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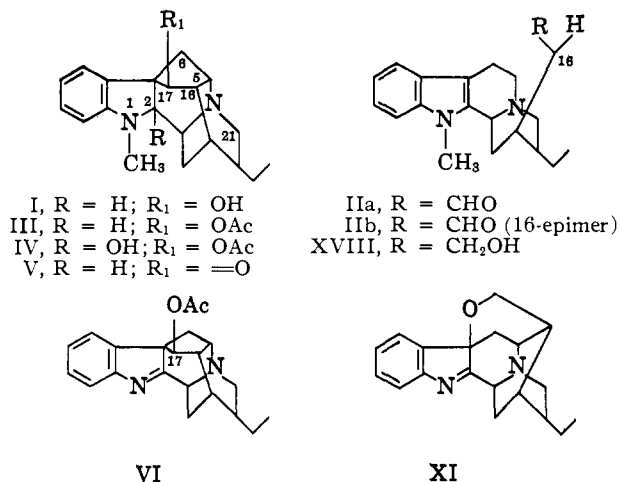
## Rauwolfia Alkaloids.<sup>1</sup> XLVIII. The Oxidative Demethylation and Rearrangement of Some Ajmaline Derivatives

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Lead tetraacetate, in excess, was the reagent of choice for the oxidative demethylation of certain ajmaline derivatives to their corresponding 1-demethyl- $\Delta^1$  compounds (indolenines, *e.g.*, VI). With 1 mole equivalent of the oxidant, the 2-hydroxy derivatives (*e.g.*, IV) were produced. 21-Deoxyajmalone (V) upon oxidation gave, according to the conditions, either the indoline-lactone VII (possibly IX), or the indole-lactone XII, whereas 21-deoxyajmalol-A furnished the ethers VIII (possibly X) and XI. The two latter compounds rearranged under acidic conditions to furnish the indole-ethers XIII and XIV, respectively.

21-Deoxyajmaline (I) has been shown to be susceptible to a number of oxidizing agents with fission of the cyclopentanol moiety to generate the indole-aldehydes, 21-deoxyajmalal-A (IIa) and its 16-epimer, 21-deoxyajmalal-B (IIb).<sup>2,3</sup> If the 17-hydroxyl was removed or blocked, as for example in the O-acetate III, oxidation (chromic oxide in pyridine) occurred in the environment of N<sub>1</sub> to furnish the 2-hydroxy compound IV or the 1-demethyl- $\Delta^1$  derivative VI, both of which upon hydrolysis gave the corresponding indole-aldehydes, 21-deoxyajmalal-B (IIb) and its 1-demethyl derivative, respectively.<sup>3</sup>



Since then, the possible use of other oxidants has been examined, among which were tetranitromethane and lead tetraacetate. The former reagent converted 21-deoxyajmaline (I) into the indole-aldehydes IIa and b, and the O-acetate III gave the 2-hydroxy derivative IV. Lead tetraacetate, however, at room temperature proved to be a more convenient and efficient oxidant than the others which were examined. It converted 21-deoxyajmaline O-acetate into IV with 1 mole equivalent and into VI with an excess. Satisfactory solvents for the reaction were nonpolar ones, such as chloroform, methylene chloride, acetic anhydride, or benzene, the latter being most generally used. As further examples of the usefulness of the method, 21-deoxyajmaline 17-epi-O-acetate, dideoxyajmaline, and diacetyljmaline and diacetylisoajmaline were oxidized into their corresponding 2-hydroxy or indolenine equivalents, depending on the amount of lead tetraacetate used. In the case of the diacetylisoajmaline derivatives, hydrolysis of the 21-O-acetates was noted, which made available also the 17-monoacetates.

(1) Preceding paper, part XLVII: N. Finch, W. I. Taylor, and P. R. Ulshafer, *Experientia*, **19**, 296 (1963).

(2) R. B. Woodward and K. Schenker, *Angew. Chem.*, **68**, 13 (1956).

(3) M. F. Bartlett, R. Sklar, W. I. Taylor, E. Schlittler, R. L. S. Amal, P. Beak, N. V. Bringi, and E. Wenkert, *J. Am. Chem. Soc.*, **84**, 622 (1962):

These and similar lead tetraacetate oxidations are thought to be initiated by an electrophilic attack of the lead triacetate cation,<sup>4</sup> the reaction course being dependent on which of the nucleophilic centers of the molecule being oxidized is the most susceptible to subsequent decomposition. No apparent reaction occurs about the strongest nucleophilic center (N<sup>b</sup>) because of the unfavorable stereochemical situation of the nitrogen at the bridgehead of a bicyclo[2.2.2] system. When the 17-hydroxyl is blocked, the lead triacetate cation can only attack the indoline nitrogen and easily the unhindered side, which is also *cis* to the C<sub>2</sub>-proton. Collapse of this complex with concomitant removal of the *cis* standing C<sub>2</sub>-proton leads to an intermediate indoleninium ion (equivalent to an isolated product, *e.g.* IV), rather than an alternative path in which one of the three protons of the N-methyl are detached.<sup>5</sup>

No attempt was made to determine the fate of the N-methyl which was removed by oxidation with excess reagent, although the sequence N-CH<sub>3</sub> → CH<sub>2</sub>O → HCOOH → CO<sub>2</sub> seems reasonable.<sup>6</sup>

When 21-deoxyajmalone (V) was subjected to the action of lead tetraacetate, the reaction went differently from what might have been expected from the results obtained above. An indole, C<sub>20</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub> ( $\nu_{C=O}$  1751 cm.<sup>-1</sup>), was isolated quite different from the N-methylindoline, C<sub>20</sub>H<sub>24</sub>N<sub>2</sub>O<sub>3</sub> ( $\nu_{C=O}$  1733 cm.<sup>-1</sup>), obtained when chromic acid in pyridine was the oxidant. The relationship between the two compounds was established by the acid-catalyzed conversion of the indoline into the indole. Undoubtedly, in the original lead tetraacetate oxidation, the ambient acidity was sufficient to rearrange the primary oxidation product, the indoline, into the isolated indole. Taking into account our previous findings and attributing the observed carbonyl absorptions to the presence of lactone moieties, structures VII<sup>7</sup> and XII were considered plausible for the indoline ( $\delta$ -lactone) and the indole (*cis*- $\gamma$ -lactone<sup>8</sup>), respectively. The p.m.r. spectrum<sup>9</sup>

(4) R. Criegee, *Angew. Chem.*, **70**, 173 (1958); "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, p. 1.

(5) The analogous and very efficient oxidation of simple N,N-dialkyl-anilines is on record [L. Horner, E. Winkelmann, K. H. Knapp, and W. Ludwig, *Ber.*, **92**, 288 (1959)], but here the reaction is carried out in acetic anhydride, which by N-acetylation traps the monodemethylated compound in a form stable to further oxidation. In the case of the ajmaline derivatives, however, substitution of benzene for acetic anhydride as the solvent did not alter the course of the reaction; *i.e.*, N-demethylation was observed only after oxidation at C-2.

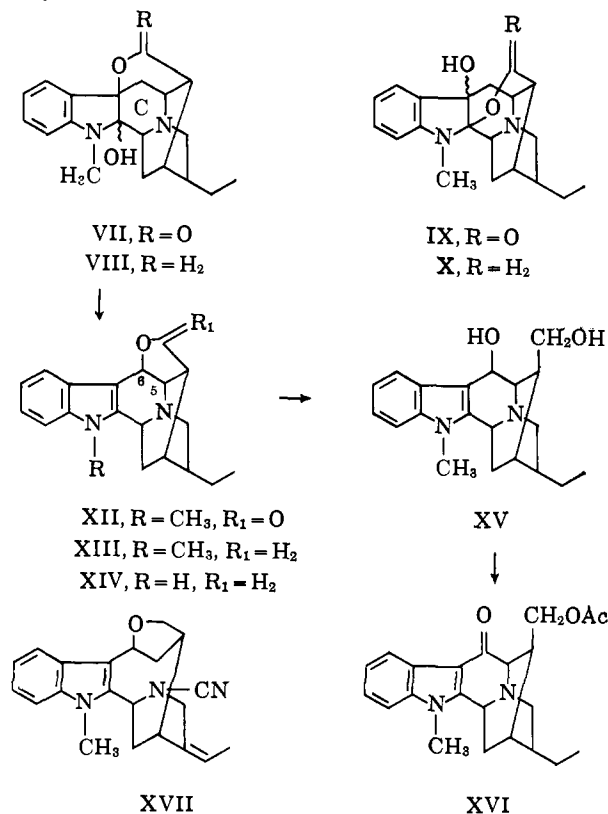
(6) Cf. R. Criegee, "Newer Methods of Preparative Chemistry," Vol. II, Academic Press, Inc., New York, N. Y., 1963, p. 369.

(7) An alternative structure IX cannot be eliminated with certainty on the basis of the evidence presented in this paper. It should be noted, however, that its formation would require that ring C be constrained in the more compressed boat form in the face of other strain-free alternatives. A similar argument might well be valid in preferring VIII over X.

(8) The observed value,  $\nu_{C=O}^{solid}$  1751 cm.<sup>-1</sup>, was in good agreement with that found for the lactone of *cis*-2-hydroxycyclohexanecetic acid,  $\nu_{C=O}^{liquid film}$  1754 cm.<sup>-1</sup>, which is at 25 cm.<sup>-1</sup> lower than that of the corre-

of the indole was in agreement with structure XII, there being a one-proton doublet centered at 6.08 p.p.m.,  $J = 9$  c.p.s., *viz.*, the C<sub>6</sub>-proton coupled to the C<sub>5</sub>-proton.<sup>10</sup>

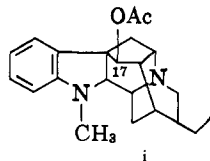
The correctness of the above conclusions as far as XII is concerned was established by its lithium aluminum hydride reduction to the diol XV, which after monoacetylation and oxidation gave a compound whose spectral properties were consistent with the expected 3-acetylindole (XVI).



A second example of the creation of a five-membered oxygen heterocyclic ring terminating at C-6 came out of a study of the lead tetraacetate oxidation of 21-deoxyajmalol-A (XVIII). In this case the primary oxidation product appeared to be the indoline VIII (or possibly X<sup>7</sup>), which was accompanied by its further oxidation product XI.<sup>11</sup> Treatment of either VIII or XI with strong acid gave the rearranged ethers XIII and XIV, respectively. The p.m.r. spectrum of sponding *trans* isomer [J. H. Brewster and C. H. Kucera, *J. Am. Chem. Soc.*, **77**, 4564 (1955)].

(9) Measured on a Varian A60 in deuteriochloroform with tetramethylsilane as internal reference.

(10) These values are almost identical with those observed for another derivative of ajmaline which contains a singlet proton in a very similar stereochemical environment, *viz.*, the C<sub>17</sub>-proton (doublet centered at 5.70 p.p.m.,  $J = 8.9$  c.p.s.) in 21-deoxyajmaline 17-*epi*-O-acetate (i) (ref. 3).



(11) The reaction probably proceeds *via* the formation of a lead triacetate alcoholate, followed by attack of the vicinal nucleophilic  $\beta$ -position of the indolic moiety to generate the indolinium ether (*cf.* a mechanistically related ring closure of deoxyajmalal-A to deoxyajmaline [M. F. Bartlett, B. F. Lambert, H. M. Werblood, and W. I. Taylor, *J. Am. Chem. Soc.*, **85**, 475 (1963)]). This view is preferred over an alternative in which the indolic system is attacked first by the lead triacetate cation and displaced by the vicinal hydroxymethyl group because under the conditions used for this oxidation 10-deoxydihydrosarpagine is unaffected [*cf.* facile oxidation of the yohimbinoindole ring system: N. Finch and W. I. Taylor, *J. Am. Chem. Soc.*, **84**, 3871 (1962); **85**, 1520 (1963)].

XIII showed the expected characteristic doublet at 5.74 p.p.m.,  $J = 8$  (XIV could not be run as it was insoluble in deuteriochloroform)

In view of the facile formation of such 6-oxygenated systems, *e.g.*, XII, such compounds may well turn up as natural products, but up until now no examples have been recognized. The only substances related to naturally-occurring alkaloids which have an oxygen at C-6 or its equivalent have been an oxidation product of ibogaine,<sup>12</sup> and the cyanogen bromide degradation product (XVII) of voachalotine.<sup>13</sup>

### Experimental

Melting points were taken in evacuated capillaries and are uncorrected. Analytical samples were routinely dried at 80° for 12 to 24 hr. *in vacuo*, the optical rotations were measured in methanol, the ultraviolet absorption spectra are expressed in  $m\mu$  ( $\epsilon$ ), and infrared absorption spectra were run in Nujol. Neutral alumina, activity III, was generally used for chromatography, and sodium sulfate was the drying agent for the organic solvent extractions.

**Lead Tetraacetate Oxidation of 21-Deoxyajmaline 17-O-Acetate.** (a).—Acetyldeoxyajmaline (500 mg.) in benzene (20 ml.) was treated with lead tetraacetate (760 mg.). After 70 min. of stirring at room temperature, the solution was washed with water. The separated aqueous phase was adjusted to pH 7 with sodium hydroxide, filtered, and extracted with methylene chloride, yielding amorphous 2-hydroxy-21-deoxyajmaline 17-O-acetate (IV)<sup>3</sup> (100 mg.), containing a small amount of the indoline VI.

(b).—21-Deoxyajmaline (1.00 g.) was refluxed for 30 min. with acetic anhydride, cooled, treated with lead tetraacetate (1.57 g.), and stirred at room temperature for 1 hr. The solution was filtered, evaporated to dryness, and the residue filtered through alumina (30 by 40 mm.) with benzene (150 ml.) and methylene chloride (200 ml.), eluting material (950 mg.) which was chromatographed on basic alumina (22 by 65 mm.). Elution with 1:1 benzene-hexane (100 ml.), benzene (100 ml.), and 1:1 benzene-methylene chloride (100 ml.) gave material (760 mg.) identified as mainly 2-hydroxy-21-deoxyajmaline 17-O-acetate (IV). For analysis a sample was crystallized from ether-hexane and had m.p. 85–95°,  $[\alpha]_D -98^\circ$ .

*Anal.* Calcd. for C<sub>22</sub>H<sub>28</sub>N<sub>2</sub>O<sub>3</sub>: C, 71.71; H, 7.66. Found: C, 71.72; H, 7.46.

(c).—Lead tetraacetate (100 g.) was added to acetyldeoxyajmaline (18.8 g.) in benzene (1500 ml.) and stirred for 1 hr. The solution was filtered through a column of alumina (80 by 70 mm.), and the material (18.1 g.) eluted with benzene (2400 ml.) and crystallized from ether, yielding 1-demethyl- $\Delta^1$ -21-deoxyajmaline 17-O-acetate (VI) (9.39 g.), m.p. 171–176°. An additional quantity (2.40 g.), m.p. 175–179°, was obtained by chromatography of the mother liquors.

**Lead Tetraacetate Oxidation of 2-Hydroxy-21-deoxyajmaline 17-O-Acetate (IV).**—Lead tetraacetate (32.4 g.) was added to 2-hydroxy-21-deoxyajmaline 17-O-acetate (8.07 g.) in benzene (300 ml.) and stirred at room temperature for 20 min. The solution was chromatographed directly on alumina (38 by 120 mm.), eluting crude 1-demethyl- $\Delta^1$ -21-deoxyajmaline 17-O-acetate (VI) (5.92 g.) with 4:1 benzene-methylene chloride (500 ml.). It crystallized from ether and had m.p. 182–183° (yield 3.04 g.).

**Lead Tetraacetate Oxidation of 21-Deoxyajmaline 17-Epi-O-acetate.**—Deoxyajmaline 17-*epi*-O-acetate (2.22 g.) was oxidized with lead tetraacetate (11.73 g.), according to procedure c above. The yield of 1-demethyl- $\Delta^1$ -21-deoxyajmaline 17-*epi*-O-acetate (C<sub>17</sub>-epimer of VI) was 630 mg., m.p. 206–207°. The indolenine was also obtained by oxidation of 2-hydroxy-21-deoxyajmaline 17-*epi*-O-acetate (990 mg.) with substantially less lead tetraacetate (3.74 g.) in the same way.

**Oxidation of 21-Deoxyajmaline with Tetranitromethane.**—Deoxyajmaline (492 mg.), anhydrous ethanol (50 ml.), tetranitromethane (612 mg.), and pyridine (372 mg.) were refluxed overnight. The solvent was partially removed, and the concentrate was extracted with dilute sulfuric acid and methylene chloride. After making the acidic solution basic and extracting with methylene chloride, the crude deoxyajmalal-A (500 mg.) was purified by chromatography on alumina. The material (130 mg.) eluted with 1:1 benzene-methylene chloride gave pure 21-deoxyajmalal-A (IIa), m.p. 169–170°.

**Oxidation of 21-Deoxyajmaline 17-O-Acetate with Tetranitromethane.**—Tetranitromethane (600 mg.) in absolute ethanol (2 ml.) was added to acetyldeoxyajmaline (540 mg.) in absolute ethanol (50 ml.) and pyridine (0.24 ml.). After standing at

(12) M. F. Bartlett, D. F. Dickel, and W. I. Taylor, *ibid.*, **80**, 126 (1958).

(13) J. Pecher, International Symposium on the Chemistry of Natural Products, Brussels, June 12, 1962; M. Kaisin, *Ind. Chim. Belge*, **28**, 640 (1963).

room temperature for 10 min., the solution was evaporated to dryness. The residue was chromatographed on alumina (18 by 105 mm.), eluting crude starting material (230 mg.) with 1:1 benzene-methylene chloride (200 ml.) and 2-hydroxy-21-deoxyajmaline 17-O-acetate (IV) (190 mg.) with 1% methanol-methylene chloride (200 ml.).

**Lead Tetraacetate Oxidation of Diacetyljmaline.**—Lead tetraacetate (19.2 g.) was added to diacetyljmaline (4.27 g.) in benzene (150 ml.) and worked up in a manner analogous to the above examples to yield 1-demethyl- $\Delta^1$ -ajmaline 17,21-O,O-diacetate (1.14 g.), m.p. 160–161°, from ether,  $[\alpha]_D +22^\circ$ .

*Anal.* Calcd. for  $C_{23}H_{28}N_2O_4$ : C, 70.03; H, 6.64. Found: C, 70.24; H, 6.71.

When this reaction was repeated using 10.27 g. of diacetyljmaline, followed by careful chromatography of the reaction product on alumina, 1-demethyl- $\Delta^1$ -ajmaline 17,21-O,O-diacetate (2.28 g.), m.p. 164–165°, was isolated from the methylene chloride eluate, and 1-demethyl- $\Delta^1$ -ajmaline 17-O-acetate<sup>14</sup> (3.01 g.), m.p. 230–240°, was obtained by crystallization of the 1% methanol-methylene chloride eluate from ethyl acetate. A sample was recrystallized from ethyl acetate for analysis; m.p. 240–242°,  $[\alpha]_D +19^\circ$ .

*Anal.* Calcd. for  $C_{21}H_{24}N_2O_3$ : C, 71.57; H, 6.86. Found: C, 71.54; H, 7.00.

**Lead Tetraacetate Oxidation of Diacetyloajmaline.**—Diacetyloajmaline (14.0 g.) was oxidized with lead tetraacetate (21.6 g.) as described in the preceding procedures. The benzene and methylene chloride eluates contained a mixture of indolic and indoleninic compounds and were not investigated further. The 2 and 4% methanol-methylene chloride eluates (1000 ml.) yielded a residue (4.68 g.) which crystallized from ether, yielding 1-demethyl- $\Delta^1$ -isoajmaline 17-O-acetate (2.28 g.), m.p. 222–230°, increasing to 242–243° on recrystallization from ethanol-ether;  $[\alpha]_D -22^\circ$ .

*Anal.* Calcd. for  $C_{21}H_{24}N_2O_3$ : C, 71.57; H, 6.86. Found: C, 71.27; H, 6.99.

**Lead Tetraacetate Oxidation of Dideoxyajmaline.** (a).—Lead tetraacetate (1.73 g.) was added to dideoxyajmaline (1.05 g.) in benzene (60 ml.) and stirred at room temperature. The product was worked up as described in procedure c (above) to afford 2-hydroxydideoxyajmaline (260 mg.), m.p. 87–89°.<sup>3</sup>

(b).—Lead tetraacetate (12.80 g.) was added to dideoxyajmaline (2.12 g.) in benzene (100 ml.), stirred at room temperature for 1.5 hr., and worked up as before to furnish 1-demethyl- $\Delta^1$ -dideoxyajmaline (480 mg.), m.p. 188–189°.<sup>3</sup>

**Lead Tetraacetate Oxidation of 21-Deoxyajmalone.**—Deoxyajmalone (500 mg.) in benzene (50 ml.) was stirred for 2 hr. at room temperature with lead tetraacetate (3.57 g.). The solution was filtered through alumina (19 by 76 mm.) and gave a product (470 mg.) from the 1:1 benzene-methylene chloride eluate (300 ml.). This was rechromatographed on a column of alumina (10 by 110 mm.), and the substance (210 mg.) eluted with benzene crystallized from methanol-ether, yielding the indole-lactone XII (130 mg.), m.p. 218–221°, increasing to 226–228° upon recrystallization from methylene chloride-cyclohexane;  $[\alpha]_D +73.1^\circ$ ;  $\lambda_{max}$  223 (35,400), 280 (6,700), and 289 (6,300);  $\nu_{C=O}$  1751  $cm^{-1}$ .

*Anal.* Calcd. for  $C_{20}H_{22}N_2O_2$ : C, 74.51; H, 6.88; N, 8.69. Found: C, 74.44; H, 6.95; N, 8.73.

**Chromium Trioxide Oxidation of 21-Deoxyajmalone.**—Deoxyajmalone (1.57 g.) in pyridine (21 ml.) was added to chromium trioxide (2.0 g.) in pyridine (30 ml.) and stirred for 2 days. The reaction mixture was filtered through sintered glass, the precipitate was washed with pyridine and 5% methanol in methylene chloride, and the combined filtrates were evaporated to dryness. The residue (1.43 g.) was chromatographed on alumina (36 by 100 mm.). The material (320 mg.) eluted with 3:1 benzene-methylene chloride (400 ml.) crystallized from methylene chloride-ether, yielding the indole-lactone XII (260 mg.), m.p. 150–160°, increasing to 226–228° on successive recrystallizations from methylene chloride-cyclohexane.

The material (560 mg.) eluted with 1:1 benzene-methylene chloride (600 ml.) crystallized from methylene chloride-ether, yielding the 2-hydroxy lactone VII (420 mg.), m.p. 110–120°. On recrystallization it melted with foaming at 110–120°, resolidifying and remelting at 160°,  $\lambda_{max}$  245 (9,900) and 295 (2,700),  $\nu_{C=O}$  1735  $cm^{-1}$ .

*Anal.* Calcd. for  $C_{20}H_{24}N_2O_3$ : C, 70.56; H, 7.11; N, 8.23. Found: C, 70.77; H, 7.12; N, 8.11.

When the lactone VII (11 mg.) was dissolved in 6 *N* hydrochloric acid (2 ml.), it gave a solution with a typically indolic ultraviolet absorption spectrum. If the solution was heated on a steam bath for a few minutes, cooled, made basic with ammonium hydroxide, and extracted with methylene chloride, it furnished the indole-lactone XII.

(14) This derivative was found to be identical in all respects with a hydrogenation product of vomilenine [W. I. Taylor, A. J. Frey, and A. Hofmann, *Helv. Chim. Acta*, **45**, 611 (1962)].

**Reduction of the Indole-Lactone XII.**—The indole-lactone (716 mg.) was extracted *via* a soxhlet apparatus into lithium aluminum hydride (2.5 g.) in dry tetrahydrofuran (80 ml.) for 18 hr. After decomposing the excess hydride with water, the mixture was filtered, the residue was washed with methylene chloride-methanol, and the filtrates were evaporated to dryness to afford a product (670 mg.), which was subjected to chromatography on alumina. The crude diol XV (354 mg.) was obtained from the 0.5% methanol in methylene chloride eluate. Without further purification the diol (325 mg.) was refluxed in acetic acid (25 ml.) for 3 hr. The resultant crude monoacetate, 360 mg.,  $\nu_{C=O}$  1730  $cm^{-1}$ , was dissolved in pyridine (20 ml.) and added to chromium trioxide (2.3 g.) in pyridine (20 ml.) and stirred at room temperature for 40 hr. The solution was filtered through alumina with 5% methanol in methylene chloride, yielding a residue (300 mg.). This was chromatographed over alumina and gave from the methylene chloride eluate the ketone XVI (42 mg.), m.p. 146–147° from ether;  $\nu_{C=O}$  1735, 1658  $cm^{-1}$ ;  $\lambda_{max}$  246 (20,200), 267 (11,500), and 306 (13,000);  $\lambda_{min}$  229 (4,880), 257 (10,700), and 278 (6,200).<sup>15</sup>

*Anal.* Calcd. for  $C_{22}H_{26}N_2O_3 \cdot 0.5H_2O$ : C, 70.32; H, 7.25. Found: C, 70.67; H, 7.04.

**Lead Tetraacetate Oxidation of 21-Deoxyajmalol-A.** (a).—Deoxyajmalol-A (444 mg.) in benzene (25 ml.) was stirred at room temperature for 2 hr. with lead tetraacetate (1.26 g.), then chromatographed on alumina. The material (237 mg.) eluted with 1:1 benzene-methylene chloride (100 ml.) crystallized from ether, yielding the 2-hydroxyindoline ether (VIII),<sup>7</sup> which melted indefinitely below 70°,  $\lambda_{max}^{HCl}$  236 (6,100), 241 (5,800), and 304–310 (3,700).

*Anal.* Calcd. for  $C_{20}H_{26}N_2O_2 \cdot 0.25H_2O$ : C, 72.60; H, 8.21. Found: C, 72.77; H, 8.30.

A sample of the free base (200 mg.) was dissolved in methanol and filtered through a column of Amberlite CG-45 ( $Cl^-$ ). The resultant hydrochloride was recrystallized from methanol-ether; m.p. 229–230°.

*Anal.* Calcd. for  $C_{20}H_{26}N_2O_2 \cdot HCl \cdot 0.25H_2O$ : C, 65.37; H, 7.54. Found: C, 65.38; H, 8.06.

(b).—Deoxyajmalol-A (1.13 g.) in benzene (50 ml.) was stirred for 80 min. with lead tetraacetate (3.24 g.), and then the solution was filtered through a column of alumina (28 by 60 mm.). The column was washed with benzene (200 ml.), 1:1 benzene-methylene chloride (200 ml.), and methylene chloride (100 ml.), eluting in all 860 mg. of substance. This was rechromatographed on alumina (22 by 90 mm.), using 1:1 hexane-benzene (300 ml.) as the developer. The material eluted with benzene (600 ml.) crystallized from ether-methylene chloride, yielding 166 mg. of the indolenine ether XI, m.p. 200–201°, increasing to 203–204° after recrystallization from ether-methylene chloride;  $[\alpha]_D -203^\circ$  ( $CHCl_3$ ),  $\lambda_{max}$  220 (23,600) and 260 (3,700).

*Anal.* Calcd. for  $C_{19}H_{22}N_2O$ : C, 77.52; H, 7.53. Found: C, 77.82; H, 7.92.

**Acid-Catalyzed Rearrangement of VIII.**—The 2-hydroxyindoline ether VIII (1.2 g.) was dissolved in 4 *N* sulfuric acid. No change was observed in the ultraviolet absorption spectrum after 1 hr. at room temperature. After heating for 30 min. on a steam bath, the typical ultraviolet absorption spectrum of an indole was observed. The solution was made basic with sodium hydroxide and extracted with methylene chloride. The extract (1.09 g.) was chromatographed on alumina (22 by 90 mm.) to give from the benzene eluate (100 ml.) the indole ether XIII, which crystallized from ether-petroleum ether, yielding 460 mg. of the pure compound, m.p. 131–133°.

*Anal.* Calcd. for  $C_{20}H_{24}N_2O$ : C, 77.88; H, 7.84; N, 9.08. Found: C, 77.94; H, 7.95; N, 8.95;  $NCH_3$ , 3.64.

**Treatment of XI with Acid.**—The indolenine ether XI (100 mg.) was dissolved in 4 *N* sulfuric acid, and there was no change 2.5 hr. later in its ultraviolet absorption spectrum. The solution was heated on a steam bath for 45 min. by which time the compound was completely converted to an indole (ultraviolet). After basifying, the solution was extracted with methylene chloride, yielding the indole ether XIV, which had m.p. 302–304°, after crystallization from methylene chloride-ether.

*Anal.* Calcd. for  $C_{19}H_{22}N_2O$ : C, 77.52; H, 7.53. Found: C, 77.41; H, 7.75.

**Acknowledgments.**—We are grateful to Dr. E. Schlittler for his constant interest and encouragement. We wish to express our thanks to Mr. L. Dorfman and his staff for the analytical and spectral data and to Mr. H. M. Werblood for assistance with some of the experiments.

(15) These data are in good agreement with those recorded for other 3-acylindoles; *inter alia*, M. F. Bartlett, D. F. Dickel, and W. I. Taylor, *J. Am. Chem. Soc.*, **80**, 126 (1958); J. A. Ballantine, C. B. Barrett, R. J. S. Beer, B. G. Boggiano, S. Eardley, B. E. Jennings, and A. Robertson, *J. Chem. Soc.*, 2227 (1957).