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Synthesis of 1*H*-Pyrrolo[1,2-*a*]indole Derivatives. III.[1] Synthesis of 2,3-Dihydro-7-hydroxy-6,9-dimethyl-5,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole

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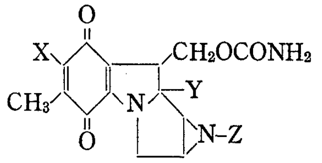
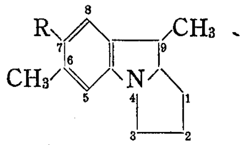
The compound related to mitomycin B, 2,3-dihydro-7-hydroxy-6,9-dimethyl-5,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole (III), was synthesized starting from 2,3,9,9a-tetrahydro-6,9-dimethyl-7-nitro-1*H*-pyrrolo[1,2-*a*]indole (II) *via* 2,3-dihydro-6,9-dimethyl-7-nitro-1*H*-pyrrolo[1,2-*a*]indole (X), 7-amino-2,3-dihydro-6,9-dimethyl-1*H*-pyrrolo[1,2-*a*]indole (XI), and 2,3-dihydro-6,9-dimethyl-7,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole (VII).

Some considerations were made on the mechanism of the formation of the dimers, 2,3-dihydro-5-(2′,3′,9′,9a′-tetrahydro-6′,9′-dimethyl-1*H*-pyrrolo[1,2-*a*]indol-7′-imino)-6,9-dimethyl-7,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole (VIII) and 2,3-dihydro-5-(2′,3′-dihydro-6′,9′-dimethyl-1*H*-pyrrolo[1,2-*a*]indol-7′-imino)-6,9-dimethyl-7,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole (IX), obtained by the oxidation of 7-amino-2,3,9,9a-tetrahydro-6,9-dimethyl-1*H*-pyrrolo[1,2-*a*]indole (V) with Fremy's salt.

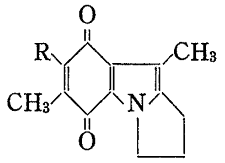
Mitomycin (I) is known as an antitumor antibiotic complex. As an approach for the synthesis of I and for the synthesis of analogs of I that might have antibacterial or antitumor activity, synthesis of 2,3,9,9a-tetrahydro-6,9-dimethyl-7-nitro-1*H*-pyrrolo[1,2-*a*]indole (II) was described in the preceding report.[1]



I
mitomycin A: X=Y=OCH_3, Z=H
mitomycin B: X=OCH_3, Y=OH, Z=CH_3
mitomycin C: X=NH_2, Y=OCH_3, Z=H
porfiromycin: X=NH_2, Y=OCH_3, Z=CH_3

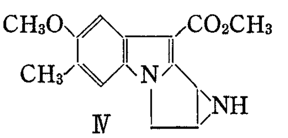


II: R=NO_2
V: R=NH_2

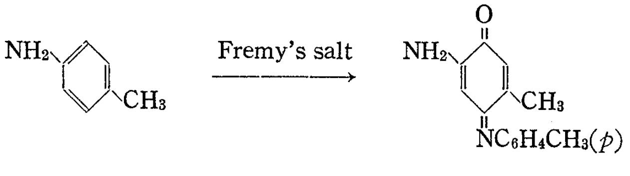


III
R=NH_2, OH, or OCH_3

In the present series of work, an attempt was made to derive II oxidatively to pyrroloindoloquinone (III), closer to I, and III (R=OH) was obtained successfully, which is described herein. The presently available report on the synthesis of compounds more closely allied to I includes that of 7-methoxymitosene[3] and a pyrroindole[4] (IV) with an aziridine ring.



IV



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[1] Part II: T. Takada, S. Kunugi, and S. Ohki, *Chem. Pharm. Bull.* (Tokyo), **19**, 982 (1971).

[2] Location: *20 Kitashinjuku 3-Chome, Shinjuku-ku, Tokyo, 160, Japan.*

[3] G.R. Allen, Jr., J.F. Poletto, and M.J. Weiss, *J. Org. Chem.*, **30**, 2897 (1965).

[4] T. Hirata, Y. Yamada, and M. Mitsui, *Tetrahedron Letters*, **19**, 4107 (1969).

Catalytic reduction of II over Raney nickel in ethanol gave oily 7-amino-2,3,9,9a-tetrahydro-6,9-dimethyl-1*H*-pyrrolo[1,2-*a*]indole (V) in a high yield. Oxidation of V should produce the mitomycin C type 7-aminopyrrolo-indoloquinone (III: R=NH_2) directly. Teuber and Jellinek[5a)] reported that oxidation of aminobenzene derivatives having alkyl or alkoxyl group in the *para*-position with Fremy's salt would give quinone-anils, just as *p*-toluidine affords a quinone-anil by this kind of oxidation, and hydrolysis of these quinone-anils would produce quinones.

However, oxidation of V with Fremy's salt at room temperature merely afforded blue crystals (VII) of mp 180—182°, bluish violet powder (VIII) of mp 185—190°, and a reddish violet resinous substance (IX) in respective low yield of 7, 3, and 5%, and the objective VI and VI′ were not obtained. The structure of VII was proved to be 2,3-dihydro-6,9-dimethyl-7,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole from its ultraviolet (UV), infrared (IR), and nuclear magnetic resonance (NMR) spectra, and from its elemental analytical data. Elemental analyses and mass spectra of VIII and IX suggested the respective molecular formulae of $C_{26}H_{29}O_2N_3$ and $C_{26}H_{27}O_2N_3$, indicating that both are probably dimers. The structure of VIII was determined as 2,3-dihydro-5-(2′,3′,9′,9a′-tetrahydro-6′,9′-dimethyl-1*H*-pyrrolo[1,2-*a*]indol-7′-imino)-6,9-dimethyl-7,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole and IX as 2,3-dihydro-5-(2′,3′-dihydro-6′,9′-dimethyl-1*H*-pyrrolo[1,2-*a*]indol-7′-imino)-6,9-dimethyl-7,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole because of the following facts. When an ethanolic solution of the quinone (VII) and the amine (V) is stirred at room temperature for 12 hr, VIII is obtained as the main product and IX as the minor product; VIII changes partly to IX when its solution in a polar solvent is allowed to stand for a long time; M^+ signal of IX in its mass spectrum is smaller than that of VIII by 2 *m/e*; in the NMR spectrum of VIII, one of the four CH_3 signals is a doublet, while that of IX shows all four CH_3 signals as singlets (Table I). As the structure of these dimers, a quinone-anil type (VIII′ and IX′) can also be considered but, if they take this type of structure, there should be a hydrogen bonding between the hydroxyl in 7-position and the carbonyl in 8-position, but the presence of a hydrogen bonding could not be recognized in their IR and NMR spectra so that they are not in a quinone-anil type but must be in an *o*-quinone type (VIII and IX).

TABLE I. Spectral Data of VIII and IX

Compound	IR_{CHCl_3} (cm^{-1})	NMR_{CDCl_3} (τ)	Mass (*m/e*)
VIII	1634 (*o*-quinone)	8.37 (3H, d, J=7.5 Hz, $C_{9'}$-CH_3) 8.45, 7.82, 7.68 (each signal 3H, s, CH_3) 3.70, 3.45 (each signal 1H, s, Ar-H)	415 (M^+)
IX	1636 (*o*-quinone)	8.52, 7.83, 7.68, 7.11 (each signal 3H, s, CH_3) 3.41, 2.96 (each signal 1H, s, Ar-H)	413 (M^+)

The amine (V) seems to be labile to oxidation, and indolines are known to be oxidized to indoles with Fremy's salt.[6)] Therefore, 9,9a-dehydro derivative (XI) of V was prepared and submitted to oxidation with Fremy's salt. It seemed difficult to obtain XI directly by the oxidation of V and, therefore, II was dehydrogenated to the 7-nitro-indole compound (X) and X was catalytically reduced over Raney nickel to the objective 7-amino-indole compound (XI), mp 94—95°. Various conditions for the dehydrogenation of II were examined and it was found that heating of II in toluene with activated manganese dioxide[7)] produced X (mp 104—106°) in a high yield.

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5) *a*) H.J. Teuber and G. Jellinek, *Chem. Ber.*, **87**, 1841 (1954); *b*) L. Horner and K. Strum, *ibid.*, **88**, 329 (1955); *c*) A.G. Holmes-Seide and B.C. Saunders, *Chem. Ind.* (London), 164 (1959).
6) H.J. Teuber and G. Staiger, *Chem. Ber.*, **89**, 489 (1956).
7) A.B.A. Jansen, J.H. Johnson, and J.R. Surtees, *J. Chem. Soc.*, **1964**, 5573.

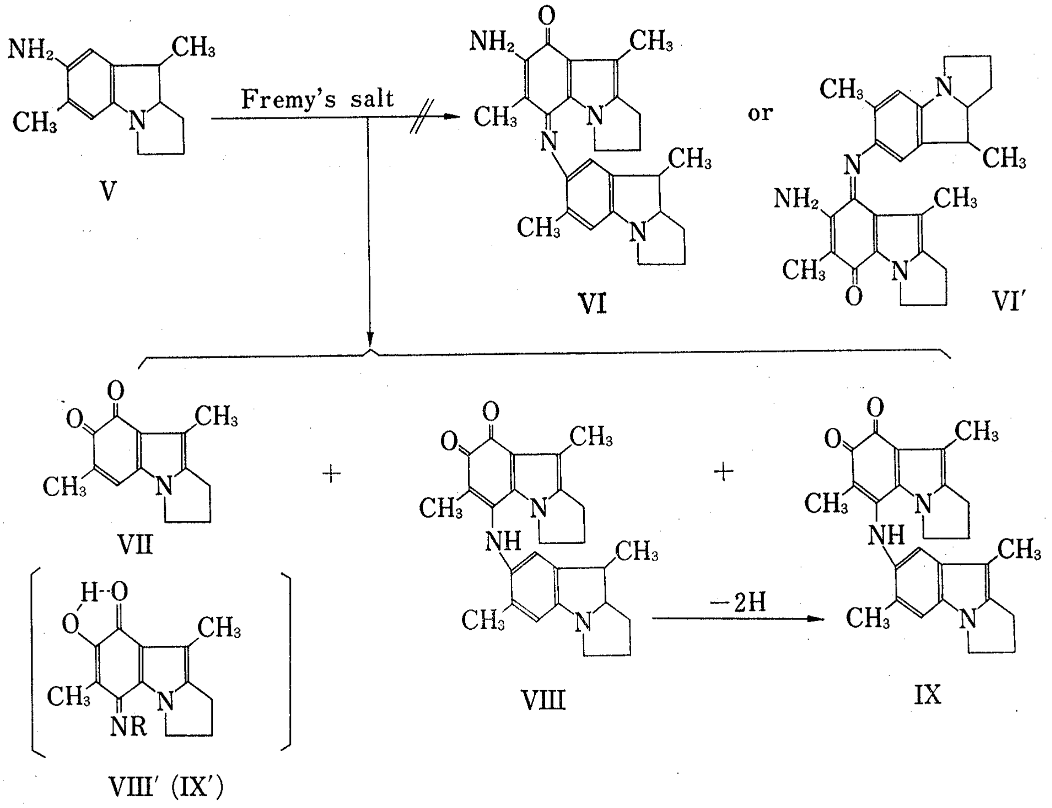

Chart 1

Oxidation of XI with Fremy's salt in acetone, at room temperature for 6 hr, afforded only VII in 43% yield, and Thiele's acetoxylation[3,8] of VII gave the triacetoxy compound (XII), which showed an ester absorption in its IR spectrum. This crude product was hydrolyzed in 20% sodium hydroxide solution followed by autoxidation, and III (R=OH) was obtained in an extremely poor yield as reddish columnar crystals, mp 187—190°. However, III (R=OH) was obtained in *ca.* 40% yield by treatment of the *o*-quinone (VII) in methanol with a small amount of boron trifluoride etherate or with a mineral acid. The above fact is rather interesting because it is contrary to the report of Allen and others[3] that, during the synthesis of 7-methoxymitosene, the said reaction in mineral acid gave a poor yield while Thiele's acetoxylation gave a good yield.

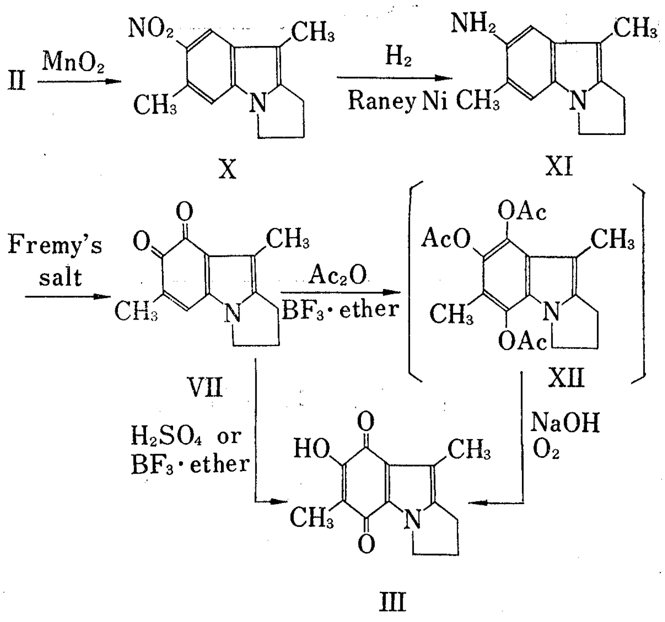

Chart 2

The structure of III (R=OH) was confirmed from its mass spectrum showing the characteristic fragmentation of *p*-quinone, with signals at *m/e* 231 (M^+), 203 (M^+—CO), 175 (M^+—2CO), and 147 ($M^+—C_4H_4O_2$), IR spectrum showing the absorption of *p*-quinone at 1650 and 1635 cm^{-1}, and

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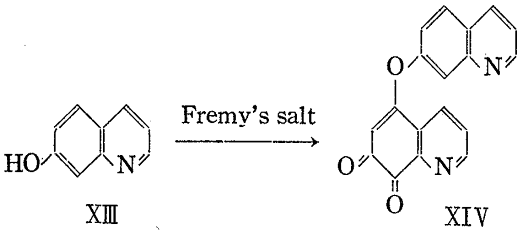
8) J. Thiele, *Chem. Ber.*, 31, 1248 (1898).

NMR spectrum having a triplet signal (J=7.5 Hz) at $5.80\,\tau$ for $-N-CH_2-$, which is shifted to a lower magnetic field by $0.33\,\tau$ from that ($6.13\,\tau$) of *o*-quinone, and a signal for hydrogen bonding at $2.67\,\tau$.

Although pyrrolido-indoloquinone related mitomycin C was not obtained in the present work, the compound (III: R=OH) closely related to mitomycin B was successfully synthesized.



Some considerations were made on the formation of the dimers (VIII and IX). As described above, formation of VIII and IX by the oxidation of V with Fremy's salt must have taken place through the initial formation of a 4,5-indoloquinone (VII) to which was added V or XI, with subsequent oxidation. An analogous reaction can be found in the oxidation of 7-hydroxyquinoline (XIII) with Fremy's salt by Teuber and Dietz[9] who also obtained an ether-linked dimer (XIV).

As a model experiment in this connection, addition reaction of 1,2-naphthoquinone (XV) with a primary amine (aniline, 1- and 2-naphthylamine) or secondary amine (pyrrolidine, piperidine, morpholine, and N-methylaniline) was carried out. Reaction of XV with an equimolar amount of one of these amines in ethanol, for 12 hr at room temperature, afforded 4-substituted naphthoquinones (XVIIa–f) in approximately quantitative yield, except in one case. This fact indicates that atmospheric air acts as an oxidant in the oxidation of XVI to XVII, rather than XV. The only exception was found in the reaction of XV with 2-naphthylamine which afforded 4-substituted quinone-anil (XVIIIb) instead of 4-substituted 1,2-naphthoquinone (XVIIg).

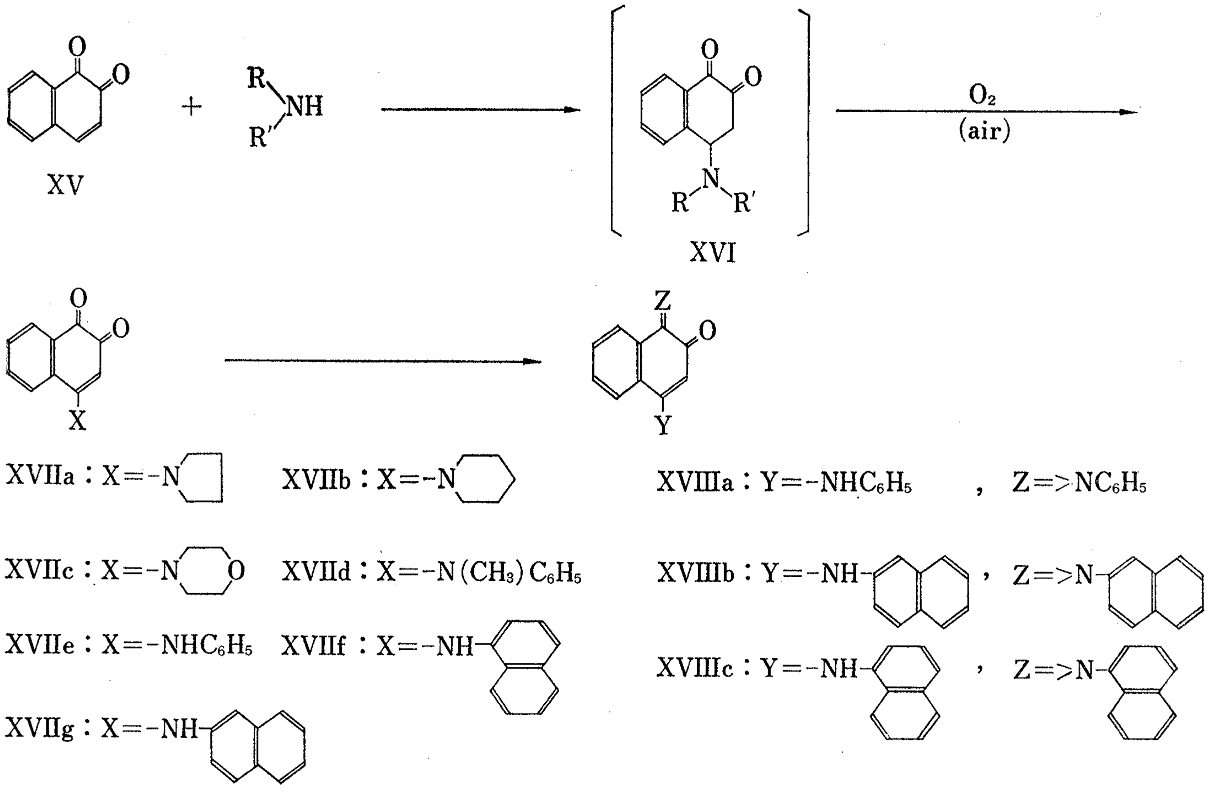


Chart 3

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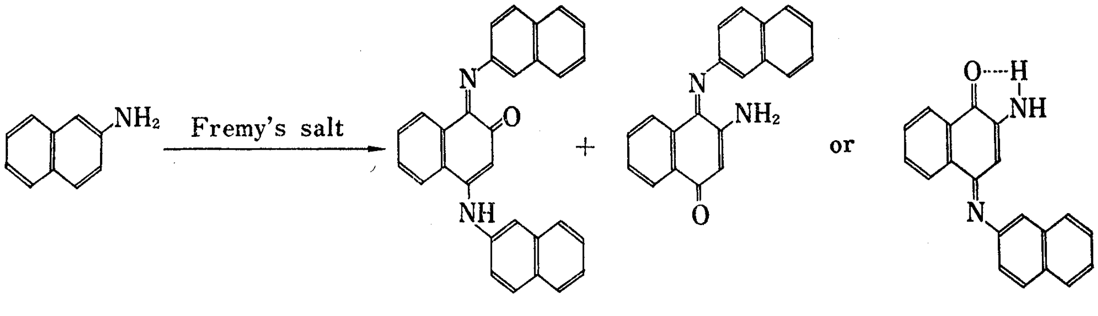
[9] H.J. Teuber and K.H. Dietz, *Angew. Chem., Int. Engl. Ed.*, **5**, 1049 (1966).

In this reaction, the use of an excess of the primary amine results in the formation of 4-substituted quinone-anil (XVIIIa—c). In this case, the reaction progresses most easily with 2-naphthylamine and XVIIIb is formed quantitatively by the reaction in ethanol at room temperature. The reaction of XV with aniline gives XVIIe when reacted at room temperature and XVIIIa when heated. The reaction of XV with 1-naphthylamine gives mainly XVIIf and only a small amount of XVIIIc is produced. These facts suggest that XVIII is formed *via* XVII and that the carbonyl in 2-position of XVII is in a vinylogous amide form, resulting in the reduction of reactivity, so that the quinone-anil would be represented by formula XVIII, which formula is supported by its IR spectrum without an absorption for an acetophenone-type carbonyl.

The interesting fact is that XVIIe reacts with 2-naphthylamine in ethanol at room temperature to form XVIIIb, by exchange of the amino group in 4-position, in a quantitative yield, while it does not react at all with 1-naphthylamine.

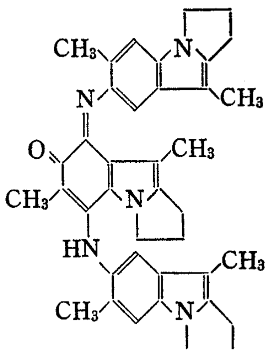
In this connection oxidation with Fremy's salt was carried out on 2-naphthylamine which is structurally similar to V and XI. Teuber and Jellinek[5a)] obtained only the quinone-anil compound (XIX or XIX′) by the same reaction, but in the present experiment, XVIIIb was obtained as the main product and the yield of XIX or XIX′ was extremely small. The structure of the latter compound is likely to be XIX rather than XIX′ because there was no evidence of a hydrogen bonding in its IR and NMR spectra. Consequently, oxidation of 2-naphthylamine type compounds with Fremy's salt preferentially produces 1,2-quinones rather than 1,4-quinones.



XVIIIb XIX XIX′

Chart 4

Reaction of *o*-quinone (VII) and the amine (XI) in ethanol at room temperature for 12 hr affords IX quantitatively but heating of the reaction mixture for 24 hr produces a minute amount of a bluish violet substance whose mass spectrum has a signal at *m/e* 525 (M^+), suggesting the formation of an aminoquinone-anil (XX) corresponding to the above XVIIIb.



XX

Formation of a small amount of dimers by the oxidation of the amine (V) with Fremy's salt but not from the amine (XI) is probably due to the weak basicity of the amino group in 7-position of V as a structure of *p*-phenylenediamine, while there is sufficient basicity in XI because the amino group is substituted in the benzene moiety of the indole ring, making it susceptible to radical oxidation by Fremy's salt and XI is preferentially oxidized to the quinone (VII).

Experimental[10)]

7-Amino-2,3,9,9a-tetrahydro-6,9-dimethyl-1*H*-pyrrolo[1,2-*a*]indole (V)——A solution of 450 mg of 2,3,9,9a-tetrahydro-6,9-dimethyl-7-nitro-1*H*-pyrrolo[1,2-*a*]indole (II) in 25 ml of dehyd. EtOH, added with Raney Ni catalyst, was submitted to catalytic hydrogenation at ordinary temperature and pressure. The catalyst and solvent were removed, and the residue was purified through silica gel chromatography to afford 360 mg (91.9%) of V as a yellow-brown oil. IR $\nu_{\max}^{\text{liq. film}}$ cm^{-1}: 3409, 3340 (-NH_2), (disappearance of absorption of -NO_2 group). Mass Spectrum: *m/e*: 202 (M^+). NMR ($CDCl_3$) τ: 3.55 and 3.63 (1H, s, aromatic proton), 6.84 (2H, s, C_7-NH_2), 7.86 (3H, d, $J=7$ Hz, C_9-CH_3).

The Oxidation of 7-Amino-2,3,9,9a-tetrahydro-6,9-dimethyl-1*H*-pyrrolo[1,2-*a*]indole (V) with Potassium Nitrosodisulfonate (Fremy's Salt)——A solution of 268 mg of 7-amino-2,3,9,9a-tetrahydro-6,9-dimethyl-1*H*-pyrrolo[1,2-*a*]indole(V) in 30 ml of acetone was added, with stirring, to a solution of 1.42 g of potassium nitrosodisulfonate in 40 ml of 1/6M potassium dihydrogen phosphate and 80 ml of water. The color of the solution turned to dark purple from light blue. The solution was extracted with $CHCl_3$. The extract was dried over Na_2SO_4, $CHCl_3$ was evaporated, and the residue was placed on a column of Florisil. Elution of the column with acetone–benzene (1:10) mixture gave 24 mg (4.9%) of 2,3-dihydro-5-(2′,3′-dihydro-6′,9′-dimethyl-1*H*-pyrrolo[1,2-*a*]indol-7′-imino)-6,9-dimethyl-7,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole (IX) as reddish blue oil. *Anal.* Calcd. for $C_{26}H_{27}O_2N_3$: 413.210295. Found: 413.21020. IR $\nu_{\max}^{\text{liq. film}}$ cm^{-1}: 3330 (=NH), 1715 (=CO). NMR ($CDCl_3$) τ: 2.96 (1H, s, Ar-H), 3.41 (1H, s, Ar-H), 7.68, 7.71, 7.83, 8.52 (s, 4CH_3). Second elution with acetone–benzene (1:5) mixture gave 13 mg (2.9%) of 2,3-dihydro-5-(2′,3′,9′,9a′-tetrahydro-6′,9′-dimethyl-1*H*-pyrrolo[1,2-*a*]indole-7′-imino)-6,9-dimethyl-7,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole (VIII) as bluish purple solid, mp 185—190° (decomp.). *Anal.* Calcd. for $C_{26}H_{29}O_2N_3$: 415.22594. Found: 415.22875. IR $\nu_{\max}^{\text{liq. film}}$ cm^{-1}: 3330 (=NH), 1710 (=CO, (w)). NMR ($CDCl_3$) τ: 3.45 (1H, s, Ar-H), 3.70 (1H, s, Ar-H), 7.68 7.82, 8.45 (s, 3CH_3), 8.73 (3H, d, $J=7.5$ Hz, $C_{9'}$-CH_3). Final elution with acetone–benzene (2:5) mixture gave 20 mg (6.9%) of 2,3-dihydro-6,9-dimethyl-7,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole (VII). Recrystallization from benzene–chloroform gave dark blue needles, mp 180—182° (decomp.). *Anal.* Calcd. for $C_{13}H_{13}O_2N$: 215.09461. Found: 215.09597. UV $\lambda_{\max}^{\text{EtOH}}$ mμ: 248, 370, 590. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1649, 1630 (shoulder) (*o*-quinone), (disappearance of absorption of -NH_2 group and benzene ring). NMR ($CDCl_3$) τ: 3.25 (1H, s, C_5-H), 6.13 (2H, t, $J=7.5$ Hz, C_3-H).

2,3-Dihydro-6,9-dimethyl-7-nitro-1*H*-pyrrolo[1,2-*a*]indole (X)——a) A solution of 265 mg of II dissolved in 10 ml of toluene, added with 1.06 g of activated MnO_2, was refluxed with stirring for 24 hr. After removal of the MnO_2 by filtration, the solvent was evaporated and the residue was chromatographed over silica gel, eluted with benzene, and the product was recrystallized from EtOH to yellow needles, mp 104—106°. Yield 202 mg (76.9%). *Anal.* Calcd. $C_{13}H_{14}O_2N_2$: 230.10551. Found: 230.10294. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1512, 1310 (-NO_2). NMR ($CDCl_3$) τ: 1.72 (1H, s, C_8-H), 3.25 (1H, s, C_5-H), 4.00 (2H, t, $J=7.5$ Hz, C_3-H), 7.30 (3H, s, C_9-CH_3). 7.75 (3H, s, C_6-CH_3).

b) To a solution of 100 mg of II dissolved in 2 ml of *p*-cymene. 10% Pd-C was added and the mixture was refluxed for 24 hr. The catalyst and solvent were removed and the residue was treated in the same way as above described. 35 mg (35.3%) of X was obtained.

7-Amino-2,3-dihydro-6,9-dimethyl-1*H*-pyrrolo[1,2-*a*]indole(XI)——A solution of 180 mg of X dissolved in 5 ml of dehyd. EtOH and 2 ml of EtOAc, added with Raney Ni catalyst, was submitted to catalytic hydrogenation at ordinary temperature and pressure. After removal of the catalyst and solvent, the residue was treated in the same way as V. Recrystallization from *n*-hexane gave white needles, mp 94—95°, yield 120 mg (77%). *Anal.* Calcd. for $C_{13}H_{16}N_2$: C, 77.96; H, 8.05; N, 13.99. Found: C, 77.88; H, 8.29; N, 13.67. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3390, 1630—1640 (-NH_2). NMR ($CDCl_3$) τ: 2.09 (1H, s, Ar-H), 2.23 (1H, s, Ar-H), 6.10 (2H, t, $J=7.5$ Hz, C_3-H), 6.72 (2H, broad s, NH_2). Mass Spectrum *m/e*: 200 (M^+).

2,3-Dihydro-6,9-dimethyl-7,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole(VII)——A solution of 67 mg of XI in 10 ml of acetone was added to a stirred solution of 356 mg of potassium nitrosodisulfonate in 20 ml of water and 10 ml of 0.167 M KH_2PO_4 solution. The resulting brown solution was stirred for 4 hr. The crude product was extracted with $CHCl_3$ and chromatographed on Florisil. The material eluted by benzene and acetone was recrystallized from hexane–$CHCl_3$ to give 31 mg (43%) of dark blue needles. This material was identical with that prepared previously.

2,3-Dihydro-7-hydroxy-6,9-dimethyl-5,8-dioxo-1*H*-pyrrolo[1,2-*a*]indole (III)——A mixture of 20 mg of VII, 20 ml of acetic anhydride, and 0.002 ml of $BF_3\cdot$ether was warmed on the steam bath and then allowed to stand at room temperature for 24 hr. The reaction mixture was then poured into water and extracted with $CHCl_3$. The extract was washed with water, dried over Na_2SO_4, and solvent was evaporated. The residue did not crystallize. The IR spectrum of the residue showed absorptions of ester.

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10) All melting points are uncorrected. NMR spectra were measured by JNM 4H-100 (100 Mc) spectrophotometer and tetramethylsilane was used as internal reference. Mass spectra were measured on a Hitachi RMU-7L mass spectrometer. IR and UV spectra were measured on a Hitachi 215 IR spectrophotometer and on a Hitachi EPS-3 UV spectrophotometer, respectively.

A suspension of the residue in 2 ml of water was treated with 0.2 ml of 25% aqueous NaOH solution. The reaction mixture was heated on the steam bath, with stirring, for 0.5 hr. After filtration the color of the filtrate turned into dark blue, on exposure to air. After 0.5 hr the solution was acidified, whereupon an orange solution resulted. The solution was extracted with $CHCl_3$. The extract was dried over Na_2SO_4, the solvent was evaporated, and the residue was purified by silica gel column chromatography. Elution of the column with acetone–benzene (1:20) gave 0.6 mg (2.8%) of III as red solid.

b) To a solution of 30 mg of VII in 1 ml of MeOH was added 1 drop of $BF_3\cdot$ether, and the solution was heated on the steam bath for about 3 min, and then kept at room temperature for 2 hr. The solvent was evaporated and the residue was chromatographed over silica gel (benzene). The solid eluted was recrystallized from ether to orange-red needles, mp 189—192°. Yield, 13 mg (40.3%). The identity of this material with that of method a) was showed by the usual criteria. *Anal.* Calcd. for $C_{13}H_{13}O_3N$: 231.08953. Found: 231.08837. UV $\lambda_{\max}^{\mathrm{EtOH}}$ mμ: 234, 290, 299, 363. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1650, 1635 (*p*-quinone). Mass Spectrum *m/e*: 231 (M^+), 203 (M^+-CO), 175 (M^+-2CO), 147 ($M^+-C_4H_4O_2$). NMR ($CDCl_3$) τ: 2.67 (1H, s, OH), 5.80 (2H, t, J=7.5 Hz, C_3-H), 7.75 (3H, s, CH_3), 8.05 (3H, s, CH_3).

Reactions of Quinone (VII) with Amines (V and XI)——To a solution of 13 mg of VII dissolved in 1 ml of EtOH, a solution of 12 mg of V in 1 ml of EtOH was added and the mixture was stirred for 12 hr. EtOH was evaporated under a reduced pressure and the residue was purified by column chromatography over silica gel, using benzene–acetone mixture (10:1). 2 mg of dimer (IX) was obtained from initial fraction and 11 mg of dimer (VIII) from second fraction. These materials were identical with those prepared previously.

The same reaction was carried out on a solution of 5 mg of VII and 5 mg of XI in 1 ml of EtOH, and dimer(IX) was obtained in quantity. On the other side, a solution of 10 mg of VII and 10 mg of XI in 2 ml of EtOH was heated on a steam bath for 24 hr. The same treatment as above afforded 8 mg of dimer (IX) and 1.6 mg of trimer (XX) of viscous oil. Mass Spectrum *m/e*: 595 (M^+).

Reactions of 1,2-Naphthoquinone with Amines——To a solution of 1,2-naphthoquinone (10^{-3} mole) in 20 ml of EtOH, amine (1.2×10^{-3} mole) in 5 ml of EtOH was added and the mixture was stirred for 12 hr at room temperature. EtOH was evaporated under a reduced pressure and the residue was purified by column chromatography.

Table II. The Physical Constants of the Reaction Products of 1,2-Naphthoquinonone with Amines

Compound	Formula	Mass spectrum *m/e* M+	Mass spectrum *m/e* M++2	IR spectrum cm^{-1} C=O	NMR spectrum ($CDCl_3$) τ Vinyl proton	Yield (%)	mp (°C)
XVIIa	$C_{14}H_{14}O_2N$	227	229	1706 (w)	3.90	82	—
XVIIb	$C_{15}H_{15}O_2N$	241	243	1695 (w)	4.00	85	—
XVIIc	$C_{14}H_{13}O_3N$	243	245	1698 (w)	3.98	74	201—203
XVIId	$C_{17}H_{13}O_2N$	263	265	1707 (w)	3.70	91	—
XVIIe	$C_{16}H_{11}O_2N$	249	251	1700 (m)	—	quantitative	168—170
XVIIf	$C_{20}H_{13}O_2N$	299	301	1692 (m)	3.53	13	241—243
XVIIIb	$C_{30}H_{20}ON_2$	424		—	—	quantitative	256—258
XVIIIc	$C_{30}H_{20}ON_2$	424		—	—	40	—

Reactions of 4-Anilino-1,2-naphthoquinone(XVIIe) with Aromatic Amines——A solution of XVIIe (10^{-4} mole) in 30 ml of EtOH was added to a solution of aromatic amine (1-naphthylamine, 2-naphthylamine, and aniline) (1.2×10^{-4} mole) in small amount of EtOH. The solution was allowed to stand for 12 hr at room temperature. 4-(2′-Naphthylamino)-1-(2′-naphthylimino)-2-oxo-naphthalene (XVIIIb), which was obtained from the reaction of XVIIe with 2-naphthylamine in almost quantitative yield, was recrystallized from EtOH to give reddish purple solid, mp 256—258°. *Anal.* Calcd. for $C_{30}H_{20}ON_2$: 424.157540. Found: 424.157057. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3300 (=NH), disappearance of absorption of CO group. 2-Oxo-4-phenylamino-1-phenylimino-naphthalene(XVIIIa) obtained from the reaction of XVIIe with aniline was recrystallized from EtOH to give red solid, mp 176—178°. Mass Spectrum *m/e*: 324 (M^+). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3298 (=NH), disappearance of absorption of CO group. NMR (DMSO) τ: 1.5—2.8 (14H, Ar-H), 4.15 (1H, broad s, vinyl proton).

The Oxidation of 2-Naphthylamine with Fremy's Salt——A solution of 2-naphthylamine (10^{-3} mole) in 5 ml of MeOH was added, with stirring, to a solution of 536 mg of potassium nitrosodisulfonate in 8 ml of 1/6 M KH_2PO_4 and 30 ml of water. The solution was allowed to stand at 5—10°, and the brownish red solid that precipitated were recrystallized from EtOH to afford 55 mg (13%) of XVIIIb. The filtrated solution was extracted with $CHCl_3$. The extract was dried over Na_2SO_4, $CHCl_3$ was evaporated, and the residue was purified through silica gel column chromatography ($CHCl_3$) to afford 16 mg (5.4%) of 2-amino-1-naphthylimino-4-oxo-naphthalene(XIX) as red solid, mp 145—148°. IR ν_{max}^{KBr} cm^{-1}: 3370, 3520 ($-NH_2$). NMR ($CDCl_3$) τ: 3.84 (1H, s, vinyl proton), 5.33 (2H, broad, $-NH_2$). Mass Spectrum *m/e*: 298 (M^+).

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