Chem. Pharm. Bull.
29(12)3499—3506(1981)

Reactions of Indole with Hydroxyl Radicals and X-Ray Crystal Structure of a Novel Indole Trimer, 14-Acetyldiindolo[2,3-*a*: 2′,3′-*c*]carbazole[1]

TAKAO KANEKO,[a] MITSUYOSHI MATSUO,*,[a] and YOICHI IITAKA[b]

Tokyo Metropolitan Institute of Gerontology,[a] 35-2 Sakae-cho, Itabashi-ku,
Tokyo, 173, Japan and Faculty of Pharmaceutical Sciences,
University of Tokyo,[b] Bunkyo-ku, Tokyo, 113, Japan

(Received May 15, 1981)

When indole reacted with titanium(III)- or iron(II)-hydrogen peroxide systems, the products varied widely, depending on the pH of the reaction solutions. Under acidic conditions, indole gave rise to oxindole, 2,3′-biindole and a novel indole trimer, diindolo-[2,3-*a*: 2′,3′-*c*]carbazole. Under neutral conditions, indole was converted to oxindole, hydroxyindoles and 3,3′-biindole. The structure of the trimer was determined by X-ray diffraction analysis of its monoacetyl derivative. A possible mechanism for the formation of the products is proposed.

Keywords——indole trimer; diindolocarbazole; hydroxyl radical; Fenton's reagent; titanium(III)-hydrogen peroxide system; X-ray crystallographic analysis; ^{1}H-NMR; ^{13}C-NMR

The reactions of indoles with hydroxyl radicals have been studied using a variety of systems, *e.g.*, Fenton's reagent [iron(II)-hydrogen peroxide],[2] Udenfriend's system [iron(II)-molecular oxygen-ascorbic acid],[3] cobalt(II)- or copper(I)-molecular oxygen systems[4] and pulse radiolysis.[5] It has so far been found that under neutral conditions hydroxyl radicals add to indoles to produce hydroxylated derivatives.[2,3] However, we have observed that the reaction of indole with a titanium(III)-hydrogen peroxide system under acidic conditions gave a novel indole trimer, diindolo[2,3-*a*: 2′,3′-*c*]carbazole (3).[6]

Norman and his co-workers reported that both the concentration and the nature of the intermediate radicals might be strongly pH-dependent in the reactions of aromatics with Fenton's reagent,[7] while Snook and Hamilton suggested that the initial reactions were electron transfers to yield aromatic radical cations rather than addition.[8] The reaction products vary with the concentration of hydrogen ion.[9] Therefore, it was expected that a primary factor in determining what species of products were obtained from the reaction of indole with hydroxyl radicals would be the pH of the reaction systems.

In order to elucidate the character of the reactions, we have analyzed the products of reactions of indole with hydroxyl radicals under neutral and acidic conditions.

Results and Discussion

In the previous paper, we reported that, when suspended in the titanium(III)-hydrogen peroxide system, indole gave rise to oxindole (**1**), 2,3′-biindole (**2**) and diindolo[2,3-*a*: 2′,3′-*c*]-carbazole (**3**).[6] However, since we could not obtain reproducible results under the above conditions, we tried to treat indole with hydroxyl radicals in homogeneous solutions. The results are shown in Fig. 1 and Table I.

At pH 1.0, the reaction of indole with the titanium(III)-hydrogen peroxide couple gave **3** and a trace amount of **2**. Only **3** was obtained upon using iron(II) in place of titanium(III). When reacted with the iron(II)-hydrogen peroxide couple under homogeneous, weakly acidic conditions (pH 2.8), indole afforded **3** in a 19.6% yield. In this reaction mixture, **2** was not detected.

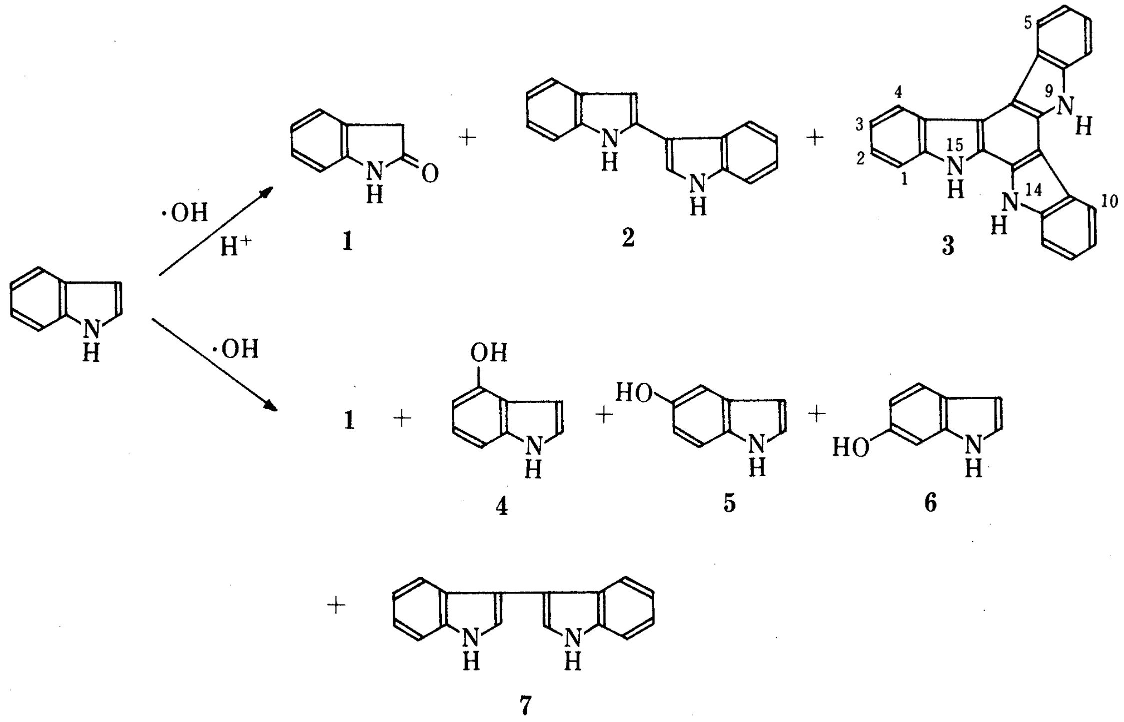


Fig. 1

TABLE I. Reactions of Indole with Hydroxyl Radicals[a)]

Run	Indole[b)] (mM)	Metal ions (mM)	H_2O_2 (mM)	Additive (mM)	EDTA (mM)	pH[c)]	% Yields (1)	(2)	(3)	(4)	(5)	(6)	(7)	Total	Indole recovered (%)
1	900[d)]	Ti^{3+}, 630	630	—	—	1.0	2.9	2.7	7.9	—	—	—	—	13.5	45.1
2	10	Ti^{3+}, 10	20	—	—	1.0	—	0.2	1.0	—	—	—	—	1.2	54.0
3	10	Fe^{2+}, 10	20	—	—	1.0	—	—	5.3	—	—	—	—	5.3	6.6
4	10	Fe^{2+}, 10	20	—	—	2.8	0.9	—	19.6	—	—	—	—	20.5	41.2
5	10	Ti^{3+}, 10[e)]	20	—	30	7.2	—	—	—	—	—	—	—	—	90.6
6	10	Fe^{2+}, 10	20	—	10	7.2	9.1	—	—	4.8	1.9	4.3	0.6	20.7	24.1
7	10	Fe^{2+}, 10	20	Cu^{2+}, 12	10	7.2	8.6	—	—	8.0	1.4	4.6	2.1	24.7	23.6
8	10	Fe^{2+}, 10	20	Mannitol, 20	10	7.2	12.9	—	—	5.7	5.4	5.4	5.8	35.2	46.3

a) All experiments were performed at room temperature.
b) Reactions were carried out in homogeneous solutions except for run 1.
c) At pH 1.0, a 0.2 N HCl–KCl buffer; at pH 2.8, 50 mM $HClO_4$; at pH 7.2, a 0.1 M potassium phosphate buffer.
d) Indole was in suspension.
e) Titanium(III) was precipitated as titanium(III) hydroxide.

On the basis of the reported data on the reactions of aromatics with hydroxyl radicals,[2,9)] indole was expected to provide other products in addition to **2** and **3** on treatment with hydroxyl radicals under neutral conditions. However, the titanium(III)-hydrogen peroxide system employed here could not function under neutral conditions, because titanium was precipitated from the solution as titanium(III) hydroxide. By the use of the neutral iron(II)-hydrogen peroxide system containing ethylenediaminetetraacetic acid to prevent iron from precipitating, indole was converted to **1**, 4-hydroxyindole (**4**),[3)] 5-hydroxyindole (**5**),[3)] 6-hydroxyindole (**6**)[3)] and 3,3′-biindole (**7**).[10)]

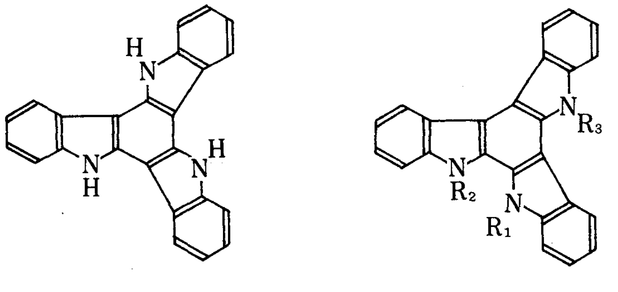
Since the addition of copper(II) has been found to increase the yields of phenolic products in the radical oxidation of benzene and its derivatives,[9)] the effect of copper(II) on the reaction of indole with hydroxyl radicals was examined. Copper(II), however, caused no significant increase in the yields of the hydroxyindoles.

The addition of mannitol, which can act as a hydroxyl radical scavenger,[11] resulted in increased yields of the products, and decreased formation of polymeric substances. In this case, mannitol may act as an inhibitor of a chain reaction leading to the formation of polymeric substances rather than as a trapper of hydroxyl radicals.

On the basis of the molecular ion peaks (both, *m/e* 232) in their mass spectra, **2** and **7** were anticipated to be indole dimers. In the ^{13}C nuclear magnetic resonance (NMR) spectrum, **2** exhibited sixteen signals, all of which were due to sp^2 carbons. The two signals at 134.9 and 110.2 ppm were assigned to C_2 and $C_{3'}$ bearing no hydrogen atom in an indole-indole dimer, respectively, by analogy with the chemical shifts of C_2 (135.4 ppm) in 2-methylindole and C_3 (111.2 ppm) in 3-methylindole.[12] Consequently, **2** was identified as 2,3′-biindole.[13] Since the ^{13}C-NMR spectrum of **7** showed only eight sp^2 carbon signals, **7** was ascertained to be a symmetric indole dimer. The signal at 111.6 ppm was assigned to quaternary C_3 in the dimer. This implies that **7** is 3,3′-biindole.[10] Oxindole (**1**) and hydroxyindoles (**4**—**6**) were identified on the basis of the melting points, the *Rf* values on thin-layer chromatography, the color characteristics with Ehrlich's reagent and the spectral data.[3,10]

By means of mass spectrometry and elemental analysis, the molecular formula of **3** was proved to be $C_{24}H_{15}N_3$ corresponding to an indole trimer. The ^1H- and ^{13}C-NMR spectra revealed that there was neither an aliphatic proton nor an sp^3 carbon atom in the molecule. The trimer was expected to be fully aromatized; the two candidates for the structure of the trimer are **3** and **8** (Figs. 1 and 2). Since the symmetric structure (**8**) may be ruled out in view of the fact that the trimer exhibits sixteen ^{13}C-signals, the trimer is presumed to be **3**. Recently, the N,N,N-trimethyl derivative of **3** has been prepared from the reactions of 3,3-bis(N-methyl-3-indolyl)-N-methylindoline with 2,3-dichloro-5,6-dicyanobenzoquinone, and of 2,3-bis(N-methyl-3-indolyl)-N-methylindole with *n*-butyllithium and copper(II) chloride.[14]

On acetylation, **3** gave two acetyl derivatives. As will be described later, it was shown by means of X-ray crystallographic analysis that the major derivative was **9a** (Figs. 2 and 3). Therefore, its mother compound was established to be **3**. Each of the derivatives displayed the same molecular ion peak at *m/e* 387 and a ^1H-signal due to an acetyl group (**9a**, 3.08 ppm; the other product, 3.06 ppm). They regenerated **3** upon treatment with sodium hydroxide solution. These results indicate that the minor product as well as **9a** is a monoacetyl derivative



8

9a: R_1=Ac, R_2=R_3=H
9b: R_2=Ac, R_1=R_3=H
9c: R_3=Ac, R_1=R_2=H

Fig. 2

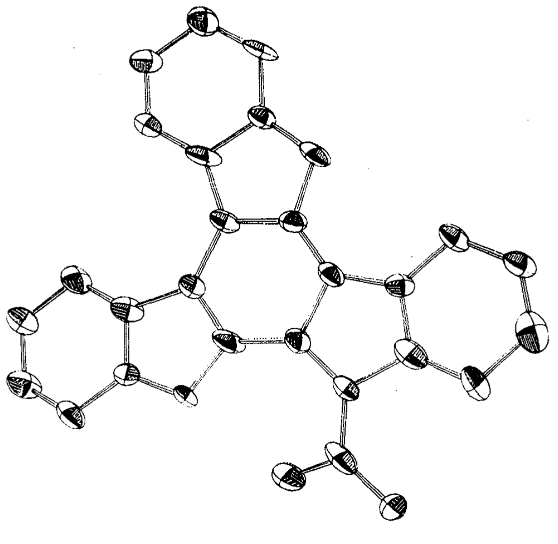


Fig. 3. The Molecular Structure of **9a** with Thermal Ellipsoids Drawn at the 30% Probability Level

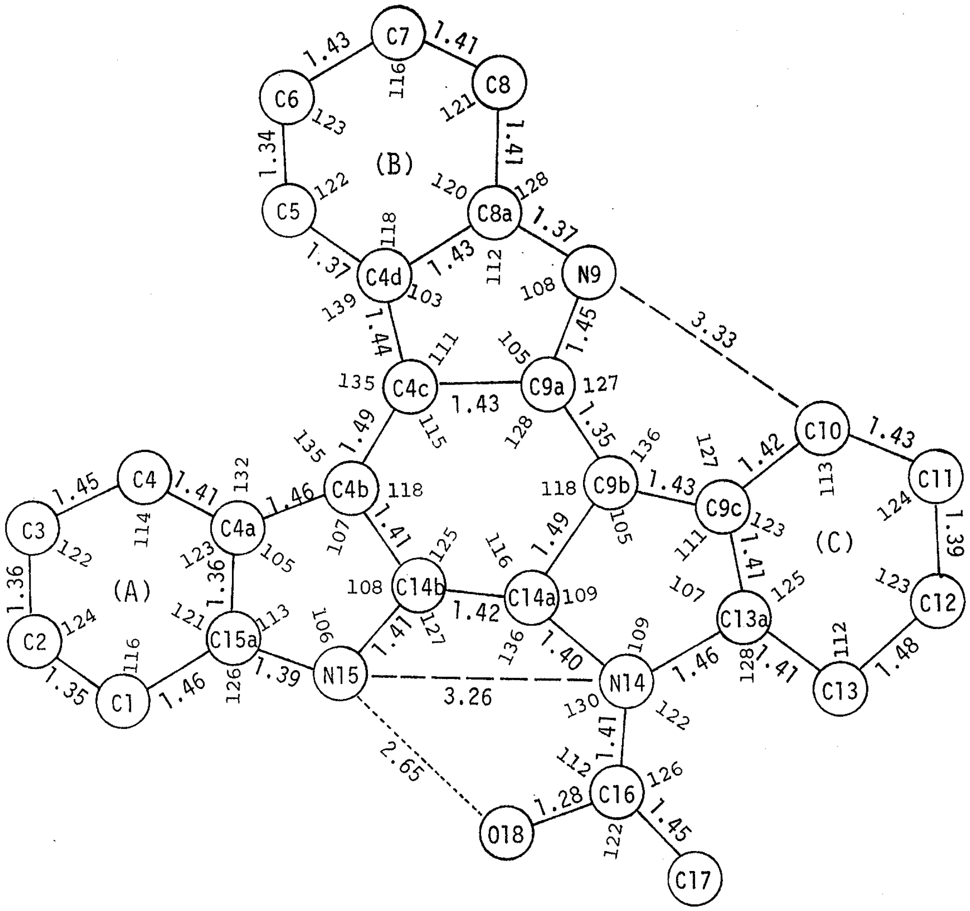


Fig. 4. Bond Lengths (Å) and Bond Angles (°) Together with Atomic Numbering in Compound (**9a**)

The dotted line between N_{15} and O_{18} suggests hydrogen bonding. Broken lines indicate close intramolecular interatomic distances. A, B and C represent, respectively, the indole rings (A), (B) and (C) given in the figure, and ∠A, B or ∠A, C is the interplanar angle between the (A) and (B) rings, or the (A) and (C) rings, respectively.

∠A,B=8.0°, ∠A,C=3.8°.

TABLE II. Crystal Data for **9a**

Molecular formula	$C_{26}H_{17}N_3O$
Molecular weight	387.4
Color and habit	Very thin platy, slightly yellow crystals
Size, mm	0.3×0.3×0.01
Crystal system	Monoclinic
a, Å	16.851±0.015
b, Å	8.562±0.008
c, Å	13.046±0.013
β, degree	102.13±0.08
U, Å^3	1840.2
Absent reflections	$h0l$ when h=odd, $0k0$ when k=odd
Space group	$P2_1/a$
Z	4
Density (calculated), g/cm^3	1.40

of 3, being either **9b** or **9c** (Fig. 2). Although we could obtain no conclusive evidence for the structure determination, it is likely to be **9b** rather than **9c** on the basis of the results of X-ray analysis described below.

As 3 was light-labile in the air, the major acetyl derivative (**9a**) was subjected to single-crystal X-ray diffraction analysis. The crystal data are presented in Table II. An ORTEP drawing of the molecular structure is shown in Fig. 3.[15] The bond lengths and bond angles are given in Fig. 4 and the fractional atomic coordinates are listed in Table III.

TABLE III. Fractional Atomic Coordinates and Temperature Factors ($\times 10^4$)

Atom	x	y	z	$\beta 11$	$\beta 22$	$\beta 33$	$\beta 12$	$\beta 13$	$\beta 23$
C (1)	3243(9)	2349(24)	8755(14)	23(6)	210(44)	84(17)	−1(14)	−2(8)	−26(22)
C (2)	3385(10)	1371(24)	9587(16)	31(7)	161(41)	121(20)	3(15)	−6(10)	49(24)
C (3)	2804(10)	464(27)	9871(16)	32(8)	286(54)	105(20)	−18(17)	3(10)	−4(28)
C (4)	2010(9)	274(24)	9199(15)	23(6)	222(44)	95(19)	18(15)	6(9)	−4(23)
C (4a)	1858(8)	1275(22)	8322(14)	21(6)	133(37)	107(18)	20(13)	10(8)	13(22)
C (4b)	1169(9)	1407(23)	7442(13)	23(6)	199(41)	67(15)	−2(14)	6(8)	−1(21)
C (4c)	333(8)	759(19)	7201(13)	18(5)	87(33)	90(16)	3(11)	8(7)	−2(19)
C (4d)	−132(8)	−216(23)	7760(15)	15(5)	178(41)	130(21)	0(13)	15(9)	23(24)
C (5)	−42(9)	−941(22)	8711(13)	23(6)	159(40)	75(16)	−6(13)	6(8)	−5(21)
C (6)	−650(10)	−1721(22)	8996(15)	33(7)	170(40)	98(19)	−8(14)	21(10)	20(22)
C (7)	−1399(10)	−2050(26)	8285(15)	31(7)	273(49)	95(19)	22(16)	13(9)	−12(26)
C (8)	−1518(8)	−1287(25)	7307(15)	13(6)	233(45)	127(20)	−20(14)	10(9)	−2(27)
C (8a)	−892(8)	−395(21)	7032(13)	20(6)	119(36)	81(16)	2(12)	3(8)	20(19)
N (9)	−907(7)	401(18)	6115(11)	12(4)	219(35)	97(14)	6(11)	5(6)	−22(19)
C (9a)	−142(8)	1219(22)	6206(13)	23(6)	154(37)	70(15)	−2(13)	14(8)	10(21)
C (9b)	92(8)	2073(22)	5456(13)	18(6)	203(40)	64(15)	1(13)	6(8)	−28(21)
C (9c)	−286(8)	2707(20)	4460(13)	23(6)	112(34)	80(16)	12(12)	14(8)	18(19)
C (10)	−1062(9)	2303(23)	3857(15)	19(6)	178(41)	99(18)	10(13)	0(8)	2(23)
C (11)	−1266(9)	3125(23)	2880(15)	23(6)	182(43)	105(19)	−2(13)	8(9)	3(22)
C (12)	−746(11)	4129(28)	2511(15)	50(9)	310(56)	88(20)	43(19)	6(11)	−45(28)
C (13)	62(9)	4560(26)	3132(15)	30(7)	272(52)	95(19)	4(16)	−12(9)	5(26)
C (13a)	248(9)	3727(25)	4085(15)	24(7)	211(46)	108(20)	10(15)	5(9)	−15(26)
N (14)	1012(6)	3711(17)	4857(10)	17(4)	151(29)	71(12)	2(10)	1(6)	−5(16)
C (14a)	915(8)	2803(23)	5709(13)	20(6)	222(43)	62(15)	6(14)	7(7)	−4(22)
C (14b)	1401(8)	2423(23)	6703(15)	15(6)	199(43)	117(20)	−1(13)	0(8)	41(24)
N (15)	2171(6)	3038(16)	7144(10)	15(4)	157(30)	60(11)	−11(9)	−3(6)	−5(15)
C (15a)	2431(8)	2258(24)	8086(13)	23(6)	235(45)	60(15)	−10(14)	10(8)	8(22)
C (16)	1717(9)	4410(26)	4650(15)	19(6)	270(50)	113(20)	−1(15)	−6(9)	−36(27)
C (17)	1751(10)	5480(23)	3795(14)	45(8)	195(44)	75(18)	−23(16)	−1(10)	56(23)
O (18)	2362(6)	3910(18)	5259(10)	28(5)	328(34)	116(14)	−15(11)	6(6)	35(19)

The anisotropic temperature factors are of the form:
$T=\exp[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+2\beta_{12}hk+2\beta_{13}hl+2\beta_{23}kl)]$

The central benzene ring and three indole rings of **9a** are substantially coplanar, the average value of the deviation of atoms in each ring being 0.02—0.04 Å, so that all the carbon atoms in this system are expected to be conjugated with each other. Interestingly, the C_{9a}–C_{9b} bond (1.35 Å) is short relative to the other C–C bonds in the central benzene ring, and the N_9–C_{9a}–C_{9b} and C_{9b}–C_{9c}–C_{10} angles (both, 127°) are rather small. This suggests congestion of atoms around N_9. The C_{10}–H group may cover the N_9–H bond and protect N_9 from acetylation. Figure 4 shows that the N_{14}–H and N_{15}–H groups are located close together and project outwards. It seems reasonable that only one of them can be acetylated.

When indole reacts with hydroxyl radicals, the products vary widely, depending on the pH of the reaction solution, *i.e.*, **2** and **3** are formed under acidic conditions, and **4**—**6** and **7** under neutral conditions. In acidic media, a radical cation may play an important role as an intermediate. It is plausible that the radical **10** generated by the addition of a hydroxyl radical to indole is either oxidized to oxindole or converted to the radical cation **11**. Further, **11** may lose a proton to lead to the production of **2** and **3** and, in part, be reduced with iron(II) or titanium(III) to regenerate the starting material. A possible mechanism for the formation of the products is illustrated in Fig. 5.

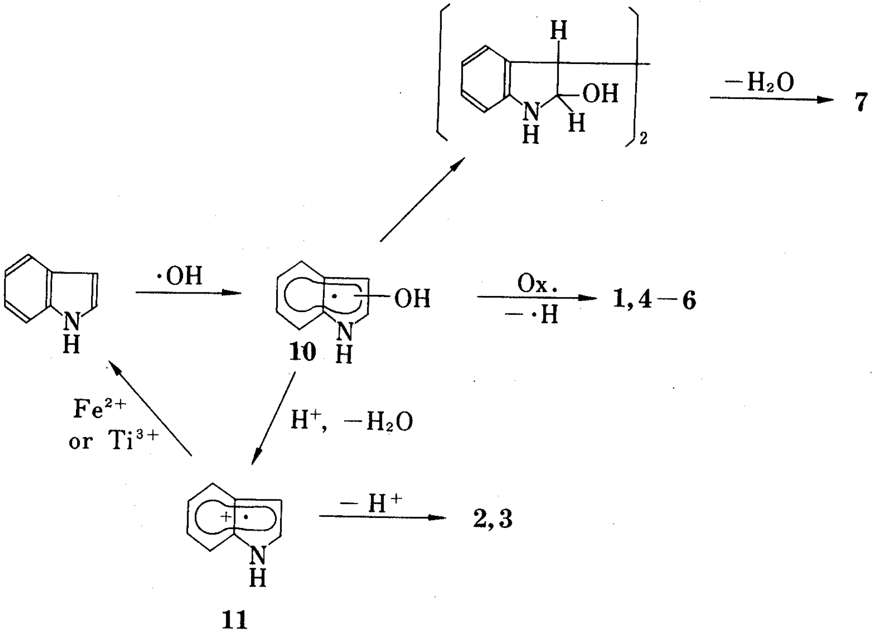


Fig. 5

Experimental

All melting points were determined on a Yamato melting point apparatus MP-21 and are uncorrected. Infrared spectra were recorded on a JASCO IRA-2 spectrophotometer. Ultraviolet spectra were measured on a Cary 118C spectrophotometer. Mass spectra were obtained on a Shimadzu-LKB 9000 gas chromatograph–mass spectrometer equipped with a Shimadzu GC-MSPAC 300 computer. All ^{1}H- and ^{13}C-NMR spectra were taken on a Varian XL-100-12WG spectrometer interfaced with a Varian 620/L computer, and with tetramethylsilane as an internal standard. Gas–liquid chromatography (GLC) was performed at 280°C on a Shimadzu GC-5A gas chromatograph with a flame ionization detector. Each of the GLC columns employed was a 0.5×150 cm glass tube containing 5% OV-1 on Chromosorb W 80—100 mesh. Thin-layer chromatography (TLC) and preparative TLC were carried out on silica gel F_{254} (Merck, Darmstadt, BRD). Silica gel (Wako gel C-200) was used for column chromatography. Indole, titanium(III) chloride, iron(II) sulfate and Wako gel C-200 were purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan). A 30% aqueous solution of hydrogen peroxide was obtained from Mitsubishi Edogawa Chemical Co., Ltd. (Tokyo, Japan).

Reaction of Indole Suspended in the Titanium(III)–Hydrogen Peroxide System at pH 1.0——Indole (6.9 g, 59 mmol) was suspended in water (70 ml) to which 30% H_2O_2 (2.0 g, 18 mmol) had been added, and the suspension was adjusted to pH 1.0 with dilute H_2SO_4. Under N_2, a 20% aqueous solution of $TiCl_3$ (14 g, 18 mmol) was added dropwise to the ice-cold suspension over 20 min with stirring. The stirring was continued below 4°C for a further 24 h. The products were extracted with a mixture of tetrahydrofuran (THF) and ethyl acetate (EtOAc) (4: 1 v/v). The extract was washed with water, dried over Na_2SO_4, and then evaporated to dryness under reduced pressure. The resulting residue was applied to a silica gel column and eluted with a gradient formed from hexane and ether. Crude products were purified by preparative TLC (eluent: CH_2Cl_2) to give oxindole (**1**) (227 mg, yield: 2.9%), 2,3′-biindole (**2**) (185 mg, 2.7%) and diindolo-[2,3-*a*: 2′,3′-*c*]carbazole (**3**) (536 mg, 7.9%).

i) Oxindole (**1**): mp 125—126°C from H_2O (lit.[16] mp 126—127°C). ^{13}C-NMR ($CDCl_3$) δ (ppm): 178.5 (s), 142.8 (s), 127.8 (d), 125.3 (s), 124.4 (d), 122.1 (d), 109.9 (d), 36.3 (t).

ii) 2,3′-Biindole (**2**): mp 201—202.5°C from benzene–hexane (lit.[13] mp 203.5—205°C). ^{13}C-NMR (acetone-d_6) δ (ppm): 137.9 (s), 137.2 (s), 134.9 (s), 130.6 (s), 126.1 (s), 123.2 (d), 122.8 (d), 121.3 (d), 120.7 (d), 120.5 (d), 120.1 (d), 119.8 (d), 112.5 (d), 111.2 (d), 110.2 (s), 98.5 (d).

iii) Diindolo[2,3-*a*: 2′,3′-*c*]carbazole (**3**): mp 302—304°C (dec.) from THF–hexane. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3390 (>NH), 1610 (C=C), $\delta_{\max}^{\text{KBr}}$ cm^{-1}: 737 (CH). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 391.5 (4.24), 373 (4.23), 346.5 (4.62), 332 (4.45), 317 sh (4.39), 305 (4.81), 298 sh (4.74), 271.5 sh (4.23), 253.5 (4.91), 215.5 (4.62). MS *m/e* (% rel. int.): 346 (M$^+$+1, 28), 345 (M$^+$, 100), 344 (M$^+$−1, 34), 173 (6), 172.5 (M$^+$/2, 25), 172 (7). ^{1}H-NMR (DMSO-d_6) δ (ppm): 11.68 (3H, br s, NH), 9.02—8.80 (3H, m, indolic 4-H), 7.98—7.76 (3H, m, indolic 7-H), 7.66—7.32 (6H, m, indolic 5,6-H). ^{13}C-NMR (DMSO-d_6) δ (ppm): 138.9 (s), 138.5 (s), 129.4 (s), 126.0 (s), 123.9 (d), 123.3 (s), 123.2 (s), 122.4 (d), 121.8 (s), 121.2 (d), 119.3 (s), 118.8 (d), 114.1 (s), 111.5 (d), 108.4 (s), 105.9 (s). *Anal.* Calcd for $C_{24}H_{15}N_3$: C, 83.46; H, 4.38; N, 12.17. Found: C, 83.26; H, 4.38; N, 12.08.

Reaction of Indole with the Titanium(III)-Hydrogen Peroxide System at pH 1.0——A 3% H_2O_2 solution (19 ml, 17 mmol) was added dropwise to a solution of indole (1.0 g, 8.5 mmol) in 0.2 N HCl–KCl buffer (850 ml, pH 1.0) containing $TiCl_3$ (1.3 g, 8.5 mmol) at room temperature under N_2. After being stirred for 15 min, the reaction mixture was extracted with a mixture of THF and EtOAc (4: 1 v/v). The organic phase was separated, washed with water, dried and concentrated under reduced pressure. The residue was purified by the method described above to give **2** (2 mg, 0.2%) and **3** (10 mg, 1.0%).

Reaction of Indole with the Iron(II)-Hydrogen Peroxide System at pH 2.8——A 3% H_2O_2 solution (95 ml, 85 mmol) was added to $FeSO_4\cdot7H_2O$ (12 g, 42 mmol) dissolved in an N_2-saturated, aqueous solution (2.5 l) of indole (5.0 g, 45 mmol) containing $HClO_4$ (13 g, 0.13 mol) over a period of 10 min under N_2. The reaction mixture was allowed to stand with stirring for another 30 min, and was then extracted with a mixture of THF and EtOAc (4: 1 v/v). The yield of **3** was 963 mg (19.6%).

Reaction of Indole with the Iron(II)-Hydrogen Peroxide System at pH 7.2——$FeSO_4\cdot7H_2O$ (2.3 g, 8.3 mmol) and EDTA·2Na (3.1 g, 8.3 mmol) were dissolved in an N_2-saturated solution of indole (1.0 g, 8.5 mmol) in 0.1 M potassium phosphate buffer (850 ml, pH 7.2), then 3% H_2O_2 (19 ml, 17 mmol) was added with stirring to the mixture over 10 min under N_2. The stirring was continued for a further 15 min at room temperature under N_2, then the reaction mixture was extracted with a mixture of THF and EtOAc (4: 1 v/v). By means of chromatographic methods, **1** (103 mg, 9.1%), 4-hydroxyindole (**4**) (55 mg, 4.8%), 5-hydroxyindole (**5**) (22 mg, 1.9%), 6-hydroxyindole (**6**) (49 mg, 4.3%) and 3,3′-biindole (**7**) (6 mg, 0.6%) were obtained.

i) 4-Hydroxyindole (**4**): mp 93—94.5°C from $CHCl_3$–hexane (lit.[3]) mp 97°C). ^{13}C-NMR (acetone-d_6) δ (ppm): 151.4 (s), 139.2 (s), 123.6 (d), 123.0 (d), 119.1 (s), 104.1 (d), 99.5 (d).

ii) 5-Hydroxyindole (**5**): mp 111.5—112.5°C from $CHCl_3$–hexane (lit.[3]) mp 107°C). ^{13}C-NMR (acetone-d_6) δ (ppm): 151.8 (s), 132.1 (s), 129.9 (s), 126.0 (d), 112.3 (d), 105.1 (d), 101.6 (d).

iii) 6-Hydroxyindole (**6**): mp 124—124.5°C from $CHCl_3$–hexane (lit.[3]) mp 126°C). ^{13}C-NMR (acetone-d_6) δ (ppm): 154.2 (s), 138.3 (s), 123.8 (d), 121.6 (s), 121.4 (d), 110.5 (d), 102.2 (d), 97.5 (d).

iv) 3,3′-Biindole (**7**): mp 283—285°C from CH_2Cl_2 (lit.[10]) mp 286—287°C). ^{13}C-NMR (acetone-d_6) δ (ppm): 137.9 (s), 127.8 (s), 122.7 (d), 122.3 (d), 120.7 (d), 120.0 (d), 112.3 (d), 111.6 (s).

Acetylation of 3——A mixture of **3** (44 mg, 0.13 mmol), Ac_2O (1.0 g, 10 mmol) and NaOAc (82 mg, 1 mmol) was heated at 45°C for 7 h, and then poured onto crushed ice. The products were extracted with benzene to give a mixture of **9a** and **9b** (**9a**+**9b**: 42 mg, 86.0%). As estimated by the gas chromatographic method, the ratio of **9a** and **9b** was 4: 1. They were purified by fractional crystallization from THF–hexane as yellow crystals. The purity was checked by GLC.

i) **9a**: mp 304—306°C (dec.). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3390 (>NH), 1680 (C=O), 1610 (C=C), $\delta_{\max}^{\text{KBr}}$ cm^{-1}: 737 (CH). UV $\lambda_{\max}^{\text{dioxane}}$ nm (log ε): 413.5 (4.08), 362 (4.49), 312 sh (4.29), 300 sh (4.40), 280.5 (4.69), 243 (4.94). MS *m/e* (% rel. int.): 388 (M$^+$+1, 29), 387 (M$^+$, 97), 345 (M$^+$−CH_2CO, 100), 344 (95), 172.5 (5). ^{1}H-NMR (DMSO-d_6) δ (ppm): 11.97 (1H, s, NH), 11.14 (1H, s, NH), 9.00—8.80 (3H, m), 8.24—8.10 (1H, m, N-Ac-indolic 7-H), 7.98—7.82 (2H, m), 7.70—7.32 (6H, m), 3.08 (3H, s, $C\underline{H}_3CO$). ^{13}C-NMR (DMSO-d_6) δ (ppm): 171.4 (s), 140.2 (s), 138.4 (s), 137.3 (s), 127.9 (s), 125.7 (d), 124.8 (d), 124.2 (d), 123.8 (d), 123.2 (d), 122.3 (d), 122.0 (d), 121.3 (d), 119.1 (d), 118.8 (d), 116.7 (s), 115.5 (d), 113.1 (s), 111.8 (d), 109.5 (s), 27.6 (q). GLC t_R: 52 min. *Anal.* Calcd for $C_{26}H_{17}N_3O$: C, 80.60; H, 4.42; N, 10.85. Found: C, 80.83; H, 4.43; N, 10.76.

ii) **9b**: MS *m/e* (% rel. int.): 388 (M$^+$+1, 21), 387 (M$^+$, 69), 345 (82), 344 (100), 172.5 (4). ^{1}H-NMR (DMSO-d_6) δ (ppm): 12.02 (1H, s, NH), 11.16 (1H, s, NH), 9.01—8.72 (3H, m), 8.26—8.10 (1H, m), 7.95—7.81 (2H, m), 7.68—7.32 (6H, m), 3.06 (3H, s, $C\underline{H}_3CO$). GLC t_R: 43 min.

Determination of the Crystal Structure of 9a——Crystals of the major acetyl derivative (**9a**) of the trimer (**3**) were grown in a THF-hexane mixed solution as very thin, pale yellow plates flattened on (100). A crystal of approximate dimensions (0.3×0.3×0.01 mm) was mounted on a Philips PW 1100 four-circle X-ray diffractometer, and the unit cell parameters and intensity data were collected by using Cu-*Kα* radiation monochromated by means of a graphite plate. The crystal data are given in Table II.

A total of 884 reflections was measured as being above the 2σ(I) level in the 2θ range of 6—130°. The intensities were measured by utilizing the θ-2θ scan method with a scan speed of 4°/min in θ. The scans were repeated twice when the total counts obtained during the single scan were less than 5000. The background was measured at each end of the scan range for half the total scan time.

The crystal of **9a** was rather stable to X-ray radiation. The intensities of three standard reflections were monitored at every 120 min and it was found that they decreased by about 2.3% of the original value during the whole measurement.

The crystal structure was solved by the direct method utilizing the computer program MULTAN[17] and refined by the block diagonal least-squares method. The final R value was 0.104 without hydrogen atoms. Since the aim of the present X-ray study was to confirm the structure of **9a**, no further refinement of the crystal structure was attempted.

The final atomic parameters are given in Table III and the bond lengths and bond angles are given in Fig. 4. The average standard deviations of these values are estimated to be 0.025 Å and 1.6°, respectively. The atoms at the circumference of the molecule undergo larger thermal vibrations than those at the central part. The e.s.d.'s of bond lengths involving these atoms are about 20% larger than the above value.

References and Notes

1) TMIG-I No. 34.
2) A. Cier and C. Nofre, *Bull. Soc. Chim. Fr.*, **1959**, 1523.
3) E. Eich and H. Rochelmeyer, *Pharm. Acta Helv.*, **41**, 109 (1966).
4) M.N. Dufour-Ricroch and A. Gaudemer, *Tetrahedron Lett.*, **1976**, 4079.
5) R.C. Armstrong and A.J. Swallow, *Radia. Res.*, **40**, 563 (1969).
6) T. Kaneko, M. Matsuo, and Y. Iitaka, *Heterocycles*, **12**, 471 (1979).
7) R.O.C. Norman and R.J. Prichett, *J. Chem. Soc.* (*B*), **1967**, 926; C.R.E. Jefcoate and R.O.C. Norman, *ibid.* (*B*), **1968**, 48.
8) M.E. Snook and G.A. Hamilton, *J. Am. Chem. Soc.*, **96**, 860 (1974).
9) C. Walling and R.A. Johnson, *J. Am. Chem. Soc.*, **97**, 363 (1975).
10) S.A. Faseeh and J. Harley-Mason, *J. Chem. Soc.*, **1957**, 4141.
11) P. Neta and L.M. Dorfman, *Advan. Chem. Ser.*, **81**, 222 (1968).
12) R.J. Pugmire, M.J. Robins, D.M. Grant, and R.K. Robins, *J. Am. Chem. Soc.*, **93**, 1887 (1971).
13) T.E. Young, *J. Org. Chem.*, **27**, 504 (1962).
14) J. Bergman and N. Eklund, *Tetrahedron*, **36**, 1445 (1980).
15) C.K. Johnson, ORTEP Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1965.
16) A.B. Neil, *J. Am. Chem. Soc.*, **75**, 1508 (1953).
17) G. Germain, P. Main, and M.M. Woolfson, *Acta Cryst.*, **A27**, 368 (1971).