilane as an internal standard. Solutions were dried over anhydrous magnesium sulfate and concentrated under reduced pressure on a rotary evaporator.

7-Benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole Oxime (IIa).—A suspension of 276 mg. (1 mmole) of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (I) in 4 ml. of ethanol and 4 ml. of pyridine was treated with 140 mg. (2 mmoles) of hydroxylamine hydrochloride, and the mixture was heated on a steam bath for 2 hr. and then concentrated under reduced pressure. The white residue was triturated with water and extracted with hot ethanol. The insoluble residue was 260 mg. (89%) of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole oxime (IIa): m.p. 217°; λ_{max} 2.9 (m) μ; λ_{max} 215 mμ (ε 32,000), 313 mμ (ε 24,000).

Anal. Calcd. for $C_{18}H_{16}N_2O_2$ (292.32): C, 73.95; H, 5.52; N, 9.58. Found: C, 73.34; H, 5.55; N, 9.16.

7-Benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole Oxime *p*-Toluenesulfonate (IIb).—A solution of 487 mg. (1.67 mmoles) of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole oxime (IIa) in 150 ml. of tetrahydrofuran was cooled to 0° and treated with a solution of 1.0 g. (excess) of potassium hydroxide in 5 ml. of water, followed by 318 mg. (1.67 mmoles) of *p*-toluenesulfonyl chloride. After a few minutes the organic layer was separated, washed with brine, filtered through magnesium sulfate, and treated with hexane. The buff-colored solid (434 mg.) that formed was recrystallized from benzene–hexane, yielding 240 mg. (32%) of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]-indole oxime *p*-toluenesulfonate (IIb) as white needles, dec. pt. 150°.

(29) O. Touster, *Org. Reactions*, **7**, 337 (1953).

(30) Attempts to prepared an α-nitroso ketone by treatment of I with butyl or amyl nitrite under a variety of conditions were unsuccessful. Similarly, it was not possible to prepare an α-nitro ketone from I by base-catalyzed condensation with amyl nitrate. Attempted condensation of indole-2-carboxylate XXVII with nitroethylene also failed to give this nitro ketone.

(31) Saponification under more vigorous conditions, sodium hydroxide in ethanol at reflux temperature, resulted in cleavage of ring A.[2b]

(32) In this context we note the previous report[1] of partial interchange in this system of a methyl ester for an ethyl ester.[33]

(33) Facile interchange of a methyl for an ethyl ester, catalyzed by methoxide, was reported in the 3-carboxy-2,5-piperazinedione system by H. E. Zaugg, *et. al.* [*J. Am. Chem. Soc.*, **78**, 2626 (1956)]. We thank Professor Howard E. Zimmerman for calling this reference to our attention.

Anal. Calcd. for $C_{25}H_{22}N_2O_4S$ (446.51): C, 67.25; H, 4.97; N, 6.28; S, 7.18. Found: C, 67.14, 67.16; H, 5.05, 5.22; N, 6.51; S, 7.16.

7-Benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole Dimethylhydrazone (VI).—A suspension of 1.38 g. of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (I) in 8 ml. (excess) of 1,1-dimethylhydrazine was heated on a steam bath overnight, cooled, and filtered. The yellow solid that was collected (334 mg.) had an infrared spectrum identical with that of the aldol condensation product of I (see below) and did not depress the melting point of this product. The filtrate was concentrated and the residue was dissolved in 75 ml. of the upper and 75 ml. of the lower phase of a methanol–heptane system, mixed with 100 g. of Celite[34] diatomaceous earth, and packed atop a column prepared from 600 g. of Celite and 450 ml. of the lower phase. This column was eluted with the upper phase and the effluent was passed through a recording ultraviolet spectrophotometer set at 328 mμ. Concentration of effluent in hold-back volumes (h.b.v.) 2–3.3 (880 ml./h.b.v.) afforded 157 mg. of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole dimethylhydrazone (VI) as pale yellow plates, m.p. 134–135°, λ_{max} 6.2 μ, λ_{max} 328 mμ.

Anal. Calcd. for $C_{20}H_{21}N_3O$ (319.39): C, 75.21; H, 6.63; N, 13.16. Found: C, 75.49; H, 6.82; N, 12.49, 12.52.

Concentration of the effluent in hold-back volumes 3.3–4.2 afforded a small amount of starting material.

1-(7-Benzyloxy-2,3-dihydro-1H-pyrrolo[1,2-*a*]indole) Hydrazine (VIII).—A mixture of 5.52 g. of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (I), 5.0 ml. of hydrazine hydrate, and 100 ml. of ethanol was heated at reflux temperature for 2 hr. then cooled overnight. This procedure afforded 5.27 g. of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole hydrazone (VII) as pale yellow solid, m.p. 165–185°. Without further purification, a portion of this hydrazone was converted directly to the hydrazine.

A suspension of 716 mg. of hydrazone VII and 57 mg. of platinum oxide in 200 ml. of ethanol was shaken in a Parr apparatus with hydrogen at an initial pressure of 31 p.s.i. After 20 hr. the mixture was filtered and the filtrate was concentrated. Crystallization of the residue from methanol afforded 1-(7-benzyloxy-2,3-dihydro-1H-pyrrolo[1,2-*a*]indole) hydrazine (VIII) as white granules, dec. pt. 190°, λ_{max} 278 mμ.

Anal. Calcd. for $C_{18}H_{19}N_3O$ (293.36): C, 73.69; H, 6.53; N, 14.33; O, 5.45. Found: C, 73.54; H, 6.50; N, 13.60 (by difference, direct determination of nitrogen was unsatisfactory); O, 6.36.

***cis*-7-Benzyloxy-2-bromo-2,3-dihydro-1-hydroxy-1H-pyrrolo-[1,2-*a*]indole (XI).**[12]—A suspension of 2.0 g. (5.62 mmoles) of 7-benzyloxy-2-bromo-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (X) in 200 ml. of ethanol was treated with 425 mg. (11.2 mmoles) of sodium borohydride. The mixture was stirred 3.5 hr. at ambient temperature and concentrated, and the residue (1.66 g.) was dissolved in 50 ml. of the upper phase and 50 ml. of the lower phase of the system heptane–ethyl acetate–2-methoxyethanol–water (80:20:20:4), admixed with 100 g. of Celite and packed atop a column of 600 g. of Celite and 300 ml. of the lower phase. This column was eluted with the upper phase and the effluent was passed through a recording spectrophotometer that had been set at 278 mμ. The fraction contained in hold-back volumes 4 and 5 (1050 ml./h.b.v.) was concentrated. In this manner was obtained 1.182 g. (59%) of *cis*-7-benzyloxy-2-bromo-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole (XI) as a cream-colored solid: m.p. 112° dec.; λ_{max} 2.80 μ; λ_{max} 278 mμ; n.m.r. τ 7.19 (complex multiplet, C-2 proton), 6.10 (two protons, complex multiplet, C-3 proton), 5.15 (two protons, benzylic), 4.80 (doubled doublet, $J_{1,2}$ = 4.5 c.p.s., $J_{1,OH}$ = 6.0 c.p.s., changes to doublet, $J_{1,2}$ = 4.5 c.p.s. on deuteration, C-1 proton), 4.50 (doublet, $J_{1,OH}$ = 6.0 c.p.s., disappears on deuteration, OH proton), 3.73 (C-9 proton), 3.12 (doubled doublet, $J_{5,6}$ = 9 c.p.s., $J_{6,8}$ = 2 c.p.s., C-6 proton), 2.78 (doublet, $J_{6,8}$ = 2 c.p.s., C-8 proton), 2.52 (doublet, $J_{5,6}$ = 8 c.p.s., C-5 proton), 2.51 (five protons, phenyl).

Anal. Calcd. for $C_{18}H_{16}BrNO_2$ (358.227): C, 60.35; H, 4.50; Br, 22.31; N, 3.91. Found: C, 60.38; H, 4.73; Br, 22.15; N, 3.98.

At 5 and 2.5% in acetonitrile XI had an OH stretching frequency in the infrared of 3460 cm.$^{-1}$, compared with a stretching frequency of 3490 cm.$^{-1}$ for XIV[1] in this solvent at the same concentrations.

Dehydrobromination of *cis*-7-Benzyloxy-2-bromo-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole (XVI).[12]—A mixture of 170 mg. of *cis*-7-benzyloxy-2-bromo-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole (XI) and 11 ml. of 5% methanolic potassium hydroxide was heated at reflux temperature for 90 min., cooled, and filtered. The yellow solid was dissolved in methylene chloride, washed with brine, and concentrated, and the residue was crystallized from chloroform–petroleum ether (b.p. 60–70°). This procedure afforded the aldol condensation product (XVI) of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (I) as yellow needles: m.p. 254–257°; λ_{max} 5.95, 6.20 μ; λ_{max} 430 mμ.

Anal. Calcd. for $C_{36}H_{28}N_2O_3$: C, 80.57; H, 5.26; N, 5.22; mol. wt., 536.6. Found: C, 80.77; H, 5.53; N, 5.24; mol. wt., 541.

Treatment of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (I) with methanolic potassium hydroxide under the conditions described above afforded an aldol condensation product identical in infrared absorption spectrum with and not depressing the melting point of the sample of XVI described above.

***trans*-2-Azido-7-benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo-[1,2-*a*]indole (XII).**—A solution of 4.39 g. (67.5 mmoles) of sodium azide in 30 ml. of water was added to a solution of 4.86 g. (13.5 mmoles) of *cis*-7-benzyloxy-2-bromo-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole (XI) in 450 ml. of hot ethanol. The reaction mixture was refluxed for 65 hr. and then concentrated *in vacuo* to 75 ml. The concentrate was diluted with 300 ml. of water. On cooling, a tan solid precipitated. This solid was collected, washed with water, and dried *in vacuo* at 55–60° for 18 hr. to give tan solid (3.30 g.) which was purified by partition chromatography. The sample was dissolved in 75 ml. of the upper phase and 75 ml. of the lower phase of the methanol–heptane system and mixed with 150 g. of Celite. The mixture was packed on a column prepared from 500 g. of Celite and 250 ml. of the lower phase. The column (5.5 × 74 cm.) was eluted with the upper phase and the effluent was passed through a recording spectrophotometer which had been set at 277 mμ. The desired material was eluted in hold-back volumes 4.5 to 7.5 and the peak absorption was in the sixth hold-back volume (2250 ml./h.b.v.). A total of 3.280 g. of the desired material was obtained by low-temperature concentration *in vacuo* of the eluted fractions. This material was repartitioned in the same system and the residue was recrystallized twice from boiling methanol to give *trans*-2-azido-7-benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole (XII): m.p. 126–129°; λ_{max} 2.95, 4.70 μ; λ_{max} 217 mμ (ε 32,000), 276 (7800), 310 sh (3000); n.m.r. τ 5.95 (multiplet, C-2 proton), 5.42 (two protons, multiplet, C-3 proton), 4.73 (three protons, superimposed peaks, benzylic methylene and C-1 proton), 3.73 (doublet, $J_{1,OH}$ = 6 c.p.s., disappears on deuteration, OH proton), 3.55 (C-9 proton), 2.92 (doubled doublet, $J_{5,6}$ = 9 c.p.s., $J_{6,8}$ = 2 c.p.s., C-6 proton), 2.65 (doublet, $J_{6,8}$ = 2 c.p.s., C-8 proton), 2.44 (five protons, phenyl), 2.42 (doublet, $J_{5,6}$ = 9 c.p.s., C-5 proton).

One fraction (750 mg.) of the once-partitioned material was recrystallized from methanol to give 388 mg. of crystals which were dissolved in 40 ml. of methylene chloride and chromatographed on 7.0 g. of Florisil[35] magnesia–silica gel adsorbent (60–100 mesh) in a 10-mm.-diameter column. The sample was eluted with methylene chloride. The first 50 ml. of effluent contained pale yellow solid (181 mg.), m.p. 127–131°, which was recrystallized from 10 ml. of methanol. Pale yellow crystals (68 mg.) of *trans*-2-azido-7-benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole (XII), m.p. 123–128°, were obtained.

Anal. Calcd. for $C_{18}H_{16}N_4O_2$ (320.34): C, 67.48; H, 5.03; N, 17.49. Found: C, 67.00; H, 5.11; N, 16.47, 16.98 (high temperature).

***trans*-2-Amino-7-benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo-[1,2*a*]indole (XIII).**—A suspension of 1.29 g. of *trans*-2-azido-7-benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole (XII) in 120 ml. of ethanol was treated with 125 mg. of platinum oxide and the mixture was shaken with hydrogen in a Parr apparatus at an initial pressure of 35 p.s.i. After 6 hr., the mixture was filtered and concentrated and the residue was crystallized from methanol–water and recrystallized from ethanol. This procedure furnished 530 mg. (45%) of *trans*-2-amino-7-benzyloxy-2,3-di-

(34) Celite is Johns-Manville's registered trade-mark for diatomaceous earth products.

(35) Florisil is the registered trade-mark of the Floridin Co. for a magnesia–silica gel adsorbent.

hydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole (XIII) as white prisms: m.p. 158–164°; λ_{max} 3.0, 3.1, 3.2 μ; λ_{max} 278 mμ (ϵ 40,100).

Anal. Calcd. for $C_{18}H_{18}N_2O_2 \cdot 0.25H_2O$ (298.84): C, 72.35; H, 6.25; N, 9.34; H_2O, 1.51. Found: C, 71.63; H, 6.26; N, 8.16; H_2O (Karl Fischer), 1.71.

***trans*-2-Acetamido-1-acetoxy-7-benzyloxy-2,3-dihydro-1H-pyrrolo[1,2-*a*]indole (XIV).**—A mixture of 490 mg. of *trans*-2-amino-7-benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole (XIII), 500 mg. of sodium acetate, and 20 ml. of acetic anhydride was heated on a steam bath for 2 hr. It was cooled and treated with ice and sodium bicarbonate solution until the excess anhydride hydrolyzed. The solid diacetyl product was taken up in methylene chloride, washed with water, dried and concentrated. Washing the residue with ether afforded 310 mg. (51%) of *trans*-2-acetamido-1-acetoxy-7-benzyloxy-2,3-dihydro-1H-pyrrolo[1,2-*a*]indole (XIV): m.p. 151–154°; λ_{max} 2.9, 5.75, 6.07 μ. An analytical sample, recrystallized from methylene chloride–hexane, had m.p. 158–159°.

Anal. Calcd. for $C_{22}H_{22}N_2O_4$ (387.41): C, 69.82; H, 5.86; N, 7.40. Found: C, 69.59; H, 6.08; N, 7.10.

***trans*-2-Acetamido-7-benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole.**—To a solution of 250 mg. (0.69 mmole) of *trans*-2-acetamido-1-acetoxy-7-benzyloxy-2,3-dihydro-1H-pyrrolo[1,2-*a*]indole (XIV) in 8 ml. of purified tetrahydrofuran was added 50 mg. of 50% sodium hydride in oil suspension (1.0 mmole). The mixture was stirred overnight at room temperature, then heated at reflux temperature for 6 hr. Water and methylene chloride were added, and the organic layer was washed with water, dried, and concentrated. Crystallization of the residue from acetone–hexane gave 137 mg. (59%) of *trans*-2-acetamido-7-benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole as white plates: m.p. 222–225°; λ_{max} 2.98, 3.05, 6.12 μ.

Anal. Calcd. for $C_{20}H_{20}N_2O_3$ (336.38): C, 71.41; H, 5.99; N, 8.33. Found: C, 71.72; H, 6.21; N, 8.58.

2-Acetoxy-7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]-indole (XIX).[19]—A solution of 356 mg. (1.0 mmole) of 7-benzyloxy-2-bromo-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (X) and 1.00 g. of potassium acetate in 8 ml. of glacial acetic acid was heated at reflux temperature with magnetic stirring for 90 min. The cooled solution was diluted with water, and the precipitated solid was recrystallized from methylene chloride–petroleum ether (b.p. 60–70°) and then three times from methanol to give 155 mg. (46%) of 2-acetoxy-7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo-[1,2-*a*]indole (XIX) as pale yellow plates, m.p. 145–147°. Material from a similar experiment had m.p. 149–151°; λ_{max} 5.72, 5.80 (doublet), 6.15 μ; λ_{max} 216 mμ (ϵ 37,400), 248 sh (13,100), 327 (22,100).

Anal. Calcd. for $C_{20}H_{17}NO_4$ (335.34): C, 71.63; H, 5.11; N, 4.18. Found: C, 71.55; H, 5.34; N, 4.23.

2-Acetoxy-7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]-indole Oxime (XX).—A mixture of 175 mg. (0.5 mmole) of 2-acetoxy-7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (XIX), 35 mg. (0.5 mmole) of hydroxylamine hydrochloride, 2 ml. of ethanol, and 2 ml. of pyridine was heated on a steam bath for 2 hr. It was then concentrated and toluene was distilled from the residue to remove traces of pyridine. The residue was treated with water, and the insoluble material was dried and then crystallized from methanol. This procedure gave 32 mg. (17%) of 2-acetoxy-7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo-[1,2-*a*]indole oxime (XX) as white needles: m.p. 162–166°; λ_{max} 3.0, 5.75 μ; λ_{max} 319 mμ (ϵ 20,000). An analytical sample, recrystallized from methanol, had m.p. 166–172°.

Anal. Calcd. for $C_{20}H_{18}N_2O_4$ (350.26): C, 68.56; H, 5.18; N, 8.00. Found: C, 68.71; H, 5.24; N, 7.94.

Repetition of the above preparation on a 1.9-g. scale, with cooling of the mixture to 0° after the 2-hr. heating period, afforded directly a 72% yield of crystalline XX, m.p. 164–172°.

7-Benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole Methoxime.—A mixture of 276 mg. (1 mmole) of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (I), 83.5 mg. (1 mmole) of methoxyamine hydrochloride, 4 ml. of ethanol, and 4 ml. of pyridine was heated on a steam bath for 2 hr. Cooling the resulting solution to 5° afforded 223 mg. (73%) of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole methoxime as white plates, m.p. 146–149°, λ_{max} 319 mμ. An analytical sample, recrystallized from methanol, had m.p. 153–155°.

Anal. Calcd. for $C_{19}H_{18}N_2O_2$ (306.35): C, 74.49; H, 5.92; N, 9.15. Found: C, 74.23; H, 6.19; N, 9.04.

Diborane Reduction of 7-Benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole Oxime.—Diborane, prepared from 38 mg. of sodium borohydride, 213 mg. of boron trifluoride etherate, and 5 ml. of diglyme,[21] was swept by nitrogen into a suspension of 146 mg. of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]-indole oxime (IIa) in 30 ml. of tetrahydrofuran. After 1 hr. the resulting clear solution was treated with 1 ml. of ethanol and concentrated. This procedure afforded the diborane derivative (XVII) of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole oxime (IIa) as pale yellow solid: m.p. 152° with gas evolution; λ_{max} 4.15, 4.3, 4.4 μ (B–H).

Anal. Calcd. for $C_{18}H_{20}B_2N_2O_2$ (317.99): C, 68.21; H, 6.03; N, 8.84. Found: C, 69.03; H, 6.84; N, 8.33.

On treatment with 1 ml. of 10% sodium hydroxide in 5 ml. of tetrahydrofuran for 1 hr. at steam-bath temperature, borane derivative XVII reverted to oxime IIa.

1-Amino-2,3-dihydro-7-hydroxy-1H-pyrrolo[1,2-*a*]indole (XVIII).—A mixture of 1.17 g. of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole oxime (IIa), 1.0 g. of 10% palladium on charcoal, and 150 ml. of ethanol was shaken in a Parr apparatus with hydrogen at an initial pressure of 39 p.s.i. After 48 hr. the mixture was filtered and concentrated. Crystallization of the residue from methanol gave 1-amino-2,3-dihydro-7-hydroxy-1H-pyrrolo[1,2-*a*]indole (XVIII), m.p. 184–189° dec., λ_{max} 278 mμ, soluble in aqueous hydrochloric acid.

Anal. Calcd. for $C_{11}H_{12}N_2O$ (188.22): C, 70.18; H, 6.43; N, 14.88. Found: C, 69.83; H, 7.74; N, 14.10.

Hydrogenation of 2-Acetoxy-7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole Oxime (XX).—A warm solution of 2.0 g. of 2-acetoxy-7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole oxime (XX) in 250 ml. of ethanol was treated with 300 mg. of platinum oxide and shaken in a Parr apparatus with hydrogen at an initial pressure of 35 p.s.i. for 60 hr. The mixture was filtered and concentrated and the residue was treated with methanol and ether. The while solid that formed was crystallized from methanol, affording *cis*-1-acetamido-7-benzyloxy-2,3-dihydro-2-hydroxy-1H-pyrrolo[1,2-*a*]indole (XXIII) as white needles: m.p. 204°; λ_{max} 2.9, 3.05, 6.15 μ; λ_{max} 278 mμ; n.m.r. τ 1.75 (doublet, J = 8.5 c.p.s., disappears on deuteration, NH), 4.47 (doubled doublet, J = 8.5, 5.0 c.p.s., becomes doublet J = 5 c.p.s. on deuteration, C-1 proton), 8.0 [C(=O)CH_3].

Anal. Calcd. for $C_{20}H_{20}N_2O_3$ (336.38): C, 71.41; H, 5.99; N, 8.33. Found: C, 72.39; H, 5.79; N, 8.04.

Treatment of XXIII with acetic anhydride and sodium acetate afforded an O,N-diacetyl derivative (λ_{max} 5.75, 6.07 μ).

Concentration of the mother liquor from the above methanol crystallization afforded white crystals: m.p. 119–123°; very weak carbonyl absorption in the infrared; λ_{max} 278 mμ; n.m.r. τ 4.7 (J = 5 c.p.s., C-1 proton), 8.33 (>C–CH_3), small peak at 8.0 (XXIII impurity). These data suggest oxazoline structure XXIV. No satisfactory analysis could be obtained on this material. It was not possible to purify it by fractional crystallization.

***cis*-7-Benzyloxy-1,2-diacetoxy-2,3-dihydro-1H-pyrrolo[1,2-*a*]-indole (XXVI).**—A suspension of 1.675 g. (5 mmoles) of 2-acetoxy-7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (XIX) in 65 ml. of methanol was treated with 378 mg. (10 mmoles) of sodium borohydride. Most of the yellow solid dissolved and within a few minutes white solid precipitated from the mixture. After 1 hr. at room temperature, the reaction solution was clear and pale yellow. The solvent was removed *in vacuo* at 25° to give an off-white solid (1.698 g.) that was insoluble in water and only sparingly soluble in ether or methylene chloride. This solid was recrystallized from 40 ml. of methanol to give 536 mg. of white solid, m.p. 270–280°.

Anal. Found: C, 68.78, 68.78; H, 5.13; 5.17; N, 4.38; ash, 16.9.

To 257 mg. of this crude solid was added 143 mg. of sodium acetate and 7 ml. of acetic anhydride. The mixture was heated on a steam bath 90 min., cooled, and poured into water. The white precipitate that slowly formed was washed with water and dissolved in methylene chloride. This solution was washed with sodium bicarbonate solution, dried, and concentrated on a steam bath as *n*-hexane was added. Cooling the solution when the first crystals appeared gave 270 mg. of *cis*-7-benzyloxy-1,2-diacetoxy-2,3-dihydro-1H-pyrrolo[1,2-*a*]indole (XXVI) as white plates: m.p. 114–116°; λ_{max} 5.70, 8.05 μ; λ_{max} 278 mμ.

Anal. Calcd. for $C_{22}H_{21}NO_5$ (379.40): C, 69.64; H, 5.58; N, 3.69. Found: C, 69.34; H, 5.82; N, 3.70.

7-Benzyloxy-2-cyano-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (ii).—To a solution of potassium *t*-butoxide, prepared by dissolving 0.624 g. (16 mg.-atoms) of potassium in 30 ml. of *t*-

butyl alcohol, was added a solution of 4.53 g. (15.5 mmoles) of ethyl 7-benzyloxy-2-indolecarboxylate (XXVII) in 20 ml. of *t*-butyl alcohol. The mixture was stirred for 15 min., treated with 0.85 g. (16 mmoles) of acrylonitrile, and heated at reflux temperature for 2 days. It was poured into water and acidified with dilute hydrochloric acid, and the precipitate that resulted was washed with water and dried. Crystallization of this precipitate from acetone–petroleum ether (b.p. 60–70°) afforded 2.35 g. (53%) of 7-benzyloxy-2-cyano-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (ii), as pale yellow plates: m.p. 225–230°; λ_{max} 4.4 (C≡N), 5.85 (C=O) μ; λ_{max} 328 mμ (ϵ 21,000).

Anal. Calcd. for $C_{19}H_{14}N_2O_2$ (302.32): C, 75.48; H, 4.67; N, 9.27. Found: C, 75.80; H, 5.04; N, 9.11.

Lithium Borohydride Reduction of 7-Benzyloxy-2-cyano-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (ii).—A suspension of 431 mg. (1.4 mmoles) of 7-benzyloxy-2-cyano-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole (ii) in 20 ml. of tetrahydrofuran was treated with 62 mg. (2.8 mmoles) of lithium borohydride. The mixture was stirred 16 hr., acidified with acetic acid, and concentrated. The dried residue (310 mg.) was dissolved in 20 ml. of the lower phase of the system heptane–ethyl acetate–methanol–water (85:15:17:4) and mixed with 40 g. of Celite. This pack was placed atop a column (3.7 cm. diam.) of 300 g. of Celite admixed with 150 ml. of the lower phase described above and eluted with the upper phase. The hold-back volume was 490 ml. The effluent was passed through a recording spectrophotometer that had been set at 278 mμ. The product appeared in two parts: the first part in hold-back volumes 4.0–6.0; the second part in hold-back volumes 6.4–8.0. Both parts were concentrated. The first part afforded 100 mg. of white plates: m.p. 192–196°; λ_{max} 2.9 (O–H), 4.4 (C≡N) μ; λ_{max} 250 mμ (ϵ 44,000), 278 (9300), 300 sh (4400), 312 sh (2900); n.m.r. τ 5.90 (complex multiplet, C-2 proton), 5.50 (two protons, complex multiplet, C-3 proton), 4.85 (two protons, benzylic); 4.45 (doubled doublet, $J_{1,2}$ = 4.5 c.p.s., $J_{1,OH}$ = 7.5 c.p.s., changes to doublet $J_{1,2}$ = 4.5 c.p.s. on deuteration, C-1 proton), 3.62 (C-9 proton), 3.50 (doublet, $J_{1,OH}$ = 7.5 c.p.s., disappears on deuteration, hydroxyl proton), 3.05 (doubled doublet, $J_{5,6}$ = 9 c.p.s., $J_{6,8}$ = 2 c.p.s., C-6 proton), 2.75 (doublet, $J_{6,8}$ = 2 c.p.s., C-8 proton), 2.60 (doublet, $J_{5,6}$ = 9 c.p.s., C-5 proton), 2.50 (5 protons, phenyl group). The second part afforded 40 mg. of white plates: m.p. 185–192°; λ_{max} 2.09 (O–H), 4.4 (C≡N) μ; λ_{max} 220 mμ (ϵ 44,000), 278 (9300), 300 sh (4400), 312 sh (2900); n.m.r. τ 5.90 (complex multiplet, C-2 proton), 5.60 (two protons, complex multiplet, C-3 protons), 4.85 (two protons, benzylic), 4.65 (doubled doublet, $J_{1,2}$ = 6 c.p.s., $J_{1,OH}$ = 7.5 c.p.s., becomes doublet $J_{1,2}$ = 6 c.p.s. on deuteration, C-1 proton), 3.65 (doublet, $J_{1,OH}$ = 7.5 c.p.s., disappears on deuteration, hydroxyl proton), 3.61 (C-9 proton), 3.05 (doubled doublet, $J_{5,6}$ = 9 c.p.s., $J_{6,8}$ = 2 c.p.s., C-6 proton), 2.73 (doublet $J_{6,8}$ = 2 c.p.s., C-8 proton), 2.60 (doublet, $J_{5,6}$ = 9 c.p.s., C-5 proton), 2.50 (5 protons, phenyl group). One of the two isomers described above is considered to be *cis*-7-benzyloxy-2-cyano-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole and the other is the corresponding *trans* isomer.

7-Benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole-2-carboxamide (XXIX).—A warm solution of ethyl 7-benzyloxy-2-indolecarboxylate (XXVII) (14.77 g., 50 mmoles) in 100 ml. of freshly distilled tetrahydrofuran was added to a suspension of freshly prepared potassium *t*-butoxide (5.61 g., 50 mmoles) in 150 ml. of tetrahydrofuran. Acrylamide (3.91 g., 55 mmoles) was added to the solution, and the resulting mixture was heated at reflux temperature for 65 hr., cooled, and acidified with concentrated hydrochloric acid. The mixture was concentrated and the solid residue (25.47 g.) was extracted three times with 150-ml. portions of boiling methylene chloride. The dark brown extract was concentrated to give a solid (11.10 g.) whose ultraviolet absorption spectrum indicated that it was starting material. The cream-colored residue from the extraction was washed with 100 ml. of water and then washed two times with 75-ml. portions of methylene chloride. This procedure afforded 6.688 g. of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole-2-carboxamide (XXIX). This material was used directly in the preparation of the corresponding 1-hydroxy compound. A sample recrystallized two times from boiling acetonitrile gave white lustrous plates: m.p. 228–229° dec.; λ_{max} 5.85, 6.01 μ; λ_{max} 315 mμ (ϵ 20,500).

Anal. Calcd. for $C_{19}H_{16}N_2O_3$ (320.33): C, 71.24; H, 5.03; N, 8.75. Found: C, 70.88; H, 5.15; N, 9.04.

7-Benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole-2-carboxamide (XXX).—Lithium borohydride (1.51 g., 60 mmoles) was added to a solution of 8.91 g. (28 mmoles) of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole-2-carboxamide (XXIX) in 4 l. of boiling tetrahydrofuran. The mixture was stirred overnight at room temperature and then filtered. White solid (5.40 g.) was collected and yellow solid (5.28 g.) was obtained by concentration of the filtrate. The combined solid was separately washed with dilute hydrochloric acid and water and dried *in vacuo* overnight. This solid (7.45 g., 82.5%) was used without further purification in the preparation of the corresponding 1-hydroxy-2-carboxylic acid hydrazide (see below). A 500-mg. sample of the solid was dissolved in 20 ml. of boiling tetrahydrofuran, treated with charcoal, and concentrated until solid began to precipitate. This procedure afforded 7-benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole-2-carboxamide (XXX): no melting below 350°; λ_{max} 2.92, 6.09 μ; λ_{max} 294 mμ. It was not possible to obtain satisfactory microanalyses on this sample.

7-Benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole-2-carboxylic Acid Hydrazide (XXXI)).—Unpurified 7-benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole-2-carboxamide (XXX, 0.5 g., 1.55 mmoles) was heated with 3.10 g. (62 mmoles) of hydrazine hydrate at reflux temperature for 24 hr. The reaction mixture was cooled and the solid that precipitated was washed with water. Recrystallization of this solid from 15 ml. of methanol afforded 92 mg. (17.03%) of 7-benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-*a*]indole-2-carboxylic acid hydrazide (XXXI): m.p. 177–179°; λ_{max} 2.96, 6.15 μ; λ_{max} 293 mμ.

Anal. Calcd. for $C_{19}H_{19}N_3O_3$ (337.4): C, 67.64; H, 5.68; N, 12.46. Calcd. for $C_{19}H_{19}N_3O_3 \cdot 0.5CH_3OH$: C, 66.27; H, 5.99; N, 11.89. Found: C, 66.75; H, 6.31; N, 12.16.

Methyl 2,3-Dihydro-7-methoxy-6-methyl-1-oxo-1H-pyrrolo-[1,2-*a*]indole-2-carboxylate (XXXIV).—A suspension of potassium *t*-butoxide (prepared from 936 mg. of potassium and 40 ml. of *t*-butyl alcohol) in 50 ml. of benzene was treated with a hot solution of 5.86 g. (27 mmoles) of methyl 5-methoxy-6-methyl-2-indolecarboxylate (XXXIII) in 60 ml. of benzene. The mixture was stirred for 15 min., treated with 3.10 g. (24 mmoles) of *t*-butyl acrylate, and stirred at reflux temperature for 4 days. It was cooled, poured into water, acidified with dilute hydrochloric acid, and extracted with methylene chloride. This extract was washed with brine, dried, and concentrated, and the dark tarry residue was treated with ether. Gray solid separated and was recrystallized from acetone two times. This procedure afforded methyl 2,3-dihydro-7-methoxy-6-methyl-1-oxo-1H-pyrrolo[1,2-*a*]indole-2-carboxylate (XXXIV) as white needles, m.p. 168–175°; the mixture melting point with an authentic sample (m.p. 168–176)[2] was at 168–175°. The infrared absorption spectrum was identical with that of the authentic sample.

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