hydrochloride of compound **5** and N-methylcassine hydrochloride are superimposable.[11]

A 200-mg sample of compound **5** was converted to the methiodide using 3 ml of absolute ethanol and 2 ml of methyl iodide. The reaction was allowed to proceed at room temperature overnight and the volatile material was removed under vacuum. The residue was crystallized twice from ethyl acetate to give the very hygroscopic methiodide, mp 79–84°, $[\alpha]^{23}D$ −16.3° (*c* 1.49 g/100 ml, absolute ethanol).[11] No analysis was attempted because of the hygroscopic nature of this compound.[7]

The reported physical constants for N-methylcassine methiodide are[5] mp 91–93°, $[\alpha]^{26}D$ 15.8°.

B. N-Methyl-2-(*S*)-methyl-3-(*S*)-hydroxy-6-(*R*)-(10-oxo-9-methylundecyl)piperidine (3a).—The same alkylation procedure was employed here as in part A except that 1.81 g (12.6 mmoles) of ethyl α-methylacetoacetate, 0.322 g (13.3 mmoles) of sodium hydride, and 1.54 g (4.95 mmoles) of N-methyl-2-(*S*)-methyl-3-(*S*)-hydroxy-6-(*R*)-(8-chlorooctyl)piperidine hydrochloride (**2**) were used. The yield of product was 0.45 g. The nmr spectrum of compound **3a** was almost identical with that of compound **5** except that **3a** showed a three-peak multiplet centered at about τ 8.93 (the center peak was very slightly resolved), where **5** showed a doublet centered at τ 8.87.

Compound **3a** gave a crystalline hydrochloride which was crystallized from ethyl acetate, mp 103–106°, $[\alpha]^{24}D$ −8.9° (*c* 1.07 g/100 ml, absolute ethanol). The infrared spectrum of this compound was not identical with that of N-methylcassine hydrochloride.

Anal. Calcd for $C_{19}H_{38}ClNO_2$: C, 65.58; H, 11.01; Cl, 10.19; N, 4.03. Found: C, 64.96; H, 11.04; Cl, 10.01; N, 4.26.

C. N-Methyl-2-(*S*)-methyl-3-(*S*)-hydroxy-6-(*R*)-(11-oxo-10-methyldodecyl)piperidine (3b).—The same alkylation procedure was employed here as in part A except that 2.00 g (13.9 mmoles) of ethyl α-methylacetoacetate, 0.200 g (8.33 mmoles) of sodium hydride, and 0.576 g (1.77 mmoles) of N-methyl-2-(*S*)-methyl-3-(*S*)-hydroxy-6-(*R*)-(9-chlorononyl)piperidine hydrochloride (**4**) were used. The yield of product was 0.25 g. The nmr spectrum of this compound was almost identical with that of compound **3a**.

Compound **3b** gave a crystalline hydrochloride which was crystallized from methanol–ether, mp 105–114°, $[\alpha]^{24}D$ −10.4° (*c* 1.03 g/100 ml, absolute ethanol). The infrared spectrum of this compound was not identical with that of N-methylcassine hydrochloride.

Anal. Calcd for $C_{20}H_{40}ClNO$: C, 66.36; H, 11.06; N, 3.88. Found: C, 65.88; H, 11.35; N, 4.19.

Acknowledgment.—We wish to thank Drs. R. K. Hill and R. J. Highet for helpful discussions concerning this work. We are especially grateful to Dr. Highet for supplying us with a sample of N-methylcassine hydrochloride and for his help in comparing physical constants and spectra of our compounds.

(11) We should comment on the observed melting points of our derivatives compared with those reported by Highet.[5] The hydrochloride of compound **5** has a melting point of 103–105.5°. This is below that reported in the literature for N-methylcassine hydrochloride (lit. mp 110.5–111.5°) but an authentic sample of N-methylcassine hydrochloride supplied by Dr. Highet showed a melting point of 104–106.5° on our apparatus. The methiodide of compound **5** has a melting point of 79–84°, whereas N-methylcassine methiodide is reported to have a melting point of 91–93°. We have been unable to purify the methiodide of **5** sufficiently or keep it dry enough to obtain a good melting point. The compound is extremely hygroscopic. We feel that the methiodide of **5** is pure enough to have a fairly reliable specific rotation but not to have a very good melting point, primarily because of its hygroscopic nature.

The Mitomycin Antibiotics. Synthetic Studies. XIII.[1a] Indoloquinone Analogs with Variations at C-5

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2,6-Dimethyl-1-ethyl-4-hydroxyindole (IIIa) was converted into the corresponding 3-formyl derivative VIIIa *via* acetylation, formylation, and deacetylation. The latter compound reacted poorly with Fremy's salt, but by employing an excess of this reagent at mildly elevated temperatures it could be oxidized in satisfactory yield to the corresponding 4,7-quinone (XIa). Under these conditions an oximino derivative (XII) of XIa was also isolated, presumably as a result of breakdown products of Fremy's salt combining with XIa. An alternate synthesis of XIa involving Fremy's salt oxidation of IIIa prior to formylation proved infeasible. Conversion of XIa to 3-hydroxymethyl methylcarbamate Xa was effected by standard procedures. By a route parallel to that just described the corresponding 5-methyl homolog Xb was also prepared. The antibacterial and antifungal activities of the above two carbamates are noted.

As part of our comprehensive program for preparing analogs of active indoloquinones (*e.g.*, I)[2] related to the mitomycin antibiotics, structures with variation of the substituent at C-5 of the quinone ring were important. In this paper we describe the preparation of analogs wherein the 5-methoxy group of I has been replaced by hydrogen and methyl.

For the 5-hydrogen analog Xa two routes parallel to those employed for the corresponding 5,6-unsubstituted analog II[1a] were envisioned, starting from 2,6-dimethyl-1-ethyl-4-hydroxyindole (IIIa).[3] However, the route preferred for the preparation of II was shown to be inapplicable to the present objective when it was not possible to effect in acceptable yield the first transformation in the sequence, namely, oxidation to *p*-quinone V. Thus, Fremy's salt (potassium nitrosodisulfonate)[4] treatment of IIIa afforded only 5% of V and 5% of *o*-quinone VII. In contrast, yields of 68 and 12% had been obtained for the corresponding *p*- and *o*-quinones, respectively, in the 5,6-unsubstituted series.[1a] In view of this difficulty we directed our efforts toward developing the alternate pathway. Hydroxyindole IIIa was converted to its acetate IVa and the latter compound was formylated under Vilsmeier–Haack conditions.[5] Deacetylation of the resulting 3-formyl-4-acetate VIa afforded 3-formyl-4-hydroxyindole VIIIa. Fremy's salt oxidation of VIIIa gave a result similar to that obtained with the corresponding 3-formyl-5,6-unsubstituted compound[1] in that the conversion of starting material to *p*-quinone XIa

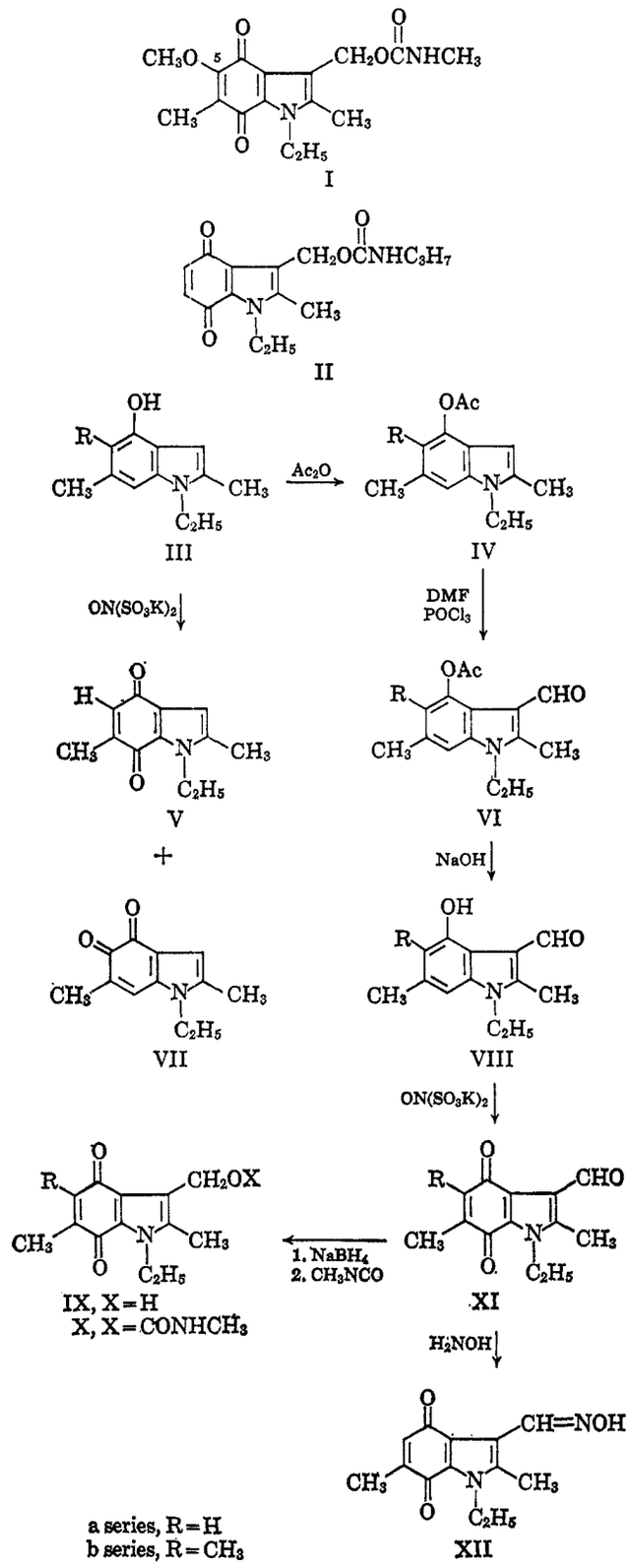
(1) (a) Preceding paper in this series: W. A. Remers and M. J. Weiss, *J. Am. Chem. Soc.*, **88**, 804 (1966); (b) to whom inquiries should be directed.

(2) G. R. Allen, Jr., J. F. Poletto, and M. J. Weiss, *J. Am. Chem. Soc.*, **86**, 3878 (1964).

(3) W. A. Remers and M. J. Weiss, *ibid.*, **87**, 5262 (1965).

(4) See H. J. Teuber and G. Jellinek, *Ber.*, **85**, 95 (1952), and subsequent papers.

(5) A. Vilsmeier and A. Haack, *ibid.*, **60**, 119 (1927).



was incomplete and the mixture obtained was difficult to separate. However, by treating VIIIa several times with excess Fremy's salt a satisfactory conversion could be obtained. In certain instances quinone XIa crystallized from the reaction mixture, although it was usually necessary to resolve the crude product by partition chromatography to obtain XIa in pure form. In addition to XIa, chromatographic separation revealed the presence of a second quinone, $C_{13}H_{14}N_2O_3$, which was shown to be the oxime XII of XIa, by infrared and nmr data. Treatment of XIa with hydroxylamine[6] also afforded XII, confirming this proposed structure.

Conversion of XIa to 3-hydroxymethylquinone IXa and thence to the methyl carbamate Xa by the usual procedures[2] was readily achieved, although Xa was obtained in low yield and partition chromatography was necessary for its purification.

Preparation of the 5-methyl analog Xb was accomplished by following a route parallel to the one just described. The starting material, 1-ethyl-4-hydroxy-2,5,6-trimethylindole (IIIb), was obtained by catalytic hydrogenation of 2,6-dimethyl-1-ethyl-4-hydroxyindole-5-carboxaldehyde.[3] Significant departures from the parallel route were observed in the acetylation of IIIb, where it proved more efficient to convert the acetate IVb directly to the corresponding 3-formyl derivative VIb, and in the preparation of 3-hydroxymethylindoloquinone IXb, where the yield was much improved. No oxime formation was detected in the preparation of indoloquinone-3-carboxaldehyde XIb.

The 5-hydrogen (Xa) and 5-methyl (Xb) analogs described in this paper showed *in vitro* activity against gram-positive bacteria and fungi; with respect to certain gram-positive bacteria and most fungi Xa was active at lower concentrations than was the lead 5-methoxyquinone I. However, Xa and Xb were less interesting than I at comparable doses when assayed against *Staphylococcus aureus* var. Smith in mice. Full details of this biological testing will be reported elsewhere.

Experimental Section

Melting points were determined on a hot-stage microscope and are corrected. **Ultraviolet spectra** were determined in methanol solution with a Cary recording spectrophotometer. **Infrared spectra** were determined in potassium bromide disks with a Perkin-Elmer Model 21 spectrophotometer. **Nuclear magnetic resonance spectra** were determined in deuteriochloroform, unless otherwise specified, with a Varian A-60 spectrometer. **Solutions** were dried over anhydrous magnesium sulfate and concentrated under reduced pressure on a rotary evaporator.

2,6-Dimethyl-1-ethyl-4,7-indoloquinone (V) and 2,6-Dimethyl-1-ethyl-4,5-indoloquinone (VII).—A solution of 1.89 g (10 mmoles) of 2,6-dimethyl-1-ethyl-4-hydroxyindole (IIIa)[3] in 320 ml of acetone was added to a solution of 10.24 g (40 mmoles) of potassium nitrosodisulfonate in 640 ml of 0.055 *M* potassium dihydrogen phosphate. After 1 hr the mixture was diluted with 1 l. of water and extracted with 600 ml of methylene chloride. This extract was washed with water, dried, and concentrated, and the residue was redissolved in methylene chloride and passed through a column of Florisil[8] (25 × 250 mm). Concentration of eluate from the orange band gave 95 mg (5%) of 2,6-dimethyl-1-ethyl-4,7-indoloquinone (V) as orange prisms: mp 115–117° after recrystallization from hexane; λ_{max} 6.10 μ; 232 (ϵ 15,200), 254 (ϵ 11,700), 346 (ϵ 2500), and 444 (ϵ 2100) mμ.

Anal. Calcd for $C_{12}H_{13}NO_3$ (mol wt, 203.22): C, 70.91; H, 6.45; N, 6.89. Found: C, 70.95, 70.61; H, 6.24, 6.43; N, 6.96.

(6) Formation of the oxime from an aldehyde by Fremy's salt has not been previously reported. However this finding is not too surprising since, at least in acid solution, the conversion of the reduction products of Fremy's salt to hydroxylamine according to the following equation was reported by Teuber and Rau.[7]

$$HON(SO_3K)_2 + HN(SO_3K)_2 \longrightarrow 3KHSO_4 + HONH_2 + H_2NSO_3K$$

(7) H. J. Teuber and W. Rau, *Ber.*, **86**, 1038 (1953).

(8) Florisil is the registered trademark of the Floridin Co. for a magnesia-silica gel adsorbent.

Elution of the Florisil column, just described, with acetone afforded 95 mg (5%) of 2,6-dimethyl-1-ethyl-4,5-indoloquinone (VII) as purple needles: mp 160–166° after recrystallization from methylene chloride–hexane; λ_{max} 6.07 μ; 243 (ϵ 28,000), 355 (ϵ 4060), and 570 (ϵ 1565) mμ.

Anal. Calcd for $C_{12}H_{13}NO_3$ (mol wt, 203.22): C, 70.91; H, 6.45; N, 6.89. Found: C, 70.97; H, 6.62; N, 6.86.

4-Acetoxy-2,6-dimethyl-1-ethylindole (IVa).—A solution of 2.487 g (13 mmoles) of 2,6-dimethyl-1-ethyl-4-hydroxyindole (IIIa)[3] in 45 ml of water containing 800 mg (20 mmoles) of sodium hydroxide was treated with 2.0 g (20 mmoles) of acetic anhydride and 1.75 g (20 mmoles) of sodium acetate. After 20 min the mixture was filtered and the solid was dissolved in methylene chloride, washed two times with sodium bicarbonate solution, dried, and concentrated. The semisolid residue was purified by adsorption chromatography on 10 g of Florisil with methylene chloride as eluent. Concentration of the eluate afforded 1.17 g (40%) of 4-acetoxy-2,6-dimethyl-1-ethylindole (IVa) as pale tan solid, mp 61–63° after recrystallization from hexane: λ_{max} 5.66 μ; 225 (ϵ 44,100) and 276 (ϵ 8600) mμ.

Anal. Calcd for $C_{14}H_{17}NO_2$ (mol wt, 231.28): C, 72.70; H, 7.41; N, 6.06. Found: C, 72.51; H, 7.16; N, 5.78.

4-Acetoxy-1-ethyl-2,5,6-trimethylindole (IVb).—A mixture of 4.35 g (20 mmoles) of 2,6-dimethyl-1-ethyl-4-hydroxy-5-indolecarboxaldehyde,[3] 2.30 g of 10% palladium on charcoal, and 150 ml of ethanol was shaken in a Parr apparatus with hydrogen at an initial pressure of 34 psi for 16 hr, filtered, and concentrated. The residual oil (4.0 g) was dissolved in 10 ml of pyridine and 200 ml of 10% sodium hydroxide containing a small amount of sodium hydrosulfite. This solution was treated with 3.00 g of sodium acetate and 3.5 ml of acetic anhydride at ice-bath temperature. Two additional portions of acetic anhydride, totaling 10 ml, were added during 1.5 hr. After 0.5 hr at room temperature the reaction mixture was poured into 200 ml of 5% sodium bicarbonate solution. A methylene chloride extract of this mixture yielded, after drying and concentration, 4.70 g of dark brown oil. This oil was dissolved in 25 ml of methylene chloride and chromatographed on 80 g of Florisil. The column was eluted with 1 l. of methylene chloride. Concentration of the eluate gave 2.5 g (52%) of 4-acetoxy-1-ethyl-2,5,6-trimethylindole (IVb) as yellow solid. A portion of this solid was recrystallized from acetone–hexane to give white crystals: mp 113–114.5°; λ_{max} 5.70 μ; 225 (ϵ 38,300) and 277 (ϵ 8800) mμ.

Although a satisfactory combustion analysis could not be obtained for this compound it was converted into VIb, for which satisfactory analytical data were obtained.

4-Acetoxy-2,6-dimethyl-1-ethyl-3-formylindole (VIa).—To an ice-cooled mixture of 5.70 g (37 mmoles) of phosphorus oxychloride and 40 ml of dimethylformamide was added a solution of 8.63 g (37 mmoles) of 4-acetoxy-2,6-dimethyl-1-ethylindole (IVa) in 40 ml of dimethylformamide. After 90 min the resulting yellow solution was poured onto ice and 10% sodium carbonate solution. The solid that formed was washed with water, dissolved in methylene chloride, washed with sodium bicarbonate solution, dried, and concentrated. The residue was crystallized two times from methanol to afford 5.3 g (55%) of 4-acetoxy-2,6-dimethyl-1-ethyl-3-formylindole (VIa) as white needles: mp 168–171°; λ_{max} 5.71 and 6.03 μ; 216 (ϵ 27,100), 248 (ϵ 15,200), 269 (ϵ 10,100), and 310 (ϵ 12,000) mμ.

Anal. Calcd for $C_{15}H_{17}NO_3$ (mol wt, 259.3): C, 69.48; H, 6.61; N, 5.40. Found: C, 69.21; H, 6.67; N, 5.38.

4-Acetoxy-1-ethyl-3-formyl-2,5,6-trimethylindole (VIb).—A solution of 1.0 g (4.0 mmoles) of 4-acetoxy-1-ethyl-2,5,6-trimethylindole (IVb) in 10 ml of dimethylformamide was added at 0° to a solution of 0.4 ml of freshly distilled phosphorus oxychloride in 4 ml of dimethylformamide. The solution was stirred for 0.5 hr at room temperature and then poured into 25 ml of 5% sodium bicarbonate. A methylene chloride extract of this mixture was dried and concentrated to give 884 mg of a brown semisolid which afforded upon treatment with methanol 347 mg (28%) of 4-acetoxy-1-ethyl-3-formyl-2,5,6-trimethylindole (VIb) as a cream-colored solid, mp 164–168°. An additional 146 mg (12%) of VIb, mp 162–166°, was obtained by work-up of the aqueous layer and methanolic mother liquor. An analytical sample, recrystallized from methanol, had mp 165–168°; λ_{max} 5.69 and 6.08 μ; 252 (ϵ 18,400) and 311 (ϵ 11,600) mμ.

Anal. Calcd for $C_{16}H_{19}NO_3$ (mol wt, 273.32): C, 70.31; H, 7.01; N, 5.13. Found: C, 70.07; H, 7.01; N, 5.17.

2,6-Dimethyl-1-ethyl-3-formyl-4-hydroxyindole (VIIIa).—A mixture of 5.19 g (20 mmoles) of 4-acetoxy-2,6-dimethyl-1-ethyl-3-formylindole (VIa), 330 ml of methanol, and 100 ml of 5% sodium hydroxide solution was stirred and gently warmed until all of the solid dissolved. The resulting solution was cooled, diluted with water, and acidified with acetic acid, affording 3.79 g (87%) of 2,6-dimethyl-1-ethyl-3-formyl-4-hydroxyindole (VIIIa) as a yellow solid, mp 178–179°, of sufficient purity for use in subsequent reactions. Two recrystallizations from methanol gave yellow needles: mp 180–181°; λ_{max} 2.9 and 6.22 μ; 221 (ϵ 32,800), 252 (ϵ 15,200), 274 (ϵ 8800) (sh), and 344 (ϵ 8400) mμ; nmr, δ 10.83 (OH), 9.55 (CHO), 6.75 and 6.40 (C-5 and C-7 protons), 4.08 (two-proton quartet, NCH_2CH_3), 2.60 (three protons, C-2 methyl), 2.38 (three protons, C-6 methyl), and 1.35 (three-proton triplet, NCH_2CH_3) ppm.

Anal. Calcd for $C_{13}H_{15}NO_2$ (mol wt, 214.2): C, 71.85; H, 6.96; N, 6.45. Found: C, 71.61; H, 6.89; N, 6.46.

1-Ethyl-3-formyl-4-hydroxy-2,5,6-trimethylindole (VIIIb).—A solution of 100 mg (3.7 mmoles) of 4-acetoxy-1-ethyl-3-formyl-2,5,6-trimethylindole (VIb) in 10 ml of warm methanol containing a small amount of sodium hydrosulfite was treated with 2.5 ml of 10% sodium hydroxide. Within 5 min the solution had become golden in color, and solid precipitated. The mixture was filtered. Additional solid was collected by diluting the filtrate with water. This procedure afforded a total of 68 mg (82%) of 1-ethyl-3-formyl-4-hydroxy-2,5,6-trimethylindole (VIIIb) as yellow needles: mp 162–163.5° after recrystallization from methanol; λ_{max} 2.95 and 6.25 μ; 218 (ϵ 28,900), 253 (ϵ 15,400), 278 (ϵ 8400), and 345 (ϵ 7600) mμ.

Anal. Calcd for $C_{14}H_{17}NO_2$ (mol wt, 231.28): C, 72.70; H, 7.41; N, 6.06. Found: C, 71.79; H, 7.63; N, 6.25.

2,6-Dimethyl-1-ethyl-3-formyl-4,7-indoloquinone (XIa) and 2,6-Dimethyl-1-ethyl-3-formyl-4,7-indoloquinone Oxime (XII).—To a solution of 19.32 g (72 mmoles) of potassium nitrosodisulfonate in 1250 ml of 0.055 *M* potassium dihydrogen phosphate buffer was added at 40° a solution of 3.95 g (18 mmoles) of 2,6-dimethyl-1-ethyl-3-formyl-4-hydroxyindole (VIIIa) in 1250 ml of acetone. The mixture was stirred at room temperature for 0.5 hr, heated to 45°, and treated with an additional 19.32 g of potassium nitrosodisulfonate in 400 ml of 0.055 *M* potassium dihydrogen phosphate. The solid which precipitated from the reaction mixture was indicated by infrared spectrum to be a mixture of starting material and product. The mixture was extracted with methylene chloride, and the extract was dried and concentrated. The residue was again treated with two 72-mmole portions of potassium nitrosodisulfonate, and the resulting mixture was worked up as described above. After this process was repeated a third time the orange solid mixture (4.14 g) obtained was resolved by partition chromatography. A 2.84-g portion of this solid was dissolved in 35 ml of the upper phase and 35 ml of the lower phase of the system methanol–heptane, mixed with 70 g of Celite[9] diatomaceous earth, and packed atop a column prepared from 1000 g of Celite and 500 ml of the lower phase (hold-back volume 1850 ml). The remaining 1.29 g of orange solid was chromatographed in similar fashion on a column prepared from 600 g of Celite and 300 ml of the lower phase (hold-back volume 1000 ml). Each column was eluted with the upper phase. Identical chromatograms (plot of ultraviolet absorption at 332 mμ *vs.* hold-back volume) were obtained, and eluates from the two columns were combined for each region of peak absorption. Concentration of the eluate in the second hold-back volume afforded 1.143 g of orange solid. Recrystallization of this solid from acetone–petroleum ether gave 2,6-dimethyl-1-ethyl-3-formyl-4,7-indoloquinone (XIa) as golden needles, mp 146–149°, that darkened on exposure to air: λ_{max} 5.95, 6.08, and 6.19 μ; 245 (ϵ 15,600), 264 (ϵ 15,800), 332 (ϵ 3700), and 410 (ϵ 1800) mμ; nmr, δ 10.48 (CHO), 6.10 (doublet, J = 1.7 cps, C-5 proton), 4.43 (two-proton quartet, $N-CH_2-CH_3$), 2.63 (three protons, C-2 methyl), 2.10 (three-proton doublet, J = 1.7 cps, C-6 methyl), and 1.35 (three-proton triplet, $N-CH_2-CH_3$) ppm.

Satisfactory combustion analyses could not be obtained for this compound, probably because air oxidation introduced impurities into the sample. However, its structure is completely defined by the nmr spectrum and it was converted into two compounds, Xa and XII, which gave good analytical data.

(9) Celite is the registered trademark of the Johns Manville Corp. for diatomaceous earth products.

Concentration of the eluate in hold-back volumes 3.5–4.5 afforded 637 mg of starting material.

The orange eluate in hold-back volumes 6–8 afforded, after concentration, 1.20 g of orange solid. Recrystallization of this solid from acetone–hexane gave 2,6-dimethyl-1-ethyl-3-formyl-4,7-indoloquinone oxime (XII) as red-orange plates: mp 204–206°; λ_{max} 6.10 μ; 264 (ϵ 19,900), 358 (ϵ 3000), and 485 (ϵ 4000) mμ; nmr, δ 12.92 (NOH), 9.23 (-CH=N), 6.35 (doublet, J = 1.5 cps, C-5 proton), 4.33 (two-proton quartet, N-CH_2-CH$_3$), 2.57 (three protons, C-2 methyl), 2.01 (three-proton doublet, J = 1.5 cps, C-6 methyl), and 1.27 (three-proton triplet, N-CH$_2$-CH_3) ppm.

Anal. Calcd for $C_{13}H_{14}N_2O_3$ (mol wt, 246.26): C, 63.40; H, 5.73; N, 11.38. Found: C, 63.26, 63.52; H, 5.75, 5.97; N, 9.89, 10.33.

A solution of 97 mg (0.42 mmole) of 2,6-dimethyl-1-ethyl-3-formyl-4,7-indoloquinone (XIa) in 10 ml of ethanol was treated with an aqueous solution of 30 mg (0.42 mmole) of hydroxylamine hydrochloride and an aqueous solution of 22 mg of sodium carbonate. The mixture was heated at reflux temperature for 1 hr, cooled, and diluted with water. The orange precipitate of 2,6-dimethyl-1-ethyl-3-formyl-4,7-indoloquinone oxime (XII) was washed with water and dried. It had an infrared absorption spectrum identical with that of the sample of XII prepared by the Fremy's salt oxidation of VIIIa described above (both samples in potassium bromide disks) and did not depress the melting point of the latter sample.

1-Ethyl-3-formyl-2,5,6-trimethyl-4,7-indoloquinone (XIb).—A solution of 104 mg (0.45 mmole) of 1-ethyl-3-formyl-4-hydroxy-2,5,6-trimethylindole (VIIIb) in 25 ml of warm acetone was added to a solution of 375 mg of potassium nitrosodisulfonate in 25 ml of 0.055 *M* potassium dihydrogen phosphate buffer. After 5 min the solution was warmed at 45° and another portion of 375 mg of potassium nitrosodisulfonate in 10 ml of buffer was added. This procedure was repeated two more times, whereupon orange solid separated from the brown solution. This solid was collected, washed with water, dried, and recrystallized from acetone–hexane to give 60 mg (54.5%) of 1-ethyl-3-formyl-2,5,6-trimethyl-4,7-indoloquinone (XIb) as an orange solid: mp 125–127°; λ_{max} 6.01 and 6.12 μ; 216 (ϵ 12,700), 247 (ϵ 7400), 257 (ϵ 7300), 278 (ϵ 6600), 281 (ϵ 5900), and 338 (ϵ 2700) mμ.

Anal. Calcd for $C_{14}H_{15}NO_3$ (mol wt, 245.27): C, 68.55; H, 6.16; N, 5.71. Found: C, 68.30, 68.79; H, 6.78, 6.63; N, 6.09.

2,6-Dimethyl-1-ethyl-3-hydroxymethyl-4,7-indoloquinone Methylcarbamate (Xa).—A solution of 665 mg (2.9 mmoles) of 2,6-dimethyl-1-ethyl-3-formyl-4,7-indoloquinone (XIa) in 150 ml of methanol, under nitrogen, was warmed to reflux temperature and treated with a solution of 1.2 g (excess) of sodium borohydride in 100 ml of ethanol. The mixture was stirred for 30 min at room temperature, treated with 12 ml of acetone, followed after 5 min by 12 ml of 0.1 *N* hydrochloric acid containing 3.24 g of ferric chloride hexahydrate. The mixture was immediately treated with methylene chloride and water. The organic layer was washed with water, dried, and concentrated to give a red oil. This oil was purified by partition chromatography on 80 g of Celite using the heptane–methanol system described above. Concentration of eluate from the principal colored band (red) gave 178 mg (26.3%) of 2,6-dimethyl-1-ethyl-3-hydroxymethyl-4,7-indoloquinone (IXa) as red-orange solid. This compound was converted directly to the methylcarbamate.

A mixture of 175 mg of IXa and 2.2 ml of freshly distilled methyl isocyanate was warmed at reflux temperature for 24 hr. The excess isocyanate was removed under reduced pressure, affording an orange solid. This solid was purified by partition chromatography on 80 g of Celite with the heptane–methanol system described above. Concentration of eluate from the red band gave 109 mg of orange oil that solidified on trituration with ether. The solid was repurified in the same manner on 40 g of Celite. The solid (97 mg) obtained after concentration of the eluate was recrystallized from methylene chloride–hexane to give 42 mg (43%) of 2,6-dimethyl-1-ethyl-3-hydroxymethyl-4,7-indoloquinone methylcarbamate (Xa) as orange needles: mp 135–138°; λ_{max} 2.95, 5.81 (carbamate), and 6.08 (quinone) μ; 228 (ϵ 14,300), 264 (ϵ 13,600), 346 (ϵ 2600), and 441 (ϵ 2000) mμ.

Anal. Calcd for $C_{15}H_{18}N_2O_4$ (mol wt, 290.31): C, 62.05; H, 6.25; N, 9.65. Found: C, 61.83; H, 6.44; N, 9.95.

1-Ethyl-3-hydroxymethyl-2,5,6-trimethyl-4,7-indoloquinone Methylcarbamate (Xb).—A solution of 100 mg (0.4 mmole) of 1-ethyl-3-formyl-2,5,6-trimethyl-4,7-indoloquinone (XIb) in 20 ml of methanol, under nitrogen, was warmed to reflux temperature and treated with 160 mg (excess) of sodium borohydride in 12 ml of ethanol. The mixture was stirred at room temperature for 30 min and treated with 1.2 ml of acetone. After 5 min a solution of 425 mg of ferric chloride hexahydrate in 1.6 ml of 0.1 *N* hydrochloric acid was added and the mixture was treated with methylene chloride and water. The organic layer was washed with water, dried, and concentrated, and the residual red oil was purified by partition chromatography on 40 g of Celite with a heptane–methanol system by the procedure described above. Concentration of eluate from the principal colored band afforded 58 mg of 1-ethyl-3-hydroxymethyl-2,5,6-trimethyl-4,7-indoloquinone (IXb) as red-orange solid. This solid was converted directly to the methylcarbamate.

A mixture of 194 mg of IXb and 2.5 ml of methyl isocyanate was warmed at reflux temperature for 24 hr. After removal of the excess isocyanate, the solid residue was crystallized from methylene chloride–hexane. This procedure gave 113 mg (47%) of 1-ethyl-3-hydroxymethyl-2,5,6-trimethyl-4,7-indoloquinone methylcarbamate (Xb) as golden needles: mp 175–178°; λ_{max} 3.02, 5.93 (carbamate), and 6.08 (quinone) μ; 228 (ϵ 16,900), 271 (ϵ 16,500), 278 (ϵ 16,400), 342 (ϵ 13,000), and 445 (ϵ 2100) mμ.

Anal. Calcd for $C_{16}H_{20}N_2O_4$ (mol wt, 304.34): C, 63.14; H, 6.62; N, 9.21. Found: C, 63.25; H, 6.72; N, 9.27.

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