5,8-dione (XXVI) in 10 ml. of dry pyridine was added 150 mg. (0.96 mmole) of phenyl chloroformate. The reaction mixture was stirred at room temperature for 2 hr. during which time the orange gum which had formed dissolved. Water was then added to the reaction mixture and the precipitate was filtered to give 366 mg. (100%) of light orange solid. An analytical sample was prepared by recrystallization from methylene chloride–petroleum ether: m.p. 137.5–138°; λ_{max} 230, 285, 345, and 450 mμ (ε 19,050, 13,900, 3800, and 950); λ 5.69, 6.03, 6.1, 6.22, and 7.85–8.1 μ.

Anal. Calcd. for $C_{21}H_{19}NO_6$ (381.37): C, 66.13; H, 5.02; N, 3.67. Found: C, 65.73; H, 5.23; N, 3.60.[38]

2,3-Dihydro-9-hydroxymethyl-7-methoxy-6-methyl-1H-pyrrolo[1,2-*a*]indole-5,8-dione Carbamate (XVIII).—Ammonia gas was passed into a solution of 256 mg. (0.67 mmole) of 2,3-dihydro-9-hydroxymethyl-7-methoxy-6-methyl-1H-pyrrolo[1,2-*a*]indole-5,8-dione phenylcarbonate (XXVII) in 15 ml. of methylene chloride, chilled in an acetone–Dry Ice bath, for 0.5 hr. The acetone–Dry Ice bath was removed, and the reaction mixture was magnetically stirred at room temperature for several hours. The excess ammonia was removed by warming on a water bath. Additional methylene chloride was added to cause solution, and the solution was washed with water. The dried solution was evaporated and the residue was recrystallized from methylene chloride–petroleum ether to give 151 mg. (74% yield) of orange needles, m.p. 206–207°. Recrystallization from ethyl acetate gave orange needles: m.p. 206–207°; λ_{max} 230, 287, 345, and 460 mμ (ε 19,200, 14,600, 3870, and 1390); λ 2.9, 2.99, 5.86, 5.96, 6.05, 6.18, 9.04, 9.5, and 9.65 μ; p.m.r. τ 3.40 ($CONH_2$), 4.90 (≥C–CH_2–O), 5.82 (>N–CH_2–, triplet, J = 7 c.p.s.), 6.03 (OCH_3), and 8.15 (CH_3–C≤).

Anal. Calcd. for $C_{15}H_{16}N_2O_5$ (304.29): C, 59.20; H, 5.30; N, 9.21. Found: C, 59.50; H, 5.57; N, 8.97.[38]

Acknowledgment.—We wish to thank Drs. D. B. Cosulich, J. B. Patrick, W. A. Remers, and J. S. Webb for helpful discussions. Generous supplies of certain intermediates were made by Mr. S. Peluso of the Preparations Laboratory with the cooperation of Drs. H. G. Arlt, Jr., and J. L. Fedrick. Spectral data were furnished by Mr. W. Fulmor and his associates. Microanalyses were determined by Mr. L. Brancone and his group, and partition chromatograms were carried out by Mr. C. Pidacks and his staff. We thank Mr. A. C. Dornbush and the late Miss M. Hauck for the *in vitro* antibacterial data, Mr. G. S. Redin and his associates for *in vivo* antibacterial assays and acute toxicity data, and Dr. A. Vogel for the antitumor assays.

The Mitomycin Antibiotics. Synthetic Studies. VI.[1] Transformations in the 2,3-Dihydro-1H-pyrrolo[1,2-*a*]indole System

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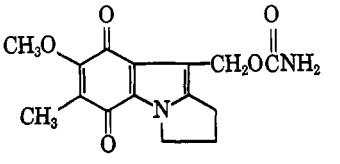
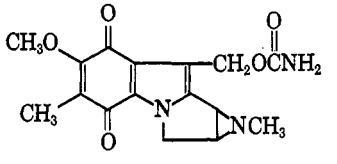
Certain transformations in the relatively rare 2,3-dihydro-1H-pyrrolo[1,2-*a*]indole system are described. Monobromination of the 2,3-dihydro-1H-pyrrolo[1,2-*a*]indol-1-ones Va and Vb results in attack at the β-indolic carbon to give the 9-bromo derivatives VIa and VIb, respectively. Treatment of ketone Va with 2 equiv. of bromine furnishes the 2,9-dibromide XIII. The order of preference observed in the reaction of this system with bromine may be reversed *via* the intermediacy of an enamine derivative. Hence, bromination of enamine XV gives the 2-bromide XVII. Various approaches to the unknown 3H-pyrrolo[1,2-*a*]indole structure, *e.g.*, XXIII, are discussed. Catalytic reduction of enamine XV affords tertiary amine XIX, the methiodide of which, on treatment with potassium *t*-butoxide, furnishes the 9H-pyrrolo[1,2-*a*]indole XXV.

As the basis for a synthetic program related to the mitomycin antibiotics, we have developed methods for the preparation of the 2,3-dihydro-1H-pyrrolo[1,2-*a*]-indole system,[1] the introduction of a 9-aldehyde function into such a structure,[2] the elaboration of the hydroxymethyl carbamate from the resulting aldehyde,[1] and the preparation of the indoloquinone chromophore.[1,3] Subsequently, the compatibility of these procedures was demonstrated in the synthesis of 7-methoxymitosene (I),[1] an antibacterial agent. A major structural feature of the mitomycins and the biologically important 7-methoxy-1,2-(N-methylaziridino)mitosene (II)[4] for which we lacked appropriate synthetic procedures is the fused aziridine moiety. We describe here certain transformations in the pyrrolo[1,2-*a*]indole system which were designed to set the stage for the introduction of this moiety.

Our procedure[1] for the preparation of the pyrrolo[1,2-*a*]indole system afforded a 1-keto derivative,



I



II

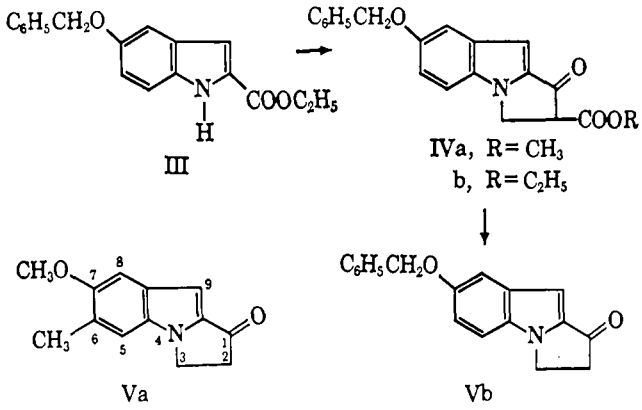
e.g., V, which seemed particularly useful for the present purpose. As a model for this study we chose the benzyloxy derivative Vb, since it was readily accessible from the commercially available ethyl 5-benzyloxyindole-2-carboxylate (III). Thus, condensation of III with methyl acrylate afforded a mixture of the methyl (IVa) and ethyl (IVb) β-keto esters, which could be separated, but was more conveniently decarboxylated to give the benzyloxy ketone Vb. A preliminary attempt to avoid this mixture by the use of ethyl acrylate in the condensation with indole

(1) Paper V: G. R. Allen, Jr., J. F. Poletto, and M. J. Weiss, *J. Org. Chem.*, **30**, 2897 (1965).

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

(3) W. A. Remers, P. N. James, and M. J. Weiss, *J. Org. Chem.*, **28**, 1169 (1963).

(4) 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).

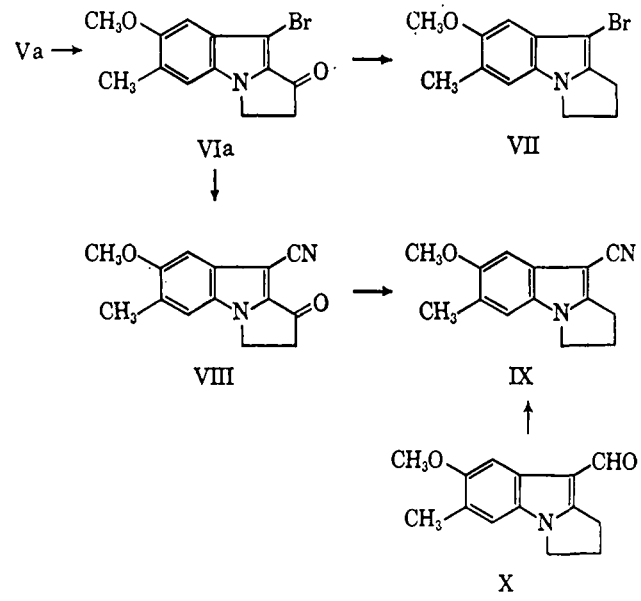


ethyl ester III resulted in a lower total yield of β-keto ester IVb and was not pursued.

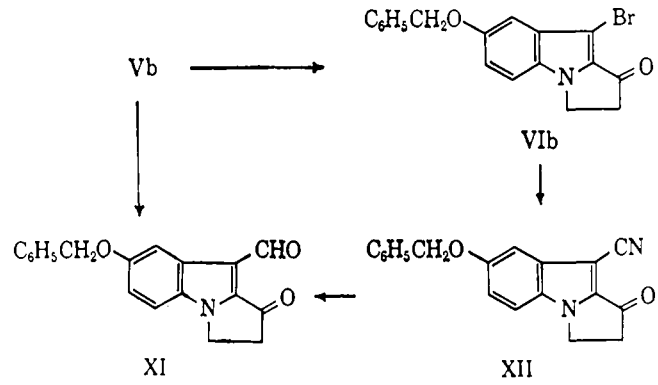
In principle, a major approach to the fused aziridine from the 1-keto system required the functionalization of C-2. Therefore, bromination of ketone Vb was initially investigated. Treatment of Vb with 1 molar equiv. of bromine in glacial acetic acid resulted in the rapid consumption of the halogen and the formation in high yield of a monobromo ketone. However, certain subsequent transformations indicated that this product was not the desired 2-bromo 1-ketone. Thus, reduction of the bromo ketone with sodium borohydride gave an impure, somewhat labile alcohol, treatment of which with methanolic potassium hydroxide was ineffective, since the recovered material was oxidized by the pyridine–chromium trioxide complex to give starting bromo ketone. Confirmation that the bromine had not entered the 2 position was furnished by a comparison of the p.m.r. spectrum of this product with that of its progenitor which revealed no change in the A_2X_2 pattern characteristic of the C-2 and C-3 methylene groups.

Since the remainder of these spectra were complicated by the presence of the benzyloxy proton signals, we turned to the simpler 7-methoxy-6-methyl series in an attempt to determine the site of bromination. Monobromination of ketone Va was readily effected as described for the 7-benzyloxy series, and the same p.m.r. spectral observations with regard to the C-2 and C-3 protons were noted. Since it was not possible to distinguish the *bz*-proton resonances from that of the C-9 proton in the parent Va (three-proton signals at τ 2.90, 3.04 and 3.17) because of deshielding of the latter by the 1-keto function, we examined the spectra of the corresponding 1-deoxy derivatives, which were prepared by Wolff–Kishner reduction. The spectrum of the nonbrominated Wolff–Kishner product[1] showed *bz*-proton signals at τ 3.21 and 3.24 and the C-9 proton resonance at τ 4.10.[5] Inasmuch as the latter signal is not observed in the spectrum of the brominated Wolff–Kishner product, this compound and its precursor ketone are assigned the 9-bromo structures VII and VIa.

Chemical confirmation of these assignments was obtained as follows. Treatment of the 9-bromo ketone VIa with cuprous cyanide[6] gave the ketonitrile



VIII, which on Wolff–Kishner reduction furnished the 9-nitrile IX, identical with the product obtained by the action[7] of O,N-bistrifluoroacetylhydroxylamine on the unequivocal 9-aldehyde X.[2]



That the 7-benzyloxy ketone Vb had behaved analogously on bromination was demonstrated in the following manner. The bromo ketone VIb was converted into the corresponding ketonitrile XII with cuprous cyanide. Reduction of XII with lithium triethoxyaluminum hydride[8] gave, in low yield, the ketoaldehyde XI, which had been prepared previously by formylation of ketone Vb.[2]

The ease with which the 1-oxopyrrolo[1,2-*a*]indole system V undergoes bromination at C-9 is of some interest, for it contrasts with the behavior of this system in the Vilsmeier–Haack aldehyde synthesis.[2] In the latter reaction ketone Vb yielded only 7% of the ketoaldehyde XI, and this under forcing conditions.

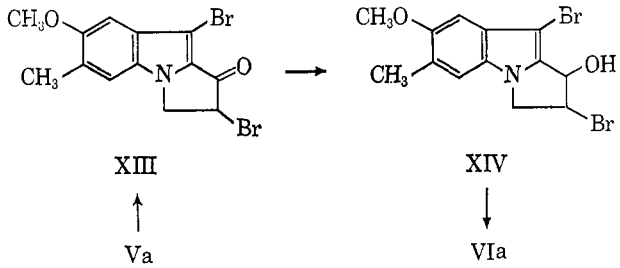
Having determined the nature of the monobromo derivatives of ketones Va and Vb, it was of interest to ascertain whether reaction with excess bromine would give an α-bromo ketone. For this purpose the methoxymethyl ketone Va was treated with 2 molar equiv. of bromine and a dibromide was isolated in good yield. Reduction of this substance with sodium borohydride gave an unstable alcohol XIV, which on treatment with

(5) It has been shown that the β-indole proton resonance appears at higher field than those of the *bz* protons [L. A. Cohen, J. W. Daly, H. Kny, and B. Witkop, *J. Am. Chem. Soc.*, **82**, 2184 (1960)]. Moreover, X, derived by 9-formylation of the Wolff–Kishner product, does not show this high-field signal.[1]

(6) (a) L. Friedman and H. Shechter, *J. Org. Chem.*, **26**, 2522 (1961); (b) M. S. Newman and H. Boden, *ibid.*, **26**, 2525 (1961).

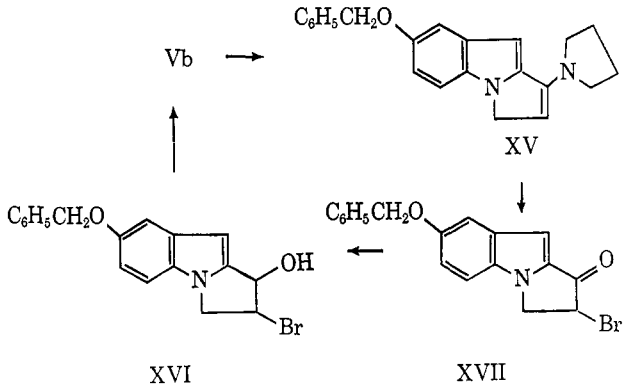
(7) J. H. Pomeroy and C. A. Craig, *J. Am. Chem. Soc.*, **81**, 6340 (1959).

(8) (a) G. Hesse and R. Schrödel, *Ann.*, **607**, 24 (1957); (b) H. C. Brown, C. J. Shoaf, and C. P. Garg, *Tetrahedron Letters*, **No. 3**, 9 (1959); (c) H. C. Brown and C. J. Shoaf, *J. Am. Chem. Soc.*, **86**, 1079 (1964); (d) H. C. Brown and C. P. Garg, *ibid.*, **86**, 1085 (1964).



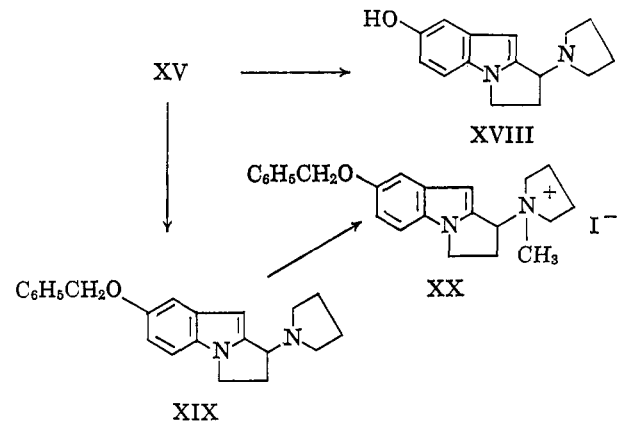
methanolic potassium hydroxide furnished the 9-bromo ketone VIa in 32% over-all yield. This observation establishes the position of the second bromine as C-2 and the structure of the dibromo ketone as XIII. Inasmuch as the bromo alcohol XIV gave a ketone on base treatment it is presumed to have the *cis* configuration.

The observed order of preference for the bromination of the ketopyrrolo[1,2-*a*]indole system was reversed *via* an enamine derivative. Thus, reaction of pyrrolidine enamine XV, prepared from the 7-benzyloxy ketone Vb, with N-bromoacetamide afforded the presumed 2-bromo ketone XVII. Confirmation of this assignment was obtained when base treatment of the derived alcohol XVI gave ketone Vb in 47% yield.[9] In view of these observations alcohol XVI is also presumed to have the *cis* configuration. Efforts to utilize α-bromo ketone XVII for the preparation of an aziridinopyrrolo[1,2-*a*]indole are described in an accompanying paper.[10] Finally, with respect to the bromo ketones we would note that the presence of a 2-bromo substituent (XIII and XVII) results in a bathochromic shift of about 15 mμ in the principal ultraviolet absorption band[11]; the 9-bromo grouping had no apparent effect.



A second approach to the fused aziridine system was predicated on the introduction of 1,2 unsaturation to give the unknown 3H-pyrrolo[1,2-*a*]indole ring system, *e.g.*, XXIII, from which several pathways to an aziridine were envisioned. However, many attempts to effect elimination to this olefinic system with the 1-ols derived from ketones Va and Vb by borohydride reduction were singularly unsuccessful.

We next investigated the possibility of effecting the elimination of a 1-tertiary-amino group or certain of its derivatives, inasmuch as at least one 2-vinylindole has been prepared by such a procedure.[12] For this purpose enamine XV was converted into tertiary amine XVIII (concomitant debenzylation) by hydrogenation using a palladium-on-charcoal catalyst. On reaction with acetic anhydride this amine gave, in low yield, a high melting, crystalline material, the p.m.r. spectrum of which showed three distinct resonances ascribable to acetoxyl group protons. For this reason, as well as the lack of styryl-type (6.24 μ) infrared absorption, the high melting point, and microanalyses, this material was considered as a possible trimer and was not further investigated.



For the base-induced Hofmann elimination reaction it was desirable to block the phenolic 7-hydroxy group in XVIII with a base-stable moiety. After preliminary unsuccessful attempts to O,N-bisalkylate XVIII, it was found that hydrogenation of the 7-benzyloxy enamine XV in the presence of Adams catalyst allowed preferential reduction of the enamine with the isolation of the 7-benzyloxy tertiary amine XIX.[13] This material was smoothly transformed into the methiodide XX, treatment of which with potassium *t*-butoxide in dimethylformamide gave in good yield a product having the desired $C_{18}H_{15}NO$ composition. The ultraviolet spectrum, λ_{max} 264 and 301 mμ (log ϵ 4.28 and 3.51), of this substance differed markedly from that of XX, but was not in accord with that recorded for the 2-vinylindole XXI, λ_{max} 305 and 315 mμ (log ϵ ~4.4 and 4.4).[12] Moreover, uleine, which has been shown to have the 2-vinylindole structure XXII,[14] has a significantly different ultraviolet spectrum, λ_{max} 209

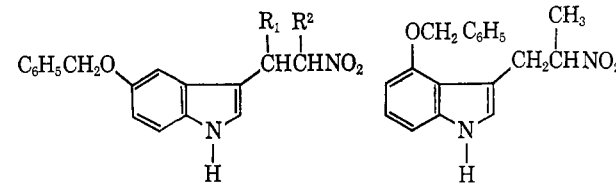
(9) In addition to ketone Vb a second product was isolated, but was not completely characterized. The nature of this material and a more careful study of this reaction is reported by Dr. W. A. Remers of this laboratory.[10]

(10) Paper VII: W. A. Remers, R. H. Roth, and M. J. Weiss, *J. Org. Chem.*, **30**, 2910 (1965).

(11) It may be noted that introduction of an α-bromo substituent in acetophenone causes a similar shift (+13 mμ): H. Keller and H. v. Halban, *Helv. Chim. Acta*, **27**, 1253 (1944).

(12) R. Goutarel, M.-M. Janot, V. Prelog, and W. I. Taylor, *ibid.*, **33**, 150 (1950).

(13) This preferential reduction is not without analogy in the literature. Thus, the reduction of the nitro group in 5-benzyloxyindoles i–iii [W. E. Noland and R. A. Hovden, *J. Org. Chem.*, **24**, 894 (1959)] and 4-benzyloxyindole iv [F. Troxler, F. Seemann, and A. Hofmann, *Helv. Chim. Acta*, **42**, 2073 (1959)] without hydrogenolysis of the benzyloxy ether has been reported.

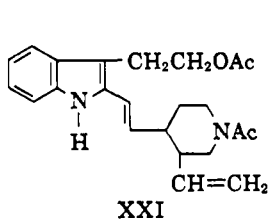


i, $R_1 = R_2 = H$
ii, $R_1 = C_6H_5$; $R_2 = H$
iii, $R_1 = C_6H_6$; $R_2 = CH_3$

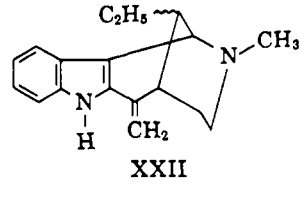
iv

(14) G. Büchi and E. W. Warnhoff, *J. Am. Chem. Soc.*, **81**, 4433 (1959).

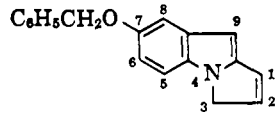
and 309 mμ (log ε 4.38 and 4.30).[15] Other evidence that the elimination product did not have the desired 3H-pyrrolo[1,2-a]indole structure (XXIII) was the lack of strong infrared absorption in the 6.24-μ region and its inability to take up hydrogen in the presence of a platinum catalyst.[16]



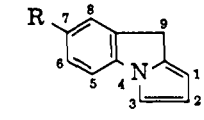
XXI



XXII



XXIII



XXIV, R = H

XXV, R = $C_6H_5CH_2O$

At this time our attention was directed to a paper by Laschtuvka and Huisgen[17] in which they reported the preparation of 9H-pyrrolo[1,2-a]indole (XXIV) by the Wolff–Kishner reduction of 9H-pyrrolo[1,2-a]-indol-9-one. Since the conditions used for the Hofmann elimination are quite similar to those of the Wolff–Kishner technique, there was a distinct possibility that our material was the 9H-pyrrolo[1,2-a]-indole XXV rather than the desired 3H-pyrrolo[1,2-a]indole XXIII. This possibility was enhanced by the similarity of the ultraviolet spectrum of the Hofmann elimination product to that reported for XXIV, λ_{max} 265 mμ (log ε ~4.15).

That, in fact, this material had the 9H-pyrrolo-[1,2-a]indole structure XXV was established from its p.m.r. spectrum,[18] the key features of which follow. (1) A single broad resonance (2 protons) at τ 7.28 and a resonance (1 proton) centered at τ 2.83 were observed. Irradiation at the radiofrequency corresponding to the former signal sharpened the τ 2.83 multiplet into a doublet with a typical *meta* coupling constant of 3 c.p.s.; the latter signal must be due to the C-8 proton, and its interaction with τ 7.28 methylene group places this group at C-9 (structure XXV), since interaction between protons at C-8 and C-3 in the alternate structure XXIII is improbable. (2) An apparent triplet at τ 3.77 (1 proton) resulting from the coincidence of two doublets with about *equal* coupling constants was noted. Irradiation at the radiofrequency corresponding to the C-3 proton multiplet (τ 2.74) transformed the τ 3.77 triplet into a sharp doublet (J = 2.5 c.p.s.). The only proton in an environment that would satisfy these observations is to be found at C-2 in the 9H-pyrrolo[1,2-a]indole structure (XXV).[19]

(15) J. Schmutz, F. Hunziker, and R. Hirt, *Helv. Chim. Acta*, **40**, 1189 (1957).

(16) The infrared spectrum of uleine (XXII) exhibits a band at 1635 cm.$^{-1}$ (6.12 μ),[14] and the alkaloid forms a dihydro derivative.[15]

(17) E. Laschtuvka and R. Huisgen, *Ber.*, **93**, 81 (1960). We are grateful to Dr. J. S. Webb for calling our attention to this paper.

(18) We are indebted to Dr. Norman S. Bhacca of Varian Associates for providing this measurement and its interpretation.

(19) Molecular orbital calculations indicate that the delocalization energy of the 9H-pyrrolo[1,2-a]indole system is greater by about 4 kcal./mole than the 3H-pyrrolo[1,2-a]indole system: W. A. Remers, *J. Am. Chem. Soc.*, **86**, 4608 (1964).

Experimental

Melting points were determined in open capillary tubes and are uncorrected. Ultraviolet spectra were determined in methanol solution unless specified otherwise, with a Cary recording spectrophotometer. Infrared spectra were determined in potassium bromide disks with a Perkin-Elmer Model 21 spectrophotometer. Proton magnetic resonance spectra were determined in deuteriochloroform, unless noted otherwise, with a Varian DP-60 (56.4 Mc.) or A-60 (60 Mc.) spectrometer using tetramethylsilane as an internal standard. The petroleum ether used was that fraction boiling at 60–70°.

Condensation of Ethyl 5-Benzyloxy-2-indolecarboxylate (III) with Methyl Acrylate.—A mechanically stirred mixture of 100 g. (0.342 mole) of ethyl 5-benzyloxy-2-indolecarboxylate, 38.3 g. (0.342 mole) of potassium *t*-butoxide, and 29.5 g. (0.342 mole, 30.6 ml.) of methyl acrylate in 2300 ml. of benzene was heated at reflux temperature for 4 days. The cooled mixture was acidified with dilute hydrochloric acid solution, whereupon all solid dissolved. The aqueous layer was extracted with methylene chloride, and the dried combined organic layers were concentrated. As a quantity of solid sufficient to cause bumping separated, it was removed by filtration and concentration of the filtrate was continued. In this manner the following six fractions were obtained: (a) 39.7 g. of **ethyl 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-a]indole-2-carboxylate (IVb)**, m.p. 160–164°; (b) 15.4 g. of **methyl 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo-[1,2-a]indole-2-carboxylate (IVa)**, m.p. 142–145°; (c) 2.0 g. of methyl ester IVa, m.p. 142–145°; (d) 7.5 g. of starting indole ester III, m.p. 160–162°; (e) 3.4 g. of methyl ester IVa, m.p. 142–145°; and (f) 5.5 g. of starting indole ester III. These amounts represent a 33% yield of ethyl ester, an 18% yield of methyl ester, and a 13% recovery of starting indole ester.

Ethyl ester from a similar experiment was recrystallized three times from ethanol to give white plates: m.p. 151–153°; λ_{max} 325 mμ (ε 23,000); λ_{max}^{HCl} 330 mμ (ε 24,100); λ_{max}^{NaOH} 356 mμ (ε 26,500) λ_{max} 5.71, 5.84, 6.15, 6.50, and 8.35 μ. In the p.m.r. spectrum[20] the presence of a triplet at τ 8.73 (3 protons) showed this substance to be the ethyl β-keto ester.

Anal. Calcd. for $C_{21}H_{19}NO_4$ (349.37): C, 72.19; H, 5.48; N, 4.01. Found: C, 71.91; H, 5.61; N, 4.00.

A sample of methyl ester from a similar experiment was recrystallized two times from methanol to give shining plates: m.p. 140–142°; λ_{max} 325 mμ (ε 22,800); λ_{max}^{NaOH} 356 mμ (ε 26,400); λ_{max} 5.69, 5.84, 6.14, 6.48, and 8.30–8.35 μ. In the p.m.r. spectrum[21] the presence of a singlet at τ 6.33 (3 protons) showed this material to be the methyl β-keto ester.

Anal. Calcd. for $C_{20}H_{17}NO_4$ (335.34): C, 71.63; H, 5.11; N, 4.18. Found: C, 71.92; H, 5.38; N, 4.11.

7-Benzyloxy-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-one (Vb).

A.—A mixture of 0.500 g. (1.5 mmoles) of methyl 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-a]indole-2-carboxylate (IVa), 40 ml. of methanol, and 10 ml. of 37% hydrochloric acid was heated at reflux for 1 hr. The product was isolated with methylene chloride and recrystallized from acetone–petroleum ether (b.p. 60–70°) to give 155 mg. (38%) of crystals, m.p. 181.0–183.5°. Three recrystallizations from the same solvent pair gave yellow plates: m.p. 183–184°; λ_{max} 320 mμ (ε 20,500); λ_{max} 5.84, 5.90 (split carbonyl), 6.15, and 6.48 μ; p.m.r.[20] τ 2.56, 2.72, 2.78 (aryl protons), 3.07 (C-9 proton), 4.85b (enzylic methylene protons), 5.62 (triplet, C-3 methylene protons), and 6.86 (triplet, C-2 methylene protons).

Anal. Calcd. for $C_{18}H_{15}NO_2$ (277.31): C, 77.96; H, 5.45; N, 5.05. Found: C, 78.16; H, 5.73; N, 5.21.

B.—A solution of 45.2 g. (0.13 mole) of ethyl 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-a]indole-2-carboxylate (IVb) and 20.8 g. (0.062 mole) of methyl 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-a]indole-2-carboxylate (IVa) in 1600 ml. of 95% acetic acid was heated at reflux temperature for 16 hr. The solution was cooled and filtered, and the solid was washed with water to give 36.0 g. of solid, m.p. 186–188°. The filtrate was diluted with water, and the precipitated solid was collected by filtration and recrystallized from acetone to give 6.0 g. (85%) of crystals, m.p. 185–187°.

7-Benzyloxy-9-bromo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-one (VIb).—A solution of 5.00 g. (18 mmoles) of 7-benzyloxy-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-one (Vb) in 500 ml. of acetic

(20) Measured with a Varian DP-60 spectrometer at 56.4 Mc.

(21) Determined with a Varian A-60 spectrometer at 60 Mc.

acid was brominated with 19.5 ml. of 0.92 *M* bromine in acetic acid solution as described below for ketone Va. The crude solid (5.45 g.) was adsorbed from benzene onto Florisil.[22] The solid eluted by methylene chloride was recrystallized from acetone–hexane to give 2.62 g. (40%) of tan crystals: m.p. 143–145° dec. after becoming dark at 125–127°; λ_{max} 218, 241, and 321 mμ (ε 33,400, 23,200, and 22,800); λ 5.84, 6.18, 6.54, 14.32 μ; p.m.r.[20] multiplets at τ 2.56–2.95 (8 aryl protons), 4.90 (benzylic methylene protons), 5.68 (triplet, C-3 methylene protons), and 6.88 (triplet, C-2 methylene protons).

Anal. Calcd. for $C_{13}H_{14}BrNO_2$ (356.22): C, 60.68; H, 3.96; Br, 22.44; N, 3.94. Found: C, 60.38; H, 3.79; Br, 22.96; N, 3.56.

A mixture of 712 mg. (2.0 mmoles) of this ketone in 50 ml. of ethanol was heated to reflux temperature and treated with 151 mg. (4.0 mmoles) of sodium borohydride. The mixture was then magnetically stirred at room temperature for 80 min., during which all solid dissolved. The solution was evaporated, and the residue was distributed between methylene chloride and a 1% sodium hydroxide solution. The organic solution was dried over magnesium sulfate and evaporated. The residue was recrystallized from ether–petroleum ether (b.p. 60–70°) to give white crystals which began decomposing at 80°. A sample from a similar experiment decomposed on standing at room temperature within 3 days.

The material from the above experiment was heated at reflux temperature for 3 hr. with 100 ml. of 5% ethanolic potassium hydroxide solution. The solution was partially concentrated, and the product was isolated with methylene chloride. The crude material was dissolved in 3 ml. of pyridine, chilled in an ice bath, and treated with a slurry of 500 mg. of chromium trioxide in 5 ml. of pyridine. The mixture was kept at room temperature for 17 hr., after which it was distributed between methylene chloride and water. The organic solution was washed with sodium bicarbonate solution and water, dried over magnesium sulfate, and evaporated. Crystallization of the residue from acetone–petroleum ether (b.p. 60–70°) gave 520 mg. (73%) of needles, darkening at 129–131° and having an infrared spectrum identical with that of the 9-bromo-1-ketone.

9-Bromo-2,3-dihydro-7-methoxy-6-methyl-1H-pyrrolo[1,2-*a*]indol-1-one (VIa) A.—A mixture of 0.855 g. (3.97 mmoles) of 2,3-dihydro-7-methoxy-6-methyl-1H-pyrrolo[1,2-*a*]indol-1-one (Va) and 100 ml. of acetic acid was heated on the steam bath until solution was effected. The solution was cooled to room temperature and treated with 2 drops of 48% hydrobromic acid solution. To this solution was added with magnetic stirring 5.4 ml. of 0.735 *M* bromine in acetic acid solution; the reaction immediately gave a negative starch–iodide test. The solution was chilled and slowly diluted with water until needles separated.

Filtration gave 0.753 g. (64%) of green needles of sufficient purity for further work. Several recrystallizations from acetone–petroleum ether (b.p. 60–70°) gave light green needles: m.p. >290°, but darkening from 125°; λ_{max} 221 and 330 mμ (ε 31,800 and 23,500); λ 5.90 and 6.50 μ; p.m.r.[20] τ 2.97 (C-5 proton), 3.26 (C-8 proton), 5.82 (triplet, C-3 methylene protons), 6.18 (methoxy protons), 6.94 (triplet, C-2 methylene protons), and 7.73 (C-6 methyl protons).

Anal. Calcd. for $C_{13}H_{12}BrNO_2$ (294.15): C, 53.08; H, 4.11; Br, 27.17; N, 4.76. Found: C, 53.24; H, 4.38; Br, 27.21; N, 5.00.

This same ketone was obtained when the bromination was carried out in the presence of sodium acetate.

B.—A slurry of 373 mg. (1.0 mmole) of 2,9-dibromo-2,3-dihydro-7-methoxy-6-methyl-1H-pyrrolo[1,2-*a*]indol-1-one (XIII, see below) in 15 ml. of boiling methanol was treated with 76 mg. (2.0 mmoles) of sodium borohydride; all solid dissolved immediately. After 45 min. at room temperature the solvent was removed from the solution, and the residue was distributed between methylene chloride and a 1% sodium hydroxide solution. The organic layer was evaporated, and the residue partially crystallized on trituration with acetone. This solid (alcohol XIV) began turning purple on standing at room temperature for about 5 min. It was dissolved in 15 ml. of methanol and treated with 750 mg. of potassium hydroxide on the steam bath for 1 hr. The product was isolated with methylene chloride and recrystallized from acetone–petroleum ether to give 95 mg. (32%) of needles which were identical with the product of method A.

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

Anal. Calcd. for $C_{13}H_{12}BrNO_2$: Br, 27.17. Found: Br, 26.94.

9-Bromo-2,3-dihydro-7-methoxy-6-methyl-1H-pyrrolo[1,2-*a*]indole (VII).—A mixture of 1.172 g. (4.0 mmoles) of 9-bromo-2,3-dihydro-7-methoxy-6-methyl-1H-pyrrolo[1,2-*a*]indol-1-one (VI), 720 mg. of potassium hydroxide pellets, and 0.44 ml. of hydrazine hydrate in 20 ml. of diethylene glycol was heated at 120–140° for 90 min. The cooled mixture was diluted with water and extracted with benzene. The combined extracts were passed through a Florisil[22] column, and the solid eluted by benzene in the first 500 ml. of eluate was recrystallized from petroleum ether to give 180 mg. (16%) of white needles which decomposed without melting at 93–95°: λ_{max} 289, 300, and 309 (sh) mμ (ε 8840, 8840, and 6740); λ 6.10, 6.30, 8.27, and 8.68 μ; p.m.r. (in carbon disulfide)[21] τ 3.28 (C-5 proton), 3.40 (C-8 proton), 6.25 (methoxy protons), 6.20 (triplet, J = 7 c.p.s., C-3 methylene protons), multiplet at 7.12–7.38 (C-1 methylene protons), multiplet at 7.38–7.72 (C-2 methylene protons), and 7.78 (C-6 methyl protons).

Anal. Calcd. for $C_{13}H_{14}BrNO$ (280.17): C, 55.73; H, 5.04; Br, 28.52; N, 5.00. Found: C, 55.69; H, 5.17; Br, 28.84; N, 5.26.

2,3-Dihydro-7-methoxy-6-methyl-1-oxo-1H-pyrrolo[1,2-*a*]indole-9-carbonitrile (VIII).—A solution of 1.178 g. (4.05 mmoles) of 9-bromo-2,3-dihydro-7-methoxy-6-methyl-1H-pyrrolo[1,2-*a*]indol-1-one (VI) and 1.30 g. (7.25 mmoles) of cuprous cyanide in 40 ml. of N-methylpyrrolidone was heated at reflux temperature for 18 hr. The dark solution was poured into a solution of 16 g. of ferric chloride in 28 ml. of water containing 4 ml. of concentrated hydrochloric acid solution. The solution was extracted several times with benzene, and the combined extracts were washed with 6 *N* hydrochloric acid solution and then 10% sodium hydroxide solution. Crystallization of the solid contained in the benzene solution from acetone–petroleum ether gave 254 mg. (26%) of solid, m.p. 227–230°. Two recrystallizations from the same solvent pair gave yellow needles: m.p. 229–230°; λ_{max} 218, 252 (sh), and 339 mμ (ε 37,500, 7450, and 19,000); λ 4.50, 5.80, 6.09, and 6.43 μ.

Anal. Calcd. for $C_{14}H_{12}N_2O_2$ (240.25): C, 69.99; H, 5.03; N, 11.66. Found: C, 69.97; H, 5.20; N, 11.58.

2,3-Dihydro-7-methoxy-6-methyl-1H-pyrrolo[1,2-*a*]indole-9-carbonitrile (IX). A.—A mixture of 183 mg. (0.76 mmole) of 2,3-dihydro-7-methoxy-6-methyl-1-oxo-1H-pyrrolo[1,2-*a*]indole-9-carbonitrile (VIII), 0.1 ml. of hydrazine hydrate, 140 mg. of potassium hydroxide pellets, and 5 ml. of diethylene glycol was heated at 120–140° for 90 min. The cooled mixture was diluted with water and extracted with several portions of benzene. The combined extracts were taken to dryness, and the residue was crystallized from methanol to give 20 mg. (11%) of white needles, m.p. 165–170°. This material was identical according to the usual criteria with that obtained in method B.

B.—A solution of 500 mg. (2.18 mmoles) of 2,3-dihydro-7-methoxy-6-methyl-1H-pyrrolo[1,2-*a*]indole-9-carboxaldehyde (X)[1] and 1.000 g. (4.45 mmoles) of O,N-bis(trifluoroacetyl)hydroxylamine in 25 ml. of benzene containing 0.5 ml. of pyridine was heated at reflux temperature for 3 hr. The cooled deep red solution was washed with water, dried, and passed through a Florisil[22] column. The column was washed with benzene, and the material eluted in the first 625 ml. of eluate was recrystallized from methanol to give 300 mg. (61%) of white needles, m.p. 170–172°. An additional recrystallization from methanol gave white needles: m.p. 173.0–173.5°; λ_{max} 278, 290, and 305 mμ (ε 9280, 9150, and 6670); λ 4.52, 6.11, 6.47, 8.06, and 9.60 μ; p.m.r.[21] τ 2.95 (C-5 and C-8 protons), 6.00 (triplet, J = 7 c.p.s., C-3 methylene protons), 6.10 (methoxy protons), multiplet at 6.75–7.25 (C-1 methylene protons), multiplet at 7.25–7.60 (C-2 methylene protons), and 7.70 (C-6 methyl protons).

Anal. Calcd. for $C_{14}H_{14}N_2O$ (226.27): C, 74.31; H, 6.24; N, 12.38. Found: C, 74.27; H, 6.52; N, 12.38.

7-Benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-*a*]indole-9-carbonitrile (XII).—A solution of 1.44 g. (4.05 mmoles) of 7-benzyloxy-9-bromo-2,3-dihydro-1H-pyrrolo[1,2-*a*]indol-1-one (VIb) in 40 ml. of N-methylpyrrolidone was treated with 1.30 g. (7.25 mmoles) of cuprous cyanide as described above. The product was recrystallized from acetone–hexane to give 74 mg. (6%) of pale yellow crystals: m.p. 224–226°; λ_{max} 219, 255, and 328 mμ (ε 48,800, 13,600, and 19,600); λ 4.53, 5.85, 6.18, 6.47, 8.16, 8.64, 9.35, and 14.25–14.40 μ.

Anal. Calcd. for $C_{19}H_{14}N_2O_2$(302.32): C, 75.48; H, 4.67; N, 9.27. Found: C, 75.74; H, 4.86; N, 9.55.

7-Benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-a]indole-9-carboxaldehyde (XI).—To a magnetically stirred solution of 19 mg. (0.5 mmole) of lithium aluminum hydride in 20 ml. of ether was added 66 mg. (0.75 mmole, 0.07 ml.) of ethyl acetate at ice-bath temperature. A solution of 151 mg. (0.5 mmole) of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-a]indole-9-carbonitrile (XII) in 15 ml. of ether was then added, and the reaction was stirred at 0° for 1 hr. Methanol was added, and the reaction was distributed between methylene chloride and water. The material isolated from the organic layer was crystallized from ethanol to give 17 mg. (11%) of tan crystals, m.p. 194–196° (lit.[2] m.p. 194–197°). This material was identical with an authentic specimen[2] according to the usual criteria.

2,9-Dibromo-2,3-dihydro-7-methoxy-6-methyl-1H-pyrrolo-[1,2-a]indol-1-one (XIII).—A solution of 0.500 g. (2.33 mmoles) of 2,3-dihydro-7-methoxy-6-methyl-1-oxo-1H-pyrrolo[1,2-a]indole in 50 ml. of acetic acid containing 2 drops of 48% hydrobromic acid was treated with magnetic stirring with 6.45 ml. of 0.726 *M* bromine in acetic acid solution. After 5 min. the reaction gave a negative starch–iodide test. Dilution with water gave 0.601 g. (69%) of orange solid, m.p. >270°. One recrystallization from acetone–petroleum ether (b.p. 60–70°) gave the analytical specimen: λ_{max} 219, 249 (sh), and 343 mμ (ε 29,100, 9710 and 19,400); λ 5.84, 6.11, 6.50, 8.24, and 6.64 μ.

Anal. Calcd. for $C_{13}H_{11}Br_2NO_2$ (373.06): C, 41.85; H, 2.97; Br, 42.84; N, 3.76. Found: C, 41.84; H, 3.08; Br, 43.00; N, 3.83.

7-Benzyloxy-1-(N-pyrrolidino)-3H-pyrrolo[1,2-a]indole (XV).—A solution of 5.840 g. (20 mmoles) of 7-benzyloxy-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-one (Vb), 200 mg. of *p*-toluenesulfonic acid hydrate, and 5.68 g. (80 mmoles, 6.7 ml.) of pyrrolidine in 250 ml. of benzene was heated at reflux temperature for 2 hr., the water being collected in a modified Dean–Stark apparatus. The solvents were removed from the cooled solution, and the residue was slurried with methanol and filtered to give 5.930 g. (90%) of golden plates, m.p. 154–157° dec. A sample for analysis was recrystallized three times from ethyl acetate to give golden plates: m.p. 151–154° dec.; λ_{max} 315 and 342 mμ (ε 14,100 and 11,900); λ 6.15, 6.25, and 6.35 μ. In the ultraviolet spectrum of this substance the 315-mμ peak is probably due to the corresponding ketone Vb, for this enamine was found to undergo facile hydrolysis in the methanol used for these spectra. The above spectrum was determined immediately after preparation of the solution; after the solution stood 30 min., the spectrum was identical with that of the parent ketone.

Anal. Calcd. for $C_{22}H_{22}N_2O$ (330.41): C, 79.97; H, 6.71; N, 8.48. Found: C, 79.46; H, 6.48; N, 8.40.

7-Benzyloxy-2-bromo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-one (XVII).—An ice-chilled magnetically stirred suspension of 7.950 g. (24 mmoles) of 7-benzyloxy-1-(N-pyrrolidino)-3H-pyrrolo[1,2-a]indole (XV) in 200 ml. of peroxide-free tetrahydrofuran was treated with 3.400 g. (24.6 mmoles) of N-bromoacetamide. All solid dissolved immediately and an aliquot gave a negative starch–iodide test after a few minutes. Water (200 ml.) containing 1 ml. of 48% hydrobromic acid solution was added; the oil that separated crystallized after the mixture was stirred at ice-bath temperature for 30 min. The crude solid (7.439 g.) was dissolved in benzene and passed through a Florisil[22] column (2.8 × 28 cm.), additional benzene being used for elution. The first liter of eluate was taken to dryness to give 3.733 g. (44%) of yellow crystals, m.p. 190–192° dec. Material from a similar experiment was recrystallized twice from acetone–petroleum ether (b.p. 60–70°) to give yellow crystals: m.p. 193–195° dec.; λ_{max} 215, 255 and 335 mμ (ε 33,200, 8900, and 18,500); λ 5.80, 6.12, 6.47, 8.30, 9.31, and 14.25 μ.

Anal. Calcd. for $C_{18}H_{14}BrNO_2$ (356.22): C, 60.68; H, 3.96; Br, 22.44; N, 3.94. Found: C, 60.60; H, 4.22; Br, 22.37; N, 4.16.

7-Benzyloxy-2-bromo-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-a]indole (XVI).[9]—A suspension of 356 mg. (1.0 mmole) of 7-benzyloxy-2-bromo-2,3-dihydro-1-oxo-1H-pyrrolo-[1,2-a]indole (XVII) in 75 ml. of boiling ethanol was reduced with 76 mg. (2.0 mmoles) of sodium borohydride in the usual manner. The product was isolated with methylene chloride and recrystallized from acetone-petroleum ether (b.p. 60–70°) to give white crystals which decomposed above 121°: λ_{max} 278, 297, and 305 (sh) mμ (ε 10,100, 4650, and 3220); λ 2.78, 6.17, 6.36, 6.49, 14.11, and 14.40 μ.

Anal. Calcd. for $C_{18}H_{16}BrNO_2$ (358.23): C, 60.34; H, 4.51; Br, 22.30; N, 3.91. Found: C, 61.62; H, 5.10; Br, 20.18; N, 4.08.

A solution of 333 mg. (0.93 mmole) of this crude bromo alcohol was dissolved in 15 ml. of methanol and heated on the steam bath with 54 mg. (1.0 mmole) of sodium methoxide for 30 min. A yellow solid began separating within a few minutes. The cooled mixture was filtered to give 156 mg. of this solid: λ_{max} 5.83, 5.92, 6.09, 6.50, 8.20, 8.30, and 14.35 μ.

The filtrate was distributed between methylene chloride and water, and the material recovered from the organic solution was recrystallized from acetone–petroleum ether (b.p. 60–70°) to give 120 mg. (47%) of 7-benzyloxy-2,3-dihydro-1H-pyrrolo-[1,2-a]indol-1-one (Vb), m.p. 193–196°.

7-Benzyloxy-2,3-dihydro-1-hydroxy-1H-pyrrolo[1,2-a]indole.—A mixture of 2.77 g. (10 mmoles) of 7-benzyloxy-2,3-dihydro-1-oxo-1H-pyrrolo[1,2-a]indole (Vb) and 250 ml. of ethanol was heated to reflux temperature. The hot suspension was treated with 0.756 g. (20 mmoles) of sodium borohydride; all solids immediately dissolved. The solution was heated at reflux temperature for 2 min. and then left at room temperature for 1 hr. The solvent was removed, and the residue was distributed between 1% sodium hydroxide solution and methylene chloride. The organic layer was dried over magnesium sulfate and taken to dryness. The residue was recrystallized from acetone–petroleum ether with the aid of activated charcoal to give 1.84 g. (66%) of crystals, m.p. 121–124°. Several recrystallizations from ether–petroleum ether (b.p. 60–70°) and then benzene–petroleum ether gave needles: m.p. 122.0–123.5°; λ_{max} 278, 298 (sh), and 310 (sh) mμ (ε 10,700, 6150, and 4110); λ 2.98, 6.13, 6.33, 6.43, and 8.50 μ.

Anal. Calcd. for $C_{18}H_{17}NO_2$ (279.32): C, 77.39; H, 6.13; N, 5.01. Found: C, 77.16; H, 6.31; N, 5.01.

2,3-Dihydro-1-hydroxy-7-methoxy-6-methyl-1H-pyrrolo[1,2-a]-indole.—A solution of 500 mg. (2.32 mmoles) of 2,3-dihydro-7-methoxy-6-methyl-1-oxo-1H-pyrrolo[1,2-a]indole (Va) in 50 ml. of ethanol was treated with 181 mg. (4.64 mmoles) of sodium borohydride as described in the above preparation. The product was isolated with methylene chloride and recrystallized three times from benzene–petroleum ether to give 313 mg. (62%) of white crystals: m.p. 143–145°; λ_{max} 280, 298 (sh), and 308 (sh) mμ (ε 8700, 6530, and 4350); λ 2.85, 6.11, and 6.45 μ.

Anal. Calcd. for $C_{13}H_{15}NO_2$ (217.26): C, 71.86; H, 6.96; N, 6.45. Found: C, 72.08; H, 7.06; N, 6.62.

2,3-Dihydro-7-hydroxy-1-(N-pyrrolidino)-1H-pyrrolo[1,2-a]-indole (XVIII).—A mixture of 5.500 g. (16.7 mmoles) of 7-benzyloxy-1-(N-pyrrolidino)-3H-pyrrolo[1,2-a]indole (XV) and 1.00 g. of 10% palladium-on-charcoal catalyst in 200 ml. of ethyl acetate was shaken under an atmosphere of hydrogen until no further pressure drop in the system was observed. The mixture was filtered, and the residue was washed with several portions of boiling acetone. The combined filtrate and washings were taken to dryness, and the solid residue was slurried with 50 ml. of acetone and collected by filtration to give 2.802 g. (70%) of needles, m.p. 220–223° dec. Two recrystallizations from ethyl acetate furnished white needles: m.p. 227–228°; λ_{max} 278, 302 (sh), and 312 (sh) mμ (ε 8970, 4380, and 3640); λ 3.34–3.80, 6.14, 6.30, and 6.48 μ.

Anal. Calcd. for $C_{15}H_{13}N_2O$ (242.31): C, 74.35; H, 7.49; N, 11.56. Found: C, 73.98; H, 7.67; N, 11.58.

Treatment of 2,3-Dihydro-7-hydroxy-1-(N-pyrrolidino)-1H-pyrrolo-[1,2-a]indole (XVIII) with Acetic Anhydride.—A solution of 1.500 g. (6.18 mmoles) of XVIII in 5 ml. of acetic anhydride was heated at steam-bath temperature for 4 hr. The excess acetic anhydride was removed, and the residue was triturated with acetone. The resulting solid was recrystallized from methylene chloride–methanol to give 125 mg. of white needles: m.p. >270°; λ_{max} 234 and 292 mμ (ε 28,200 and 6550); λ 5.70, 6.08, 6.40, 8.28, and 8.95 μ; the p.m.r. spectrum[20] of this material showed singlets at τ 7.72, 7.76, and 7.79 which comprised approximately 27% of the proton resonances by integration.

Anal. Found: C, 71.68, 71.82; H, 5.50, 5.90; N, 6.40.

1-(2,3-Dihydro-7-hydroxy-1H-pyrrolo[1,2-a]indol-1-yl)-1-methylpyrrolidinium Iodide.—A solution of 484 mg. (2.0 mmoles) of 2,3-dihydro-7-hydroxy-1-(N-pyrrolidino)-1H-pyrrolo[1,2-a]indole (XVIII) and 15 ml. of methyl iodide in 50 ml. of methanol was kept in the dark at room temperature for 18 hr. The solution was taken to dryness; addition of acetone to the residue induced crystallization. Filtration gave 0.677 g. (88%) of crystals,

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.

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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.

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