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Isolation of a Novel Oxygenated Dimer of 3-Methylindole, 5aβ(*H*),11aα(*H*)-12β-Hydroxy-10bβ,12α-dimethyl-5a,10b,11a,12-tetrahydro-6*H*-oxazolo-[3,2-*a*:4,5-*b*']diindole, and Structure Determination of Its Acetylated Derivative

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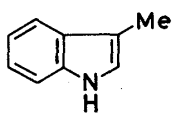
A new oxygenated dimer of 3-methylindole was isolated from the reaction mixture obtained by oxygenation of 3-methylindole in the presence of a sterically crowded cobalt catalyst, *N,N'*-(*cis*-1,2-cyclohexylene)bis(3-*tert*-butylsalicylideneaminato)cobalt(II). X-Ray crystal structure determination of its acetylated derivative revealed it to be 6-acetyl-5aβ(*H*),11aα(*H*)-12β-hydroxy-10bβ,12α-dimethyl-5a,10b,11a,12-tetrahydro-6*H*-oxazolo[3,2-*a*:4,5-*b*']diindole, with a novel C_6–C_4N–C_3NO–C_4N–C_6 ring system. Two conformers due to restricted rotation of the acetyl group of the acetylated derivative was observed by temperature-dependent ^{1}H-nuclear magnetic resonance spectroscopy.

Keywords——3-methylindole; oxygenation; dimerization; X-ray analysis; 6*H*-oxazolo[3,2-*a*:4,5-*b*']diindole; dynamic NMR

3-Methylindole (**1**) has been used as a substrate for oxygenation with several transition metal complexes used as models for tryptophan-2,3-dioxygenase, which cleaves L-tryptophan oxidatively to formylkynurenine.[1] The main product is 2-formylaminoacetophenone (**2**) in



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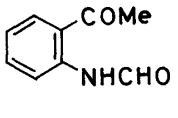

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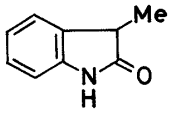

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the reaction catalyzed by *N,N'*-ethylenebis(salicylideneaminato)cobalt(II), Co(salen).[1a] A mechanistic study requires detailed product analysis but there have been few studies on the product distribution so far. On the other hand, there have been many studies in regard to the oxidation of indoles.[2] The oxidation reaction of **1** is known to proceed with ozone,[3a] peracids,[3b] hydrogen peroxide,[3c] *N*-bromosuccinimide,[3d] potassium persulfate,[3e] ascorbic acid–Fe system,[3f] and singlet oxygen (and photosensitized oxygenation),[3g] but again there seem to be few reports on product analysis, except that the main products are **2**,[3a,b,f,g] and 3-methyloxindole (**3**).[3c–e] Furthermore, oxygenation of **1** with indole side chain oxidase leads to the formation of indolemethanol.[4]

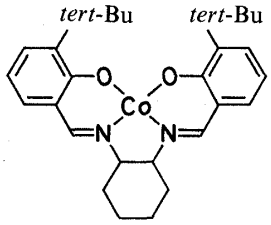
We have previously reported the catalytic oxygenation of **1** with sterically crowded Co(salen) derivatives.[5] With a larger substituent around the apical region in the square-planar Co(II) complexes, the induction period is longer but the rate of the oxygenation during the steady state is greater.[5] When methanol was used as a solvent, the main product was **2** but the use of chloroform as a solvent led to the formation of several products. We undertook

product analysis for the latter reaction, and one of the products was found to be a compound which is formed from one molecule of dioxygen and two molecules of **1** and has a novel ring structure. The results of the isolation and structural determination of this oxygenated dimer are presented here.

Results and Discussion

Oxygenation of 1 and Isolation of the Oxygenated Dimer (4)

A solution of **1** in chloroform was oxygenated in the presence of *N,N'*-(*cis*-1,2-cyclohexylene)bis(3-*tert*-butylsalicylideneaminato)cobalt(II) (**5**) at 25 °C. After 3 h, the re-



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action mixture was concentrated and chromatographed on a silica-gel column with a mixture of hexane and ethyl acetate. The chromatogram is shown in Fig. 1. The peaks were assigned by comparison of the ^{1}H- and ^{13}C-nuclear magnetic resonance (NMR) spectra with those in the literatures.[6] The fractions denoted by B and F yielded compounds which had similar spectral properties to each other. The compound **4** isolated from fraction B was subjected to a detailed study. The fraction from 6.0 through 7.9 dm^3 was collected and chromatographed again. Crystals of **4** were obtained from a mixture of ether and cyclohexane.

Properties of 4

The molecular weight of **4** was determined by high-resolution mass spectrometry which gave M^+ 294.139. In conjunction with elemental analysis (C, H, N), the formula was determined to be $C_{18}H_{18}N_2O_2$ (M^+, Calcd: 294.137). These results showed that **4** is composed of one molecule of O_2 and two molecules of **1**. The absorption maxima (λ_{max} nm (ε): 239 (18500) and 290 (4390)) indicate that **4** is not an indole or indolenine but an indoline;[7] O–H (3580 cm^{-1}) and N–H (3430 cm^{-1}) stretching absorptions were found in the infrared (IR) spectrum (CCl_4) but no carbonyl stretching absorption was found. The ^{1}H- and ^{13}C-NMR

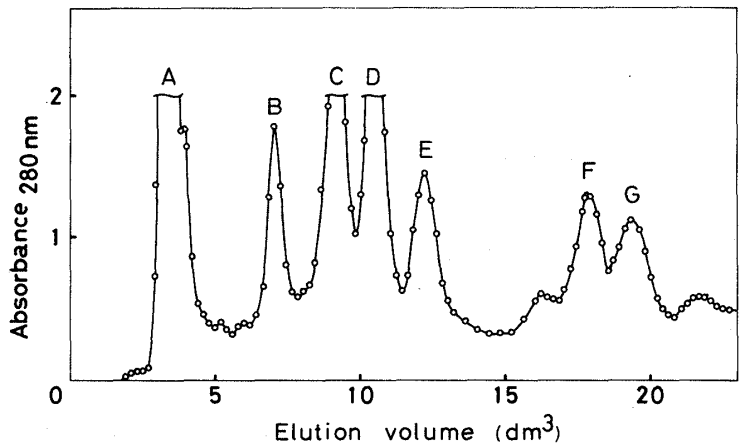


Fig. 1. Separation of Oxygenation Products of **1** on Silica Gel

spectra showed that the two molecules of **1** were unsymmetrically combined. Two ^{1}H-NMR signals (3.08 and 4.42 ppm) disappeared on addition of D_2O, as expected from the IR results. The results of NMR measurements will be discussed later.

Acetylation of 4

Acetylation with acetic anhydride in pyridine at 50 °C afforded the mono-acetylated derivative (**6**), which lacked an N–H stretching band but showed amide bands in the IR spectrum. Deacetylation was carried out with NaOH in methanol and the deacetylated product was found to be **4** from the ^{1}H-NMR spectrum. Thus, it was concluded that no change in the ring structure occurred during acetylation. An X-ray crystallographic study was carried out with **6**.

Structural Determination of 6

In order to establish the structure unequivocally, **6** was subjected to X-ray crystallographic analysis. The crystal structure was solved by the direct method with the MULTAN program[8] and refined by the block-diagonal least-squares method with the UNICS III program,[9] with anisotropic thermal factors for non-hydrogen atoms. The final R value was 0.073.

The final atomic coordinates and thermal factors are listed in Table I, together with their estimated standard deviations. Compound **6** was determined to have the structure shown in Fig. 2, and the structure of **4** is also shown. Two molecules of **1** are connected by bonds formed between the nitrogen of a molecule of **1** and the 2-position carbon of the second molecule of **1** and by the oxygen atom inserted between the 3-position and 2-position carbons of these molecules. Two oxygen atoms were incorporated separately; one as part of an ether and the other as a hydroxyl group at the 3-position of one of the parent 3-methylindole

TABLE I(a). Fractional Atomic Coordinates ($\times 10^4$) for Non-hydrogen Atoms

Atom	x	y	z
O1	5863 (2)	2649 (1)	7147 (4)
O2	4543 (2)	1530 (2)	6261 (4)
O3	9256 (3)	2888 (2)	12728 (5)
N1	8171 (3)	2917 (2)	9931 (4)
N2	7312 (3)	1917 (2)	8153 (4)
C1	7626 (3)	3556 (2)	10131 (6)
C2	7803 (4)	4035 (3)	11558 (6)
C3	7178 (5)	4626 (3)	11449 (7)
C4	6375 (4)	4753 (3)	9934 (8)
C5	6193 (4)	4272 (2)	8471 (7)
C6	6830 (3)	3671 (2)	8580 (6)
C7	6802 (3)	3092 (2)	7215 (6)
C8	7773 (3)	2622 (2)	8079 (5)
C9	6826 (4)	3335 (3)	5266 (6)
C10	8958 (3)	2616 (3)	11223 (6)
C11	7348 (3)	1465 (2)	6620 (5)
C12	8216 (3)	1332 (2)	5771 (6)
C13	8056 (4)	849 (3)	4355 (7)
C14	7081 (4)	508 (2)	3764 (6)
C15	6217 (4)	655 (2)	4630 (6)
C16	6372 (3)	1134 (2)	6077 (5)
C17	5592 (3)	1375 (2)	7271 (5)
C18	6181 (3)	2025 (2)	8213 (5)
C19	5449 (4)	829 (2)	8734 (6)
C20	9454 (4)	1938 (3)	10761 (7)

TABLE I(b). Anisotropic Temperature Factors ($\times 10^5$)[a]

Atom	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
O1	454 (21)	195 (9)	2203 (72)	−41 (11)	−79 (31)	−27 (21)
O2	399 (21)	334 (11)	1825 (68)	−53 (12)	−17 (30)	31 (23)
O3	1292 (39)	566 (17)	1919 (81)	114 (21)	−552 (45)	−255 (32)
N1	543 (26)	260 (12)	1114 (69)	−49 (15)	−24 (34)	−81 (24)
N2	383 (23)	218 (11)	1309 (68)	−41 (13)	69 (32)	−15 (23)
C1	631 (35)	227 (14)	1495 (91)	−83 (19)	267 (45)	18 (30)
C2	955 (45)	275 (17)	1938 (113)	−184 (23)	372 (58)	−254 (36)
C3	1122 (53)	248 (17)	2784 (137)	−159 (25)	631 (69)	−218 (40)
C4	782 (43)	236 (16)	3704 (162)	−43 (22)	645 (67)	−87 (42)
C5	704 (40)	172 (14)	3093 (138)	−41 (19)	346 (59)	32 (36)
C6	635 (35)	180 (13)	1857 (102)	−33 (18)	365 (48)	30 (30)
C7	515 (32)	219 (14)	1555 (91)	−36 (17)	108 (44)	17 (30)
C8	484 (30)	204 (13)	1199 (82)	13 (17)	93 (40)	43 (27)
C9	811 (42)	368 (19)	1599 (102)	44 (23)	109 (53)	239 (37)
C10	538 (35)	369 (18)	1623 (99)	−64 (21)	−130 (46)	−74 (35)
C11	480 (30)	197 (13)	1170 (81)	44 (16)	126 (39)	8 (27)
C12	508 (33)	281 (16)	1793 (101)	46 (19)	226 (46)	−58 (34)
C13	782 (42)	306 (17)	2196 (117)	55 (21)	560 (58)	−108 (37)
C14	976 (46)	242 (16)	1868 (110)	−8 (22)	343 (57)	−216 (33)
C15	685 (38)	246 (15)	1546 (98)	−52 (19)	−30 (48)	−116 (31)
C16	468 (30)	211 (13)	1123 (78)	−38 (16)	41 (39)	−36 (27)
C17	448 (30)	227 (14)	1363 (86)	−19 (17)	70 (41)	−48 (29)
C18	402 (28)	239 (14)	1238 (82)	18 (17)	72 (38)	−15 (29)
C19	692 (39)	265 (16)	1883 (108)	−66 (20)	222 (53)	112 (34)
C20	664 (39)	332 (18)	2276 (119)	16 (22)	−138 (54)	46 (38)

a) These are of the form $\exp[-(h^2B_{11}+k^2B_{22}+l^2B_{33}+2hkB_{12}+2hlB_{13}+2klB_{23})]$.

TABLE I(c). Fractional Atomic Coordinates ($\times 10^3$) and Isotropic Temperature Factors for Hydrogen Atoms

Atom	x	y	z	B/Å^2
HO2	448 (3)	182 (2)	504 (6)	5.2 (1.1)
H2	849 (3)	393 (2)	1278 (5)	4.2 (0.9)
H3	725 (4)	502 (3)	1239 (6)	7.4 (1.3)
H4	590 (3)	514 (2)	990 (5)	4.5 (1.0)
H5	557 (3)	434 (2)	717 (5)	4.9 (1.0)
H8	839 (3)	265 (2)	726 (5)	3.0 (0.8)
H91	746 (3)	356 (2)	511 (6)	5.1 (1.1)
H92	619 (3)	367 (2)	494 (5)	3.5 (0.9)
H93	672 (3)	286 (2)	450 (6)	6.3 (1.2)
H12	898 (3)	158 (2)	638 (5)	4.7 (1.0)
H13	859 (4)	77 (2)	369 (6)	7.2 (1.3)
H14	696 (3)	12 (2)	289 (5)	5.0 (1.0)
H15	550 (4)	44 (2)	410 (6)	6.0 (1.2)
H18	602 (3)	211 (2)	946 (5)	4.8 (1.0)
H191	490 (3)	105 (2)	953 (5)	4.7 (1.0)
H192	616 (3)	74 (2)	938 (5)	3.2 (0.9)
H193	515 (3)	49 (2)	819 (6)	5.4 (1.1)
H201	1011 (3)	192 (2)	1164 (5)	3.7 (0.9)
H202	896 (3)	150 (2)	1081 (5)	4.7 (1.0)
H203	960 (3)	194 (2)	955 (6)	5.4 (1.1)

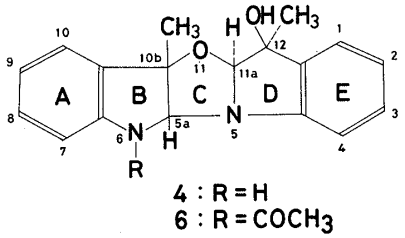


Fig. 2. Schematic Structures of **4** and **6**

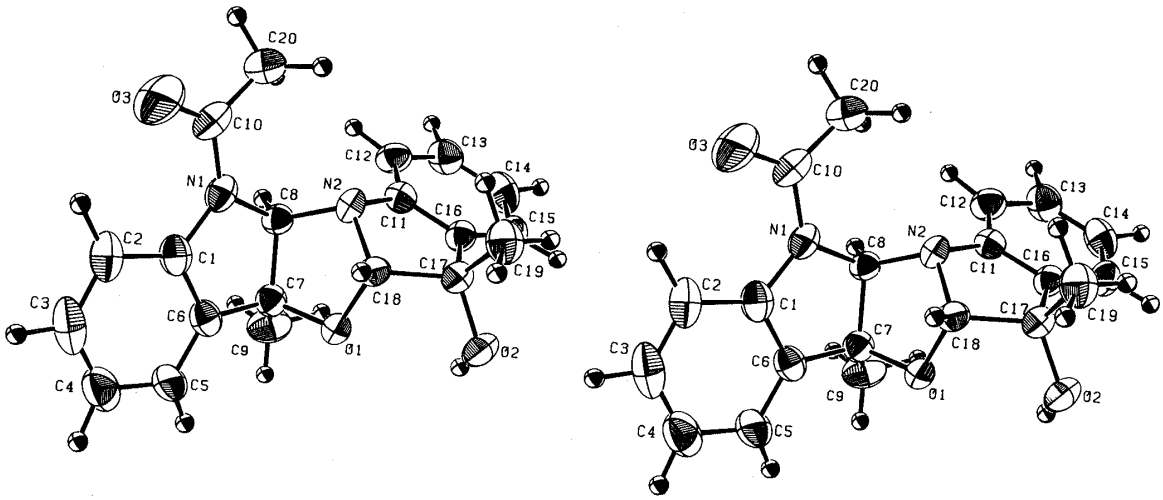


Fig. 3. A Stereoscopic Structural View and Atom Numbering of **6**

Non-hydrogen atoms are drawn as thermal ellipsoids at the 50% probability level.

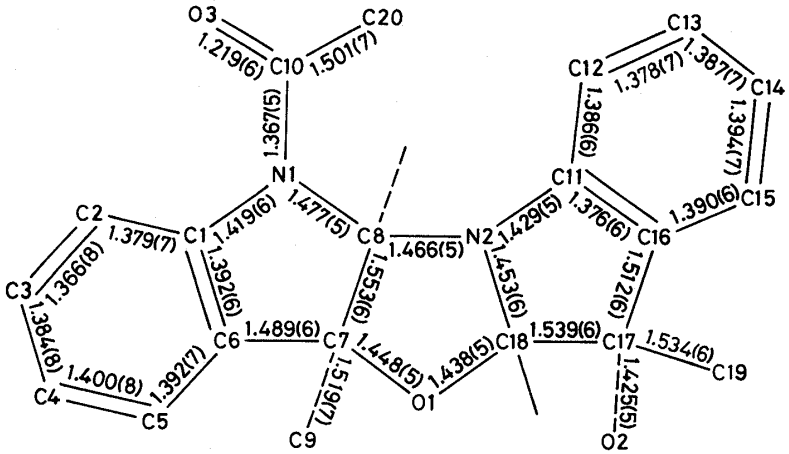


Fig. 4. Selected Bond Lengths (l/Å) in **6**

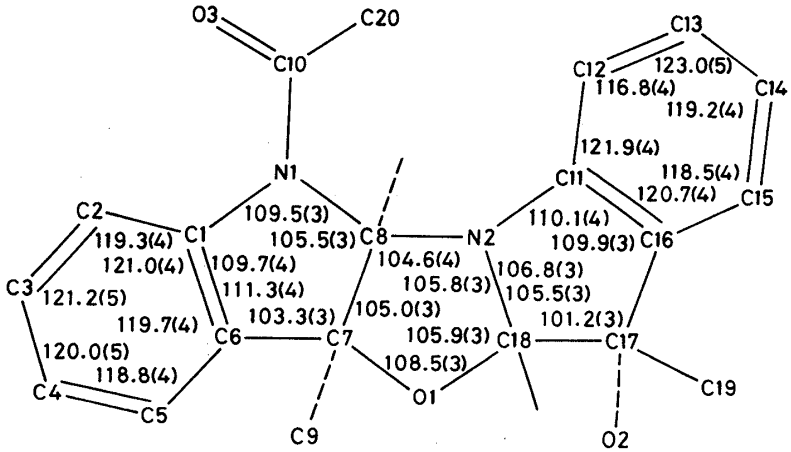


Fig. 5. Selected Bond Angles (θ/°) in **6**

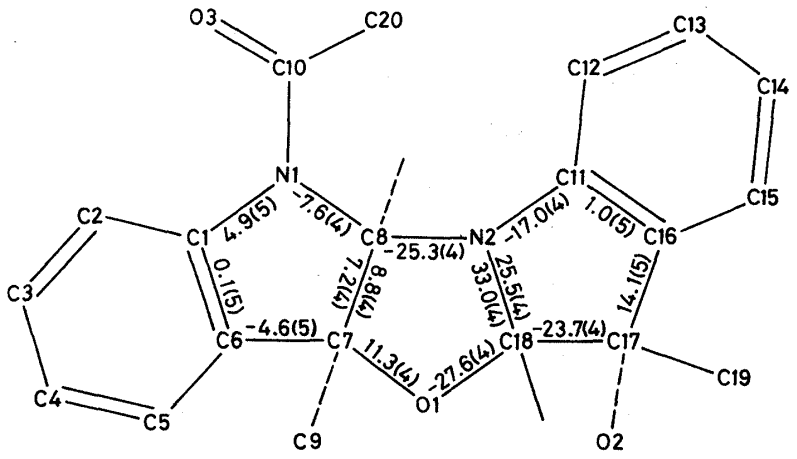


Fig. 6. Dihedral Angles (ϕ/°) in the Three Successive Five-Membered Rings in **6**

molecules. They are located *cis* to each other.

This compound is a derivative of 6*H*-oxazolo[3,2-*a*:4,5-*b*']diindole, no derivative of which has previously been reported. A stereoscopic view of the molecule is shown in Fig. 3 along with the numbering of the atoms. The central perhydrooxazole ring (C) is fused with two indole rings (AB and DE) to form a *cis–anti–cis* structure. The angle between the least-squares planes B and C is 64.8° and that between the least-squares planes C and D is 69.7°. Bond lengths and bond angles are given in Figs. 4 and 5, respectively. The torsional angles in the five-membered rings are give in Fig. 6. Owing to the outer flanks of benzene rings, the B and D rings have approximately an envelope conformation, but ring C has a deformed half-chair conformation and the dihedral angles are close to those found in the central rings of Δ9(12)-capnellene-3β,8β,10α-triol (**7**).[10] Small values of torsional angles around the C7–C8 bond, where C7 is substituted with a methyl group, have also been reported for **7**.[10]

The molecules in the crystal are connected by two hydrogen bonds, O2-H(O2)···O3, in the direction of the *c* axis, where the distance between O2 and O3 is 2.796(4) Å.

^{1}H- and ^{13}C-NMR Spectra of 4 and 6

The ^{1}H- and ^{13}C-NMR spectra of **4** and **6** are closely related and the chemical shifts of **6** are indicated in parentheses below. A feature of the NMR spectra is the fact that the corresponding two nuclei in the parent, **1**, have different chemical shifts after the oxidative dimerization. In ^{1}H-NMR of **4**(**6**), two singlets due to methine protons are observed at 4.69 (4.61) and 5.10 (5.54 and 5.71) ppm. The difference in chemical shifts is ascribed to the different numbers of heteroatoms around the α-carbons: C_{5a} has two nitrogens and one carbon, while C_{11a} has one oxygen, one nitrogen, and one carbon. The singlet of **4** at 5.10 ppm moved to 5.54 and 5.71 ppm on acetylation, and thus it is assigned to H-C_{5a}.

The temperature-dependent ^{1}H-NMR spectra of **6** in the methine region are reproduced in Fig. 7. With increase of the temperature, the two singlets at 5.54 and 5.71 ppm coalesced at 40 °C giving a singlet at 5.55 ppm. On lowering the temperature, the singlet at 4.61 ppm showed a shoulder on the high-field side and split at 0 °C into two singlets with unequal intensities at 4.63 and 4.55 ppm. At −20 °C, the lower side methyl resonance was split into two signals at 1.62 and 1.66 ppm. The intensity ratio of the set around 5.6 ppm was 0.76 to 0.26, irrespective of the temperature between 20 and −40 °C.

In the ^{13}C-NMR spectra, 18 and 20 signals were observed for **4** and **6**, respectively. In the methyl carbon region, the signals at 24.2 (24.6) and 26.0 (25.4) ppm are assigned to $\underline{C}H_3$-C_{10b} and $\underline{C}H_3$-C_{12} supplemented with a quartet at 24.9 ppm for **6**. In the region between 70 and 105 ppm, both **4** and **6** showed two singlets and two doublets. The difference in chemical shifts between the two singlets was large, 13.1 ppm (*i.e.* 77.2 (77.3) for C_{12} and 90.3 (88.1) ppm for

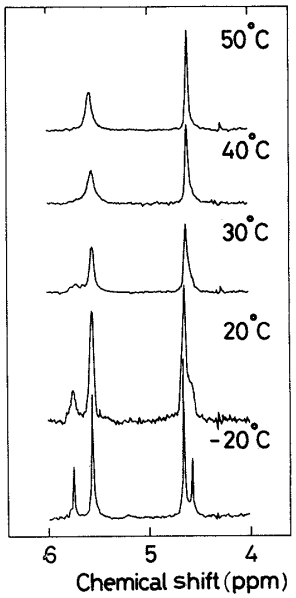


Fig. 7. Variable-Temperature ^{1}H-NMR Spectra of the Methine Protons of **6** in $CDCl_3$

C_{10b}, and is ascribed to the difference between the α-substituent effect of *tert*-alcohol (35—52 ppm) and ether (9—10 ppm downfield from the corresponding alcohol).[11] The difference in chemical shifts between the two doublets was also large, *i.e.* 11.5 ppm. The atoms adjacent to the C_{5a} and C_{11a} carbons differ in the number of heteroatoms as described in the analysis of the ^{1}H-NMR spectra, and therefore the doublets at 88.5 (89.1) and 100.3 (100.0) ppm are assigned to C_{5a} and C_{11a}, respectively.

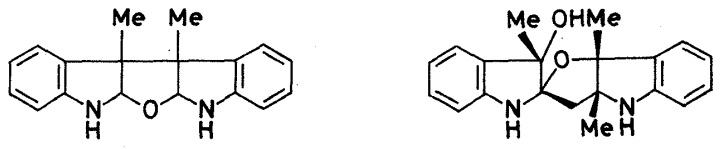
In the aromatic region, two pairs of singlets and four pairs of doublets were observed. Rings A and E should have features characteristic of the aromatic ring of indoline derivatives. Based on ^{13}C-NMR studies of indolines,[12c,d] and indole alkaloids,[13] the aromatic carbons of **4** were expected to be classified into six pairs which resonate at approximately the following chemical shifts: (C_4, C_7), 110; (C_2, C_9), 119; (C_1, C_{10}), 121; (C_3, C_8), 128; (C_{10a}, C_{12a}), 132; and (C_{4a}, C_{6a}), 149 ppm. It is difficult to assign the carbon atoms of each pair to the A and E rings. If the AB and ED rings are assumed to be indoline derivatives, factors which would influence the difference between the two skeletons are as follows: (i) the nitrogen atom is secondary for the AB ring but tertiary for the ED ring, and (ii) C_{10b} in the AB ring is adjacent to an ether oxygen while C_{12} in the ED ring is adjacent to a hydroxyl group. An application of the substituent increments rule leads to tentative assignments for **4** (see Experimental) by use of the following values:[11] Z_1, Z_o, Z_m, and Z_p (ppm) are 13.3, −0.8, 0.6, and −0.4 for $-CH_2OH$; 10.5, −0.5, 0.5, and −0.5 for $-CH_2OCH_2C_6H_5$; 21.9, −16.4, 0.6, and −12.6 for $-NHCH_3$; and 22.2, −15.8, 0.5, and −11.8 for $-N(CH_3)_2$, respectively. The acetylation of indoline nitrogen is expected to cause downfield shifts for C_7, C_8, C_9, C_{10}, and C_{10a} by 7.5, 0—0.2, 6.5, 0—2, and 6 ppm, respectively, and to cause an upfield shift for C_{6a} by 8.5 ppm.[13] Based on these values, the aromatic carbons of **6** were assigned and the results are given in Experimental. Furthermore, a small broad signal was observed at 113.8 ppm for **6**.

The temperature-dependent ^{1}H-NMR phenomena can be ascribed to either (i) ring reversal about the tertiary amine nitrogen (N_5),[14] or (ii) restricted rotation of the amide group.[15] As regards the former case, the inversion of two nitrogen atoms at the bridgehead of two fused five-membered rings has been reported for an alkyl derivative of 1,5-diazabicyclo[3.3.0]octane.[16] As regards the latter case, the hindered rotation of acyl groups has been investigated by ^{1}H- and ^{13}C-NMR spectroscopy for *N*-acyl indoline derivatives.[12] Though the acetyl methyl protons of **6** did not show any broadening on decrease of the

temperature, the temperature-dependency in the NMR spectrum was concluded to occur because of restricted rotation of the acetyl group, since (a) no broadening of the signals of H-C_{5a} and H-C_{11a} was observed even at $-50\,°C$ in the ^{1}H-NMR spectrum of **4**, (b) a broadening of the doublet at 8.3 ppm was observed in the ^{1}H-NMR spectrum of **6** on increasing the temperature (this signal can be assigned to H-C_7, which is in close proximity to the acetyl C=O group [12a,b]), and (c) a broad signal assignable to C_7 was observed at 113.8 ppm in the ^{13}C-NMR spectrum of **6**.[12c] Based on the results for *N*-acyl indole derivatives, the signals for H-C_7 and C_7 of **6** are expected to move upfield on changing from an *endo*- to an *exo*-conformer with respect to the orientation of the acetyl group.[12] The predominance of *endo*-form is in agreement with the structure determined by X-ray crystallography described above.

Reaction Path Leading to the Formation of 4

Oxidative dimerization of alkyl indoles has been reported to give 11b,11c-dimethyl-5,5a,6a,7,11b,11c-hexahydrofuro[2,3-*b*:5,4-*b*′]diindole (**8**)[1f] and 3′-hydroxy-3′,3a,8b-trimethyl-3,3a,4,8b-tetrahydrospiro[2*H*-furo[3,2-*b*]indole-2,2′-indoline] (**9**).[7,17] The former has been reported to be formed from **1** in the presence of $Cu^{II}(OCH_3)_2$, under oxygen-free conditions and the latter has been reported to be formed from 2,3-dimethylindole in the presence of oxygen. The mechanism of formation of **9** involves the reaction between 3-hydroxy-2,3-dimethyl-3*H*-indole and its enamine tautomer, which are produced from 3-hydroperoxy-2,3-dimethyl-3*H*-indole.[17]



8 **9**

However, the oxidative dimerization of **1** to **4** should proceed along paths different from those involved in the production of **8** and **9**. Two possible paths are shown in Fig. 8 to account for the bond formation between the nitrogen center of a molecule of **1** and the 2-position of the other **1**. The carbon atom in the imine is electrophilic and is expected to be susceptible to the attack of the lone pair of a nitrogen or oxygen atom. This occurs in the dimerization of two molecules of 3-hydroxy-3-methyl-3*H*-indole, derived from 3-hydroperoxy-3-methyl-3*H*-

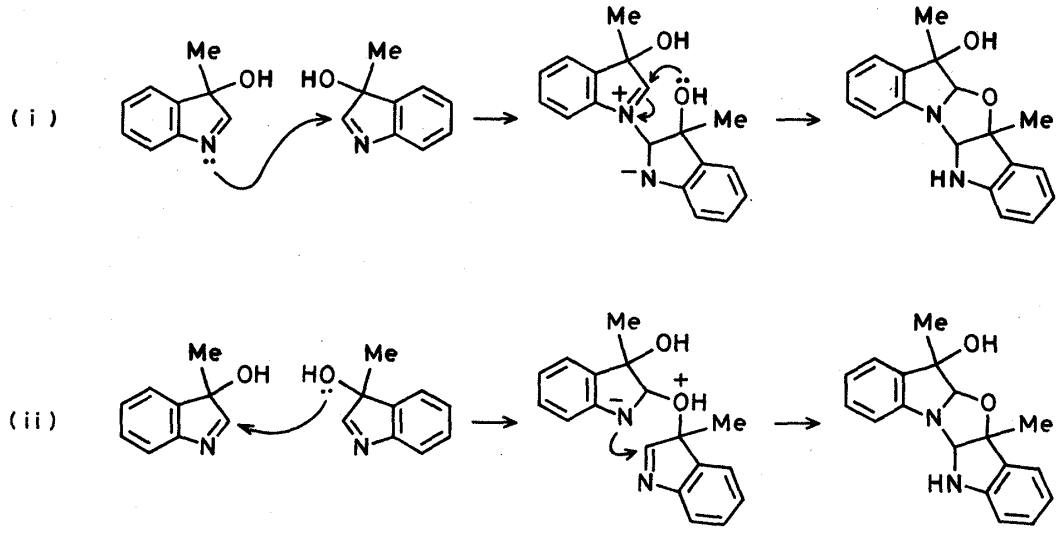


Fig. 8. Possible Mechanisms of the Formation of **4**

indole which is formed from **1** by oxygenation with the cobalt complex. In both cases, however, the second intramolecular nucleophilic attack of the hydroxyl group or the nitrogen anion in the ring closure will be non-stereospecific and two geometric isomers with respect to the relative positions of the two oxygen atoms are possible. A study on the structure of another dioxygenated dimer isolated from fraction F is under way to clarify the stereochemistry of this dimerization.

Experimental

All the materials were prepared or purified according to the methods reported previously.[5] Mass spectra (MS) were measured on a Hitachi M-80A mass spectrometer. Infrared (IR) spectra were obtained with a JASCO IRA-1 spectrophotometer. ^{1}H-NMR spectra were recorded on a JEOL MH-100 spectrometer. Temperature-dependent ^{1}H-NMR spectra were recorded on a JEOL FX-100 spectrometer operated at 99.6 MHz. Typical acquisition parameters were as follows: spectral width 2000 Hz and flip angle 45° with 8192 data points. ^{13}C-NMR spectra were recorded on a JEOL FX-100 spectrometer operated at 25.05 MHz. Typical acquisition parameters were as follows: spectral width 5000 Hz, flip angle 26°, and pulse delay 3—4 s with 8192 data points. All the chemical shifts are given in δ values relative to internal tetramethylsilane. Ultraviolet (UV) and visible spectra were recorded on a Shimadzu UV-210A spectrophotometer. All melting points are uncorrected.

Oxygenation of 1 and Isolation of 4——A Co catalyst, **5** (0.134 g, 2.7×10^{-4} mol), was added to a chloroform solution of **1** (2.5 g in 220 cm^3), and oxygen was passed through the mixture at a rate of 40 cm^3 min^{-1}. After 3 h, the resulting dark brown mixture was concentrated to a volume of about 5 cm^3. This product was chromatographed on a silica-gel column (Wakogel C-200, 6×70 cm); stepwise elution was carried out with mixtures of hexane and ethyl acetate: 5 : 1, 8 dm^3; 4 : 1, 8 dm^3; and 3 : 1, 13 dm^3. The fraction of 6.0 dm^3 through 7.9 dm^3 was collected and concentrated to give a viscous red-brown oil which eventually crystallized on standing at room temperature. Yield, 0.14 g.

The crude product was chromatographed again with a mixture of hexane and ethyl acetate (5 : 1). Yield, 96 mg. The product was recrystallized from a mixture of ether and cyclohexane. Yield, 34 mg. mp 146—148 °C. *Anal.* Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.71; H, 5.95; N, 9.38. ^{1}H-NMR ($CDCl_3$) δ: 1.44 (3H, s, CH_3), 1.55 (3H, s, CH_3), 3.08 (1H, br s, OH), 4.42 (1H, br s, NH), 4.69 (1H, s, H-C_{11a}), 5.10 (1H, s, H-C_{5a}), 6.65—7.41 (8H, m, arom. H). ^{13}C-NMR ($CDCl_3$) δ: ambiguity remains in the assignment of the signals indicated by [ ], 24.2 (q, CH_3), 26.0 (q, CH_3), 77.2 (s, C_{12}), 88.5 (d, C_{5a}), 90.3 (s, C_{10b}), 100.3 (d, C_{11a}), [109.5 (d, C_7), 112.1 (d, C_4)], [119.5 (d, C_9), 122.2 (d, C_2)], [123.9 (d, C_1), 124.4 (d, C_{10})], [129.3 (d, C_3), 130.1 (d, C_8)], [128.4 (s, C_{10a}), 135.2 (s, C_{12a})], [148.8 (s, C_{4a}), 149.5 (s, C_{6a})]. IR (2%, CCl_4): 3580 (νO–H), 3430 (νN–H) cm^{-1}. MS *m/e*: 294.137 (M^+).

Acetylation of 4——**4** (13 mg) was dissolved in pyridine (0.2 cm^3) and acetic anhydride (0.2 cm^3) was added. The mixture was stirred for 30 min at 50 °C. Chloroform (6 cm^3) was added to the mixture and the chloroform layer was washed three times with 4 cm^3 portions of water then dried over sodium sulfate. The chloroform solution was concentrated and dissolved again in a small portion of chloroform (0.05 cm^3). Petroleum ether (1.0 cm^3) was added until the solution became turbid, and the mixture was kept in an ice-water bath to yield pale brown crystals. These were recrystallized from petroleum ether. Yield, 8 mg. mp 218—220 °C (dec.). *Anal.* Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.08; H, 6.14; N, 8.15. ^{1}H-NMR ($CDCl_3$, 20 °C) δ: 1.45 (3H, s, CH_3), 1.59 (3H, s, CH_3), 2.57 (3H, s, CH_3CO), 3.00 (1H, br s, OH), 4.61 (1H, s, H-C_{11a}), 5.54 and 5.71 (1H (3 : 1), each br s, H-C_{5a}), 6.95—7.44 (7H, m, arom. H), 8.31 (*ca.* 1H, br d, J=8 Hz). ^{13}C-NMR ($CDCl_3$) δ: ambiguity remains in the assignment of the signals indicated by [ ], [24.6 (q, CH_3), 24.9 (q, CH_3CO), 25.4 (q, CH_3)], 77.3 (s, C_{12}), 88.1 (s, C_{10b}), 89.1 (d, C_{5a}), 100.0 (d, C_{11a}), 111.0 (d, C_4), 116.7 (d, C_7), [123.0 (d, C_2), 123.9 (d, C_1), 124.4 (d, C_{10}), 124.5 (d, C_9)], [129.5 (d, C_3), 130.4 (d, C_8)], 130.2 (s, C_{10a}), 135.5 (s, C_{12a}), 142.6 (s, C_{6a}), 147.8 (s, C_{4a}). IR ($CHCl_3$): 3570 (νO–H), 1670 (νC=O, amide) cm^{-1}. MS *m/e*: 336.149 (M^+, Calcd for $C_{20}H_{20}N_2O_3$: 336.148).

Deacetylation of 6——A solution of **6** (15 mg) in 0.2 N NaOH–methanol (5 cm^3) was refluxed for 12 h. The reaction mixture was concentrated to a volume of about 2 cm^3, and then diluted with chloroform (9 cm^3), washed twice with water (5 cm^3), dried, and evaporated to leave a yellowish residue. This was chromatographed on a silica-gel column (Wakogel C-200, 1.5×12 cm) with hexane–2-propanol (20 : 1). Yield, 5 mg. The ^{1}H-NMR spectrum of the deacetylated product was identical with that of **4**.

X-Ray Diffraction Study of 6——A clear pale brown crystal of **6** with approximate dimensions of $0.58 \times 0.40 \times 0.22$ mm was mounted on the end of a glass fiber. Preliminary reflection data indicated the crystal system to be monoclinic with systematically absent reflections ($h0l$ for $h \neq 2n$ and $0k0$ for $k \neq 2n$) uniquely determining its space group as $P2_1/a$.

The lattice constants were determined by a least-squares fit of 43 reflections ($20° < 2\theta < 30°$) measured with a Rigaku AFC-5 automatic diffractometer with graphite-monochromated Mo$K\alpha$ radiation (λ=0.71073 Å) by using the operating system of the AFC-5. The observed density was measured by floatation on aqueous solutions of sodium chloride and potassium iodide.

The crystal data: $C_{20}H_{20}N_2O_3$, mol. wt. 336.39, monoclinic, $P2_1/a$, $a=12.640$ (2), $b=19.000$ (2), $c=7.393$ (1) Å, $\beta=100.89$ (1)°, $U=1743.5$ (4) Å^3, $Z=4$, $D_c=1.282$, $D_m=1.275\,g\,cm^{-3}$, $\mu(MoK\alpha)=0.941\,cm^{-1}$.

The intensity data were measured on the Rigaku diffractometer by using the θ–2θ scan technique with graphite-monochromated Mo$K\alpha$ radiation; 2θ was varied from 2° to 60°. The range of each scan, taken at 3°/min, consisted of the base width of 1.1° at $2\theta=0°$ and an increment of $\Delta(2\theta)=(0.5\tan\theta)°$; backgrounds were recorded for 8 s at each extremity of the reflection scan and were assumed to very linearly across the scan. The intensities of three reflections, measured at 97 reflection intervals to monitor the stability of the system, displayed no trend of change with time.

The intensity data were reduced to values of $|F_O|$ and $\sigma(F_O)$ by using the UNICS III program.[9] Sample corrections for the effects of absorption were not made for the intensity data. The number of reflections scanned was 6098, and 2581 reflections (independent reflections: 2290) with $|F_O|>3\sigma(F_O)$ were retained for use in the subsequent structure analysis.

Structure Determination and Refinement——The structure was solved by the direct method.[8] Atomic coordinates and anisotropic thermal factors of the 25 peaks (C, N, O) obtained by Fourier synthesis were refined by a block-diagonal least-squares analysis to give the R value of 0.1371. Difference Fourier syntheses revealed all of the hydrogen atoms. Upon convergence, the R and R_w values were 0.0731 and 0.0794 for 2054 independent reflections with $|F_O|>3.0\sigma(F_O)$, where:

$$R=\frac{\sum||F_O|-|F_C||}{\sum|F_O|}$$

$$R_w=\left[\frac{\sum w(|F_O|-|F_C|)^2}{\sum w|F_O|^2}\right]^{1/2}$$

$$w=[(\sigma(F_O))^2+0.015|F_O|^2]^{-1}$$

The quantity minimized during the least-squares refinement was $\sum w(|F_O|-|F_C|)^2$.

Atomic scattering factors and corrections for anomalous dispersion were taken from ref. 19. Calculations were performed on the HITAC M-200H computer at the Institute for Molecular Science with the MULTAN78[8] and UNICS III[9] program packages.

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6) The assignments and yields of the isolated compounds were as follows: A, 3-methylindole, 0.23 g; B, **4**, 0.14 g; C, unknown, 0.12 g; D, 2-formylaminoacetophenone,[1a] 0.41 g; E, 11b,11c-dimethyl-5,5a,6a,7,11b,11c-hexahydrofuro[2,3-*b*:5,4-*b*']diindole,[1f] 0.17 g; F, the other dimer, 0.15 g; G, 3-methyloxindole,[18] 0.17 g. Fraction C was a mixture of at least eight substances as determined by high-performance liquid chromatography measurement.

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