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A [3,3] SIGMATROPIC AND NOVEL IPSO [3,3] SIGMATROPIC REARRANGEMENT OF 1-HYDROXYINDOLE CHEMISTRY[1,#]

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Abstract – Utilizing 1-aryloxyindole derivatives, we found a new type of [3,3] sigmatropic rearrangement reaction. We named it as ipso [3,3] sigmatropic rearrangement. The product structures are strictly determined by X-ray crystallographic analysis. Normal [3,3] sigmatropic rearrangement of 1-hydroxyindole derivative was found to be a useful synthetic method for 2*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4-dione derivative.

INTRODUCTION

Starting from 2,3-dihydroindoles we have created 1-hydroxyindole chemistry.[3] While investigating the reactivity of 1-hydroxyindoles, we wondered if we could get 1-aryloxyindole (**A,** depicted in Figure 1), where aryloxy group has an ortho substituent, what will happen to it. We could expect [3,3] sigmatropic rearrangement of 1-aryloxy group. Interestingly there are two possible routes. The one is a normal **a** route, migrating carbon-3 has hydrogen, producing product (**C**) through the intermediate (**B**). While in the other **b** route, product (**E**) would be obtained through the intermediate (**D**), where migrating carbon-3' is an ipso carbon having a substituent (X). We can name the **b** route as novel ipso [3,3] sigmatropic rearrangement.

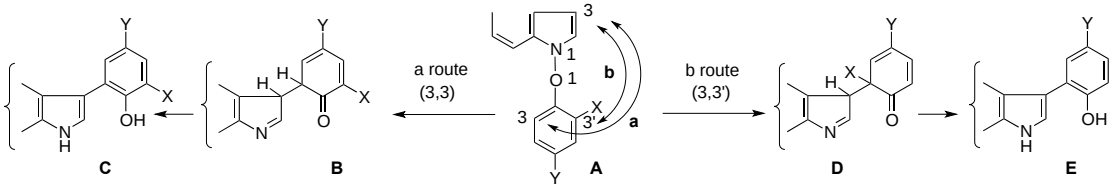


Figure 1

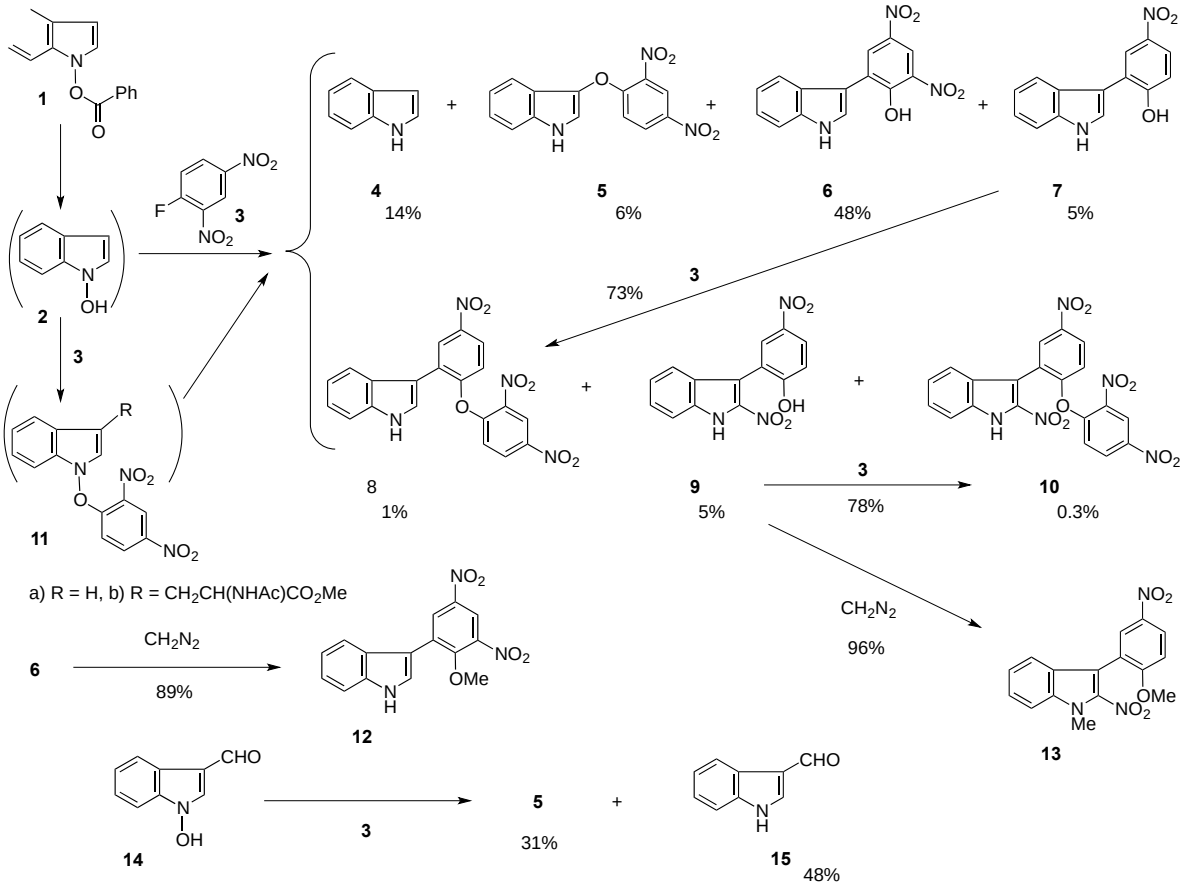
Dedicated to the 70th birthday of Professor Dr. Tohru Fukuyama

Furthermore, in this case, it is an interesting subject to elucidate what happens to X's fate. This report is a full report of previous communications[4,5] with new results.

RESULTS AND DISCUSSION

1. Novel ipso [3,3] and [1,3] sigmatropic reactions of 1-hydroxyindole (2)

1-Hydroxyindole (**2**), produced *in situ* by treatment of 1-benzoyloxyindole[3] (**1**) with sodium hydroxide, reacted with 2,4-dinitrofluorobenzene (**3**) to afford indole (**4**), 3-(2,4-dinitrophenoxy)indole (**5**), 2,4-dinitro-6-(indol-3-yl)phenol (**6**), 2-(indol-3-yl)-4-nitrophenol (**7**), 1-(2,4-dinitrophenoxy)-2-(indol-3-yl)-4-nitrobenzene (**8**), 4-nitro-2-(2-nitroindol-3-yl)phenol (**9**), and 4-nitro-2-(2-nitroindol-3-yl)-1-(2,4-dinitrophenoxy)benzene (**10**) in 14, 6, 48, 5, 1, 5, and 0.3% yields, respectively (Scheme 1).



Scheme 1

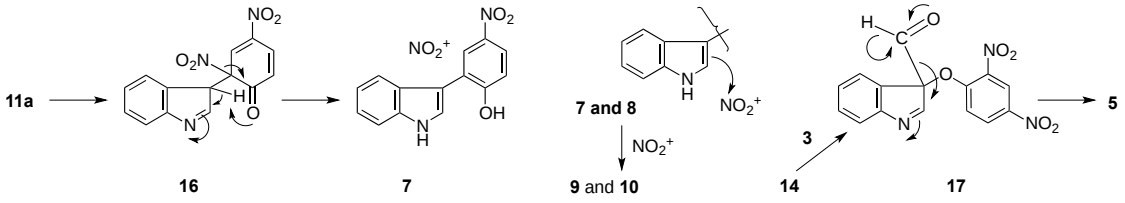
The structures of **5** and **6** were easily confirmed by the spectral data as normal [1,3] and [3,3] sigmatropic rearrangement products, respectively. The structures of the other products were unknown and strange. Therefore, mutual correlation was carried out. Thus, the reactions of **7** and **9** with **3** provided **8** and **10** in the respective yields of 73 and 78%. Interestingly a pair of compounds, **7** and **8**, had missed one nitro

group compared with the expected rearrangement products. On the other hand, a pair of compounds, **9** and **10**, were deduced to have an extra nitro group. The presence of phenol moiety in the compounds **6** and **9** were proved by reacting them with diazomethane to afford the corresponding methyl ethers, 2,4-dinitro-6-(indol-3-yl)phenol methyl ether (**12**) and 4-nitro-2-(1-methyl-2-nitroindol-3-yl)phenol methyl ether (**13**) in 89 and 96% yields, respectively. Concerning the mysterious **8** and **9**, with the spectral data alone, it was difficult to determine their structures. Therefore, X-ray single crystallographic structure analysis of **8** and **13** were carried out. The results shown in Figures 2 and 3 (Experimental section) clearly proved them to be the depicted structures in Scheme 1.

In addition, the reaction of 1-hydroxyindole-3-carbaldehyde (**14**) with **3** produced **5** and indole-3-carbaldehyde (**15**) in 31 and 48% yields, respectively. In this case ipso [1,3] sigmatropic rearrangement reaction took place.

2. Mechanism of the formation of 9 and 10

Mechanism of the formation of **9** and **10** are deduced as follows (Scheme 2). First, **1** produce 1-hydroxyindole (**2**), and it reacts with **3** to give unstable intermediate (**11a**). Normal [1,3] and [3,3] sigmatropic rearrangement of migrating group, 2,4-dinitropnenyloxy group, affords products **5** and **6**, respectively. Ipso [3,3] sigmatropic reaction of **11a** generates intermediate (**16**) followed by liberation of nitronium ion to give **7** (Scheme 2). This nitronium ion is trapped at the electron rich 2-position of indole nucleus of **7** and **8** culminating in the formation of **9** and **10**. In the reaction of **14** with **3** generates ipso [1,3] sigmatropic rearrangement intermediate **17**, followed by the liberation of carbon oxide to result in the formation of **5**. Liberations of both the nitro and formyl moieties, initially present in the 2,4-dinitrophenyl group and indole 3-position, respectively, were interesting findings.

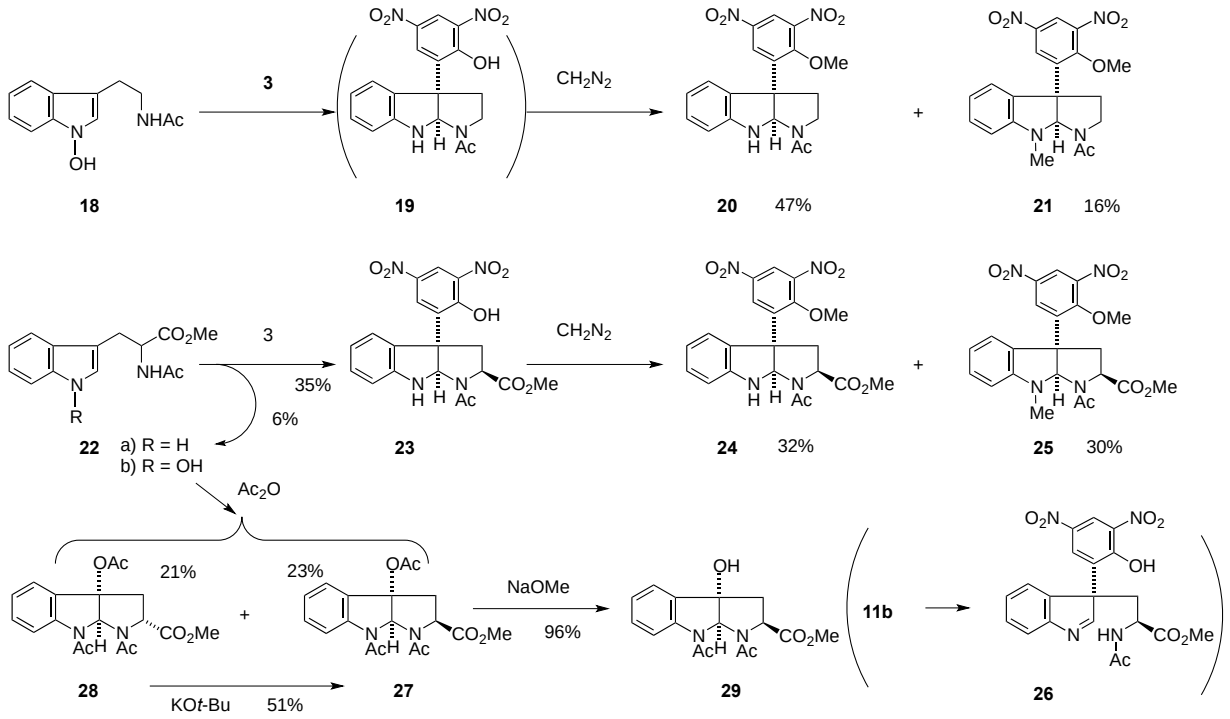


Scheme 2

3. Reaction of 1-hydroxytryptamine (18) and 1-hydroxytryptophan (22a) derivatives with 3

Next, we tried the reaction of *N*b-acetyl-1-hydroxytryptamine (**18**) with **3**. If we predict ipso [3,3] sigmatropic rearrangement to occur in this case, the intermediate would have two adjacent quaternary carbons. Because it is energetically unstable, the real reaction will not occur through the intermediate. In fact, normal [3,3] sigmatropic reaction was observed. Since the expected product (**19**) was found to be

unstable and decomposed during the purification by column chromatography, crude **19** was treated with excess diazomethane culminating in the formation of stable **20** and **21** in 47 and 16% yields, respectively. To determine the structures of **20** and **21**, we next explored the reaction of *N*-acetyl-1-hydroxytryptophan methyl ester (**22b**) with **3**. As expected, normal [3,3] sigmatropic rearrangement product (**23**) and **22a** are produced in 35 and 6% yields, respectively. The structure of **23** was confirmed by leading it to **24** and **25** by the reaction with diazomethane in 32 and 30% yields, respectively. The structure of **25** was determined by the X-ray single crystal structure analysis. The ORTEP structure of **25** is shown in Figure 4 (Experimental part).



Scheme 3

The formation of **23** could be explained by the formation of **11b**, followed by [3,3] sigmatropic rearrangement of 2,4-dinitrophenyl group resulting **26**, and subsequent ring closure of *N*b side chain to the imine carbon. Similar reaction was observed by reacting **22b** with Ac_2O affording **27** and **28** in 23 and 21% yields, respectively. Compounds **27** and **28** were the stereoisomers at the 2-methoxycarbonyl group. The stereochemistry of 2-methoxycarbonyl group in **28** was supposed to be α-position, because KO*t*-Bu treatment of **28** for 10 min gave **27** in 51% yield, which are thermodynamically stable β-isomer. The structure of **27** was determined by converting it to **29** by treatment with NaOMe in MeOH in 96% yield. The structure of **29** was determined unequivocally by X-ray crystallographic analysis (Figure 5).

4. 3,10b-Disubstituted (3*S*,5a*R*,10b*S*,11a*S*)-1,3,4,5a,6,10b,11,11a-octahydro-2*H*-pyrazino[1',2':1,5]-pyrrolo[2,3-*b*]indole-1,4-dione derivatives

We expected that normal **[**3,3**]** sigmatropic rearrangement of (–)-**30** would produce a common structure of 2*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4-dione ((–)-**31**) (Scheme 4) which is included in such bioactive indole alkaloids as sporidesmin B,[6] brevianamide E,[7] and okaramine C.8.

In fact, heating (–)-**30** in DMF at reflux produced (3*S*,5a*R*,10b*S*,11a*S*)-(–)-10b-benzoyloxy-3-isobutyl-1,3,4,5a,6,10b,11,11a-octahydro-2*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4-dione [(–)-**31**] as a sole product in 37% yield. The structure of (–)-**31** was determined by spectral data, and its stereochemistry was confirmed by the nOe experimental results in ^{1}H-NMR spectroscopy as shown in Figure 6.

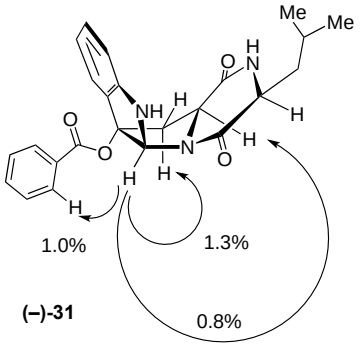
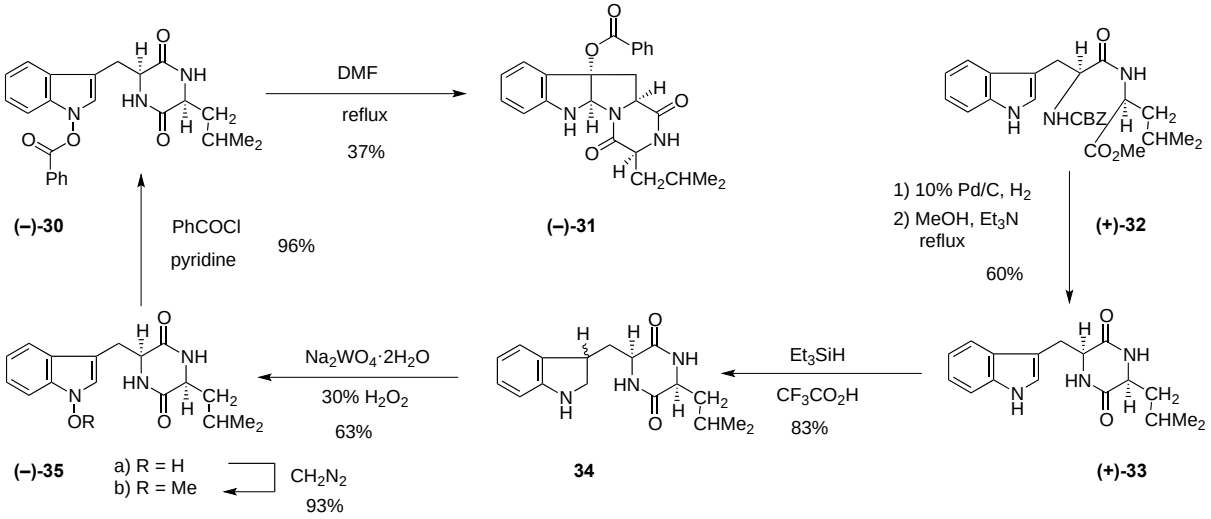


Figure 6

The conformation explains why isobutyl methyl groups of (–)-**31** resonate at higher magnetic field (δ 0.95 and 0.97), because they are just above the indole benzenoid moiety and receive its shielding effect.

Starting material (–)-**30** was prepared as follows. 2,5-Piperazinedione derivative ((+)-**33**) was prepared from (+)-*N*-benzyloxycarbonyl-*L*-tryptophan [(+)-**32**] according to the reported procedure.[9] Thus catalytic hydrogenation of (+)-**32** over 10% Pd/C, followed by cyclization in refluxing MeOH afforded (+)-**33**[9a,b] in 60% yield. Reduction of (+)-**33** with Et_3SiH in TFA[10] afforded a 1:1 mixture of diastereomers (**34**) in 83% yield.



Scheme 4

The desired (3*S*,6*S*)-(–)-6-(1-hydroxyindol-3-ylmethyl)-3-benzyl-2,5-piperazinedione [(–)-**35a**] was isolated in 63% yield, by the oxidation of **34** with $Na_2WO_4 \cdot 2H_2O$[3] and 30% H_2O_2[3] in CH_2Cl_2-MeOH-H_2O. The structure was proved by converting the 1-hydroxyindole to the corresponding 1-methoxyindole [(–)-**35b**] in 93% yield by the reaction with CH_2N_2. Benzoylation of 1-hydroxy group of (–)-**35a** with benzoyl chloride provided (–)-**30** in 96% yield.

In conclusion, we have discovered an interesting ipso [1,3] and ipso [3,3] sigmatropic rearrangement reactions and preparation method for core structure of indole alkaloids such as sporidesmin B, brevianamide, okaramine C during investigating 1-hydroxyindole chemistry. The research area is a treasure trove of new discoveries and findings.

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were determined with a Shimadzu IR-420 or Horiba FT-720 spectrophotometer, and proton nuclear magnetic resonance (^{1}H-NMR) spectra with a JEOL JNM-GSX 500 or FX100S spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) were recorded on a Hitachi M-80 or JEOL SX-102A spectrometer. Column chromatography was performed on silica gel (SiO_2, 100–200 mesh, from Kanto Chemical Co. Inc.) or activated alumina (Al_2O_3, 300 meshes, from Wako Pure Chemical Industries, Ltd.) throughout the present study.

Reaction of 1-hydroxyindole (*in situ* formation) with 2,4-dinitrofluorobenzene – Aqueous 8% NaOH (3.0 mL) was added to a solution of 1-benzoyloxyindole (**1**, 298.5 mg, 1.26 mmol) in MeOH (9.0 mL) and stirred at rt for 10 min. After adding ice-cooled brine (60 mL), the reaction mixture was made acidic (pH 4) by aqueous 8% HCl. The whole was extracted with benzene and dried over Na_2SO_4. To the benzene solution including 1-hydroxyindole (**2**), Et_3N (1.8 mL, 12.6 mmol) and a solution of (n-Bu)$_4NHSO_4$ (43.1 mg, 0.13 mmol) and 2,4-dinitrofluorobenzene (237.2 mg, 1.27 mmol) in benzene (3.0 mL) were added and the whole was stirred at rt for 2 h. To the reaction mixture $CHCl_3$-MeOH (4:1, v/v) was added and the precipitates were dissolved. Aqueous 0.8% NaOH was added to the mixture and the whole was separated to water layer and organic layer. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated to give neutral fraction residue. The water layer was made acidic by adding aqueous 8% HCl and extracted with $CHCl_3$-MeOH (4:1, v/v). The extract was dried over Na_2SO_4 and evaporated to give acidic fraction residue. The neutral fraction residue was subjected to column-chromatography on SiO_2 with CH_2Cl_2 to afford indole (**4**, 19.9 mg, 14%), **8** (2.6 mg, 1%), **5** (23.3 mg, 6%), and **10** (1.7 mg, 0.3%). The crystalline acidic fraction residue was recrystallized from MeOH to give **6** (139.7 mg). The mother liquor was subjected to column-chromatography with $CHCl_3$-MeOH (4:1, v/v) to give further crop of **6** (40.8 mg, total 180.5 mg, 48%), **7** (17.2 mg, 5%), and **9** (23.3 mg, 5%). **5:**

mp 174–175 °C (decomp., yellow plates, recrystallized from MeOH). IR (KBr): 3395, 1606, 1584, 1530, 1522, 1339, 1304, 1264, 1141, 1071, 918, 837, 821, 738 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 6.94–7.49 (5H, m), 7.12 (1H, d, *J* = 9.3 Hz), 8.04 (1H, br s, D_2O exchange), 8.21 (1H, dd, *J* = 9.3, 2.7 Hz), 8.82 (1H, d, *J* = 2.7 Hz). MS *m/z*: 299 (M^+). *Anal*. Calcd for $C_{14}H_9N_3O_5$: C, 56.19; H, 3.03; N, 14.04. Found: C, 56.10; H, 2.95; N, 14.03. **6:** mp 290 °C (decomp., orange needles, recrystallized from MeOH). IR (KBr): 3350, 3000, 1607, 1564, 1555, 1534, 1465, 1440, 1330, 1260, 1244, 752, 745, 710 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 7.13 (1H, ddd, *J* = 8.9, 7.3, 1.0 Hz), 7.20 (1H, ddd, *J* = 8.9, 7.6, 1.0 Hz), 7.50 (1H, dd, *J* = 7.3, 1.0 Hz), 7.71 (1H, dd, *J* = 7.6, 1.0 Hz), 7.90 (1H, d, *J* = 2.6 Hz), 8.52 (1H, d, *J* = 3.0 Hz), 8.63 (1H, d, *J* = 3.0 Hz), 11.59 (1H, br s). MS *m/z*: 299 (M^+). *Anal*. Calcd for $C_{14}H_9N_3O_5$: C, 56.17; H, 3.03; N, 14.04. Found: C, 56.03; H, 3.17; N, 13.94. **7:** mp 173 °C (orange prisms, recrystallized from CH_2Cl_2-hexane). IR (KBr): 3445, 3350, 1547, 1497, 1472, 1332, 1317, 1282, 1257, 1177, 1136, 1102, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 6.10 (1H, br. s), 7.12 (1H, d, *J* = 9.0 Hz), 7.24 (1H, ddd, *J* = 7.9, 7.0, 0.9 Hz), 7.34 (1H, ddd, *J* = 8.4, 7.0, 0.9 Hz), 7.44 (1H, d, *J* = 2.7 Hz), 7.52 (1H, ddd, *J* = 8.3, 0.9, 0.5 Hz), 7.57 (1H, ddd, *J* = 7.9, 0.9, 0.5 Hz), 8.19 (1H, dd, *J* = 9.0, 2.8 Hz), 8.34 (1H, d, *J* = 2.8 Hz), 8.58 (1H, br s). MS *m/z*: 254 (M^+). *Anal*. Calcd for $C_{14}H_{10}N_2O_3$: C, 66.14; H, 11.02; N, 3,96. Found: C, 66.14; H, 10.88; N, 3.87. **8:** mp 171–174 °C (yellow prisms, recrystallized from CH_2Cl_2-MeOH). IR (KBr): 3410, 3180, 1605, 1535, 1512, 1475, 1340, 1260, 755, 745 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 7.00 (1H, d, *J* = 9.3 Hz), 7.10 (1H, ddd, *J* = 7.8, 7.0, 1.0 Hz), 7.15 (1H, ddd, *J* = 8.0, 7.0, 1.0 Hz), 7.36 (1H, ddd, *J* = 8.0, 1.0, 1.0 Hz), 7.51 (1H, d, *J* = 8.8 Hz), 7.65 (1H, s), 7.72 (1H, ddd, *J* = 7.8, 1.0, 1.0 Hz), 8.18 (1H, dd, *J* = 9.3, 3.0 Hz), 8.25 (1H, dd, *J* = 8.8, 3.0 Hz), 8.67 (1H, d, *J* = 3.0 Hz), 8.72 (1H, d, *J* = 3.0 Hz). MS *m/z*: 420 (M^+). *Anal*. Calcd for $C_{20}H_{12}N_4O_7 \cdot 1/2H_2O$: C, 55.95; H, 2.82; N, 13.05. Found: C, 56.09; H, 3.08; N, 12.84. **9:** mp 242–244 °C (decomp., yellow needles, recrystallized from MeOH-H_2O). IR (KBr): 3320, 1620, 1590, 1533, 1518, 1500, 1486, 1460, 1384, 1333, 1303, 1289, 1260, 1100, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 5.91 (1H, br. s), 7.16 (1H, d, *J* = 8.8 Hz), 7.32 (1H, ddd, *J* = 8.0, 6.6, 1.0 Hz), 7.53 (1H, ddd, *J* = 8.0, 1.0, 1.0 Hz), 7.54 (1H, ddd, *J* = 8.2, 1.0, 1.0 Hz), 7.58 (1H, ddd, *J* = 8.2, 6.6, 1.0 Hz), 8.31 (1H, dd, *J* = 8.8, 2.8 Hz), 8.34 (1H, d, *J* = 2.8 Hz), 9.55 (1H, br s). MS *m/z*: 299 (M^+). *Anal*. Calcd for $C_{14}H_9N_3O_5$: C, 56.17; H, 3.03; N, 14.04. Found: C, 56.24; H, 2.93; N, 13.92. **10:** yellow oil. IR (film): 3370, 3100, 1520, 1345, 1298, 1260, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.26 (1H, d, *J* = 9.0 Hz), 7.29 (1H, d, *J* = 9.0 Hz), 7.32 (1H, ddd, *J* = 8.4, 8.3, 1.0 Hz), 7.48 (1H, ddd, *J* = 8.4, 1.0, 0.5 Hz), 7.54 (1H, ddd, *J* = 8.4, 1.0, 0.5 Hz), 7.56 (1H, ddd, *J* = 8.4, 8.3, 1.0 Hz), 8.34 (1H, dd, *J* = 9.0, 2.8 Hz), 8.43 (1H, dd, *J* = 9.0, 2.8 Hz), 8.51 (1H, d, *J* = 9.0 Hz), 8.70 (1H, d, *J* = 9.0 Hz), 9.46 (1H, br s). HR-MS *m/z*: Calcd for $C_{20}H_{11}N_5O_9$: 465.0556. Found: 465.0557.

3-(2,4-Dinitrophenoxy)indole (5) and indole-3-carbaldehyde (15) from 1-hydroxyindole-3-carbaldehyde (14) – A solution of 2,4-dinitrofluorobenzene (15.0 mg, 0.08 mmol) and anhydrous Et_3N

(0.2 mL) in anhydrous THF (1.0 mL) was added to a solution of **14** (12.9 mg, 0.08 mmol) in anhydrous THF (2.0 mL) and stirred at rt for 2 h. After evaporation of the solvent, the residue was subjected to column-chromatography on SiO_2 with CH_2Cl_2 to give **5** (7.4 mg, 31%) and **15** (5.6 mg, 48%).

2-(Indol-3-yl)-1-(2,4-dinitrophenoxy)-4-nitrobenzene (8) from 7 – 2,4-Dinitrofluorobenzene (15.0 mg, 0.08 mmol) was dissolved in CH_2Cl_2 (1.0 mL). The half of the solution (0.5 mL) was added to a solution of **7** (4.9 mg, 0.02 mmol) in CH_2Cl_2-NEt_3 (100:2.7, v/v, 1.0 mL) and stirred at rt for 2 h. After evaporation of the solvent, the residue was subjected to column-chromatography on SiO_2 with CH_2Cl_2 to give **8** (5.9 mg, 73%).

1-(2,4-Dinitrophenoxy)-2-(2-nitroindol-3-yl)-4-nitrobenzene (10) from 9 – 2,4-Dinitrofluorobenzene (15.7 mg, 0.08 mmol) was dissolved in CH_2Cl_2 (1.0 mL). The solution (0.5 mL) was added to a solution of **9** (5.4 mg, 0.02 mmol) in CH_2Cl_2 -NEt_3 (100:3, v/v, 1.0 mL) and stirred at rt for 6 h. After evaporation of the solvent, the residue was subjected to column-chromatography on SiO_2 with CH_2Cl_2 to give **10** (6.5 mg, 78%).

2,4-Dinitro2-(indol-3-yl)-1-methoxybenzene (12) from 6 – Excess diazomethane in Et_2O was added to a solution of **6** (20.0 mg, 0.07 mmol) in acetone (4.0 mL) at rt with stirring. After stirring for 20 min at rt, the solvent was evaporated under reduced pressure. The residue was subjected to column-chromatography on SiO_2 with CH_2Cl_2-hexane (1:2, v/v) as an eluent to give **12** (18.6 mg, 89%). **12:** mp 177–178 °C (orange prisms, recrystallized from MeOH). IR (KBr): 3380, 1540, 1520, 1354, 1250, 1135, 990, 755 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.69 (3H, s), 7.27 (1H, ddd, *J* = 7.9, 7.6, 1.3 Hz), 7.34 (1H, ddd, *J* = 7.9, 7.0, 1.3 Hz), 7.51 (1H, dd, *J* = 7.0, 1.3 Hz), 7.70 (1H, d, *J* = 2.6 Hz), 7.80 (1H, dd, *J* = 7.0, 1.3 Hz), 8.52 (1H, d, *J* = 3.0 Hz), 8.61 (1H, br s), 8.72 (1H, d, *J* = 3.0 Hz). MS *m/z*: 313 (M^+). *Anal*. Calcd for $C_{15}H_{11}N_3O_5$: C,57.51; H, 3.54; N, 13.41. Found: C, 57.48; H, 3.57; N, 13.39.

1-Methyl-3-(1-methoxy-4-nitrophen-3-yl)-2-nitroindole (13) from 9 – Excess diazomethane in Et_2O was added to a solution of **9** (11.5 mg, 0.04 mmol) in EtOAc (2.0 mL) at rt with stirring. After stirring for 20 min at rt, the solvent was evaporated under reduced pressure. The residue was subjected to column-chromatography on SiO_2 with EtOAc-hexane (1:2, v/v) as an eluent to give **13** (12.1 mg, 96%). **13:** mp 202–202.5 °C (yellow prisms, recrystallized from EtOAc-hexane). IR (KBr): 1515, 1503, 1468, 1378, 1339, 1318, 1270, 1020, 752 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 3.86 (3H, s), 4.13 (3H, s), 7.07 (1H, d, *J* = 8.6 Hz), 7.27 (1H, ddd, *J* = 8.0, 7.0, 1.0 Hz), 7.48 (1H, dd, *J* = 8.4, 1.0 Hz), 7.54 (1H, dd, *J* = 8.0, 1.3 Hz), 7.54 (1H, ddd, *J* = 8.4, 7.0, 1.3 Hz), 8.34 (1H, d, *J* = 2.9 Hz), 8.35 (1H, dd, *J* = 8.6, 2.9 Hz). HR-MS *m/z*: Calcd for $C_{16}H_{13}N_3O_5$: 327.0854. Found: 327.0854.

20 and 21 from 18 – A solution of 2,4-dinitrofluorobenzene (56.5 mg, 0.30 mmol) in anhydrous THF (1.0 mL) and Et_3N (0.4 mL) was added to a stirred solution of **18** (64.7 mg, 0.29 mmol) at 0 °C and stirring was continued at rt for 1 h. After evaporation of the solvent under reduced pressure, the residue

was dissolved in MeOH (3.0 mL). Then, excess amount of diazomethane in Et_2O was added and stirred at rt for 1 h. The residue obtained after evaporation of the solvent was subjected to column chromatography on SiO_2 with acetone-hexane (1:1, v/v) as an eluent to give **21** (20.0 mg, 16%) and **20** (55.8 mg, 47%) in the order of elution. **20:** mp 183–184 °C (decomp., yellow prisms, recrystallized from CH_2Cl_2-hexane). IR (KBr): 3390, 3088, 1648, 1605, 1528, 1477, 1418, 1344, 1255, 758 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: a 2:1 mixture of rotational isomers. 2.10 (2H, s), 2.21 (1H, s), 2.56 (1/3H, ddd, *J* = 12.5, 6.4, 1.7 Hz), 2.67 (2/3H, ddd, *J* = 12.5, 6.4, 1.7 Hz), 2.78 (1/3H, ddd, *J* = 12.5, 11.2, 7.7 Hz), 2.91 (2/3H, ddd, *J* = 12.5, 10.6, 7.9 Hz), 3.06 (1/3H, dt, *J* = 11.2, 6.4 Hz), 3.35 (2/3H, dt, *J* = 10.6, 6.4 Hz), 3.57 (1H, s), 3.76 (2H, s), 3.93 (2/3H, ddd, *J* = 10.6, 7.9, 1.7 Hz), 4.12 (1/3H, ddd, *J* = 11.2, 7.7, 1.7 Hz), 5.88 (2/3H, s), 5.90 (1/3H, s), 6.71 (2/3H, dd, *J* = 7.5, 0.6 Hz), 6.73 (1/3H, d, *J* = 7.5 Hz), 6.78 (1/3H, dt, *J* = 7.5, 0.9 Hz), 6.79 (2/3H, dt, *J* = 7.5, 0.9 Hz), 7.06 (1/3H, d, *J* = 7.5 Hz), 7.13 (2/3H, dt, *J* = 7.5, 0.9 Hz), 7.14 (1/3H, dt, *J* = 7.5, 0.9 Hz), 7.18 (2/3H, dd, *J* = 7.5, 0.9 Hz), 8.44 (2/3H, d, *J* = 2.4 Hz), 8.50 (1/3H, d, *J* = 2.4 Hz), 8.65 (2/3H, d, *J* = 2.4 Hz), 8.67 (1/3H, d, *J* = 2.4 Hz). MS *m/z*: 398 (M^+). *Anal*. Calcd for $C_{19}H_{18}N_4O_6 \cdot H_2O$ C, 56.02; H, 4.73; N, 13.75. Found: C, 56.06; H, 4.53; N, 13.45. **21**: mp 153–154 °C (decomp., yellow prisms, recrystallized from CH_2Cl_2-hexane). IR (KBr): 3091, 2970, 2895, 1655, 1608, 1330, 1485, 1395, 1338, 1265, 757 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: a mixture of rotational isomers. Only major isomer was assigned. 2.14 (3H, s), 2.46 (1H, ddd, *J* = 11.3, 5.4, 1.7 Hz), 2.88 (1H, ddd, *J* = 11.3, 10.3, 7.1 Hz), 3.03 (3H, s), 3.30 (1H, dt, *J* = 10.3, 5.4 Hz), 3.52 (3H, s), 3.97 (1H, ddd, *J* = 10.3, 7.1, 1.7 Hz), 6.05 (1H, s), 6.53 (1H, d, *J* = 7.6 Hz), 6.70 (1H, dt, *J* = 7.6, 0.7 Hz), 6.99 (1H, dd, *J* = 7.6, 0.7 Hz), 7.17 (1H, dt, *J* = 7.6, 0.7 Hz), 8.49 (1H, d, *J* = 2.9 Hz), 8.67 (1H, d, *J* = 2.9 Hz). MS *m/z*: 412 (M^+). *Anal*. Calcd for $C_{20}H_{20}N_4O_6$: C, 58.25; H, 4.89; N, 13.59. Found: C, 58.42; H, 4.84; N, 13.53.

23 from 22b – Anhydrous Et_3N (5.0 mL) and 2,4-dinitrofluorobenzene (0.66 mL, 5.22 mmol) were added to a solution of (*dl*)-*N*b-acetyl-1-hydroxy tryptophan methyl ester (22b, 1.201 g, 4.35 mmol) in anhydrous THF (50 mL) and stirred at rt for 1 h. After adding brine, the whole was extracted with CH_2Cl_2-MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was subjected to column chromatography with $CHCl_3$-MeOH-30% aq. NH_3 (46:2:0.2, v/v) to afford **22a** (70.3 mg, 6%) and **23** (669.1 mg, 35%). **23**: mp 198–199 °C (yellow needles, recrystallized from MeOH). IR (KBr): 3375, 3120, 1729, 1609, 1532, 1427, 1308, 1267, 740 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: a 1:1 mixture of rotational isomer. 2.03 (3/2H, s), 2.30 (3/2H, s), 2.53 (1/2H, d, *J* = 12.7 Hz), 2.78 (1/2H, d, *J* = 12.7 Hz), 3.19 (3/2H, s), 3.25 (3/2H, s), 3.50 (1/2H, dd, *J* = 12.7, 9.4 Hz), 3.65 (1/2H, dd, *J* = 12.7, 9.4 Hz), 4.95 (1/2H, d, *J* = 9.4 Hz), 6.01 (1/2H, s), 6.02 (1/2H, s), 6.66 (1/2H, d, *J* = 7.8 Hz), 6.71 (1/2H, d, *J* = 7.8 Hz), 6.82 (1/2H, td, *J* = 7.8, 0.8 Hz), 6.86 (1/2H, td, *J* = 7.8, 0.8 Hz), 7.11 (1/2H, td, *J* = 7.8, 0.8 Hz), 7.15 (1/2H, td, *J* = 7.8, 0.8 Hz), 7.20 (1/2H, d, *J* = 7.8 Hz), 7.24

(1/2H, d, *J* = 7.8 Hz), 7.77 (1/2H, d, *J* = 3.1 Hz), 7.79 (1/2H, d, *J* = 3.1 Hz), 8.70 (1H, d, *J* = 3.1 Hz). MS *m/z*: 442 (M^+). *Anal*. Calcd for $C_{20}H_{18}N_4O_8 \cdot NH_4OH$: C, 50.32; H, 4.86; N, 14.67. Found: C, 50.43; H, 4.56; N, 14.34.

24 and 25 from 23 – Excess diazomethane in Et_2O was added to a solution of **23** (101.6 mg, 0.23 mmol) in MeOH (40 mL) and stirred at rt for 30 min. The solvent was evaporated under reduced pressure to leave an orange residue which was subjected to column-chromatography on SiO_2 with hexane-EtOAc (1:2, v/v) as an eluent to give **25** (32.0 mg, 30%) and **24** (34.0 mg, 32%) in the order of elution. **24:** mp 175–176 °C (pale orange needles, recrystallized from MeOH). IR (KBr): 3347, 1731, 1648, 1606, 1540, 1482, 1409, 1341, 1252, 981, 746 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: a 10:1 mixture of rotational isomers. Major isomer: 2.07 (3H, s), 3.17 (1H, dd, *J* = 12.7, 8.1 Hz), 3.22 (1H, d, *J* = 12.7 Hz), 3.26 (3H, s), 3.96 (3H, s), 4.63 (1H, d, *J* = 8.1 Hz), 5.89 (1H, s), 6.68 (1H, d, *J* = 7.8 Hz), 6.80 (1H, dd, *J* = 7.8 Hz), 7.14 (1H, d, *J* = 7.8 Hz), 7.15 (1H, dd, *J* = 7.8 Hz), 8.38 (1H, d, *J* = 2.9 Hz), 8.58 (1H, d, *J* = 2.9 Hz). Minor isomer: 2.31 (3/10H, s), 2.99 (2/10H, d, *J* = 5.1 Hz), 3.27 (3/10H, s), 3.73 (3/10H, s), 5.15 (1/10H, t, *J* = 5.1 Hz), 5.87 (1/10H, s), 6.77 (1/10H, d, *J* = 7.8 Hz), 6.87 (1/10H, dd, *J* = 7.8 Hz), 7.05 (1/10H, d, *J* = 7.8 Hz), 7.19 (1/10H, dd, *J* = 7.8 Hz), 8.41 (1/10H, d, *J* = 2.9 Hz), 8.63 (1/10H, d, *J* = 2.9 Hz). MS *m/z*: 456 (M^+). *Anal*. Calcd for $C_{21}H_{20}N_4O_8$: C, 55.26; H, 4.42; N, 12.28. Found: C, 55.04; H, 4.43; N, 12.20.

25: mp 163–165 °C (orange prisms, recrystallized from MeOH). IR (KBr): 1739, 1660, 1604, 1531, 1409, 1340, 1257, 1239, 992, 760 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: a 7:1 mixture of rotational isomers. Major isomer: 2.15 (3H, s), 2.99 (1H, d, *J* = 12.7 Hz), 3.03 (3H, s), 3.13 (1H, dd, *J* = 12.7, 8.4 Hz), 3.28 (3H, s), 3.82 (3H, s), 4.69 (1H, d, *J* = 8.4 Hz), 6.17 (1H, s), 6.42 (1H, d, *J* = 7.5 Hz), 6.74 (1H, dd, *J* = 7.5 Hz), 7.02 (1H, d, *J* = 7.5 Hz), 7.19 (1H, dd, *J* = 7.5 Hz), 8.35 (1H, d, *J* = 2.9 Hz), 8.61 (1H, d, *J* = 2.9 Hz). Minor isomer: 2.34 (3/7H, s), 2.88 (2/7H, d, *J* = 5.7 Hz), 3.03 (3/7H, s), 3.34 (3/7H, s), 3.55 (3/7H, s), 5.34 (1/7H, t, *J* = 5.7 Hz), 5.88 (1/7H, s), 6.44 (1/7H, d, *J* = 7.5 Hz), 6.70 (1/7H, d, *J* = 7.5 Hz), 6.89 (1/7H, d, *J* = 7.5 Hz), 7.15 (1/7H, d, *J* = 7.5 Hz), 8.49 (1/7H, d, *J* = 2.9 Hz), 8.64 (1/7H, d, *J* = 2.9 Hz). MS *m/z*: 470 (M^+). *Anal*. Calcd for $C_{22}H_{22}N_4O_8$: C, 56.17; H, 4.71; N, 11.91. Found: C, 56.04; H, 4.74; N, 11.88.

2,3a-*trans*-3a-Acetoxy- (27) and 2,3a-*cis*-3a-acetoxy-1,8-diacetyl-2-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (28) from 22b – Sodium acetate (373.4 mg, 4.55 mmol) was added to a solution of **22b** (622.9 mg, 2.26 mmol) in Ac_2O (25.0 mL) and stirred at 120 °C for 12 h. Water was added to the reaction mixture and the whole was extracted with CH_2Cl_2-MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to column chromatography on SiO_2 with $CHCl_3$-MeOH-30% aq. NH_3 (100:1:0/1, v/v) as an eluent to afford **28** (170.0 mg, 21%) and **27** (187.3 mg, 23%) in the order of elution. **27**: mp 130–132 °C (colorless prisms, recrystallized from MeOH-H_2O). IR (KBr): 3460, 2950, 1747, 1661, 1478,

1403, 1383, 1233, 763 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: a 4:1 mixture of rotational isomers. 2.05 (3H, s), 2.08 (12/5H, s), 2.43 (3/5H, s), 2.45 (3/5H, s), 2.67 (12/5H, s), 2.90 (1/5H, dd, *J* = 12.7, 9.3 Hz), 3.00 (4/5H, dd, *J* = 12.7, 9.3 Hz), 3.13 (1/5H, d, *J* = 12.7 Hz), 3.19 (3/5H, s), 3.24 (12/5H, s), 4.85–4.98 (4/5H, m), 4.90 (1H, d, *J* = 9.3 Hz), 4.98 (1/5H, d, *J* = 9.3 Hz), 6.43 (4/5H, s), 6.68 (1/5H, s), 7.20 (4/5H, t, *J* = 7.8 Hz), 7.26 (1/5H, t, *J* = 7.8 Hz), 7.39–7.45 (1H, m), 7.48–7.56 (6/5H, m), 7.86 (4/5H, d, *J* = 7.8 Hz). MS *m/z*: 360 (M^+). *Anal*. Calcd for $C_{18}H_{20}N_2O_6 \cdot H_2O$: C, 57.14; H, 5.86; N, 7.40. Found: C, 57.06; H, 5.91; N, 7.39. **28:** mp 156–157 °C (colorless prisms, recrystallized from MeOH-H_2O). IR (KBr): 3475, 2950, 1742, 1678, 1602, 1478, 1403, 1368, 1231, 1043, 760 cm^{-1}. ^{1}H-NMR ($CDCl_3$-CD_3OD, 95:5, v/v) δ: a 4:1 mixture of rotational isomers. 1.81 (3/5H, s), 2.00 (3H, s), 2.25 (12/5H, s), 2.41 (12/5H,s), 2.51 (1H, dd, *J* = 12.2, 10.7 Hz), 2.63 (3/5H, s), 3.24 (4/5H, dd, *J* = 12.2, 6.4 Hz), 3.61–3.66 (1/5H, m), 3.73 (12/5H, s), 3.83 (3/5H, s), 3.91 (4/5H, dd, *J* = 10.7, 6.4 Hz), 4.20–4.23 (1/5H, m), 6.15 (1/5H, s), 6.64 (4/5H, s), 7.16 (1/5H, t, *J* = 7.8 Hz), 7.26–7.28 (8/5H, m), 7.39–7.47 (1H, m), 7.62–7.68 (1H, m) 7.97 (1/5H, d, *J* = 7.8 Hz). MS *m/z*: 360 (M^+). *Anal*. Calcd for $C_{18}H_{20}N_2O_6$: C, 60.00; H, 5.59; N, 7.77. Found: C, 60.09; H, 5.60; N, 7.76.

27 from 28 – KO*t*-Bu (23.1 mg, 0.21 mmol) was added to a solution of **28** (29.6 mg, 0.08 mmol) in anhydrous DMF (5.0 mL) and stirred at rt for 10 min under Ar atmosphere. Then Ac_2O (5.0 mL) and pyridine (5.0 mL) were added to the reaction mixture under ice cooling and stirring was continued at rt for 4 h. Water was added to the reaction mixture and the whole was extracted with CH_2Cl_2-MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column chromatography on Al_2O_3 with EtOAc-hexane (1:1, v/v) as an eluent to afford **27** (15.0 mg, 51%).

***trans*-1,8-Diacetyl-3a-hydroxy-2-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (29) from 27 (46) –** Sodium (1.4 mg, 0.06 mmol) was dissolved in anhydrous MeOH (1.0 mL) at 0 °C and a solution of **27** (5.1 mg, 0.014 mmol) in anhydrous MeOH (1.0 mL) was added to the NaOMe solution at rt. After stirring at rt for 1 h, water was added to the reaction mixture under ice cooling. The whole was acidified with 10% citric acid and extracted with CH_2Cl_2-MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column chromatography on SiO_2 with CH_2Cl_2-MeOH (95:5, v/v) as an eluent to afford **29** (4.3 mg, 96%). **29:** mp 274–275 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3285, 3012, 2931, 1702, 1668, 1635, 1597, 1479, 1125, 763 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: a 4:1 mixture of rotational isomers. 2.00 (12/5H, s), 2.33 (3/5H, s), 2.44 (3/5H, s), 2.61 (12/5H, s), 2.67 (1/5H, dd, *J* = 12.7, 9.8 Hz), 2.80 (4/5H, dd, *J* = 12.7, 9.1 Hz), 2.82 (1/5H, d, *J* = 12. 7 Hz), 2.98 (4/5H, d, *J* = 12.7 Hz), 3.15 (3/5H, s), 3.19 (12/5H, s), 4.79 (4/5H, d, *J* = 9.1 Hz), 4.81 (1/5H, d, *J* = 9.8 Hz), 5.90 (4/5H, s), 6.26 (1/5H, s), 7.16

(4/5H, td, *J* = 7.6, 1.2 Hz), 7.21 (1/5H, t, *J* = 7.6 Hz), 7.33 (4/5H, td, *J* = 7.6, 1.2 Hz), 7.37 (4/5H, dd, *J* = 7.6, 1.2 Hz), 7.41 (1/5H, d, *J* = 7.6 Hz), 7.43 (1/5H, t, *J* = 7.6 Hz), 7.86 (1H, d, *J* = 7.6 Hz). MS *m/z*: 318 (M^+). *Anal*. Calcd for $C_{16}H_{18}N_2O_5$: C, 60.37; H, 5.70; N, 8.80. Found: C, 60.37; H, 5.76; N, 8.75.

(3*S*,5a*R*,10b*S*,11a*S*)-(–)-10b-Benzoyloxy-3-isopropyl-1,3,4,5a,6,10b,11,11a-octahydro-2*H*-pyrazino-[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4-dione (–)-31 from (–)-30 – A solution of (–)-**30** (109.6 mg, 0.26 mmol) in DMF (20.0 mL) was refluxed for 1 h with stirring. After evaporation of the solvent under reduced pressure, the residual oi was purified by column chromatography on SiO_2 with CH_2Cl_2-MeOH (99:1, v/v) as an eluent to afford (–)-**31** (40.1 mg, 37%). (–)-**31:** colorless oil. $[\alpha]_D^{22}$ –438 (c 0.2, MeOH). IR (KBr): 3297, 2938, 1719, 1667, 1611, 1416, 1257, 1104, 704 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 0.95 (3H, d, *J* = 6.0 Hz), 0.97 (3H, d, *J* = 6.0 Hz), 1.59–1.64 (1H, m), 1.87–1.97 (2H, m), 2.89 (1H, dd, *J* = 12.8, 11.5 Hz), 3.34 (1H, dd, *J* = 12.8, 6.7 Hz), 4.15 (1H, ddd, *J* = 6.7, 4.6, 1.7 Hz), 4.26 (1H, ddd, *J* = 11.5, 6.7, 1.7 Hz), 6.00 (1H, s), 6.71 (1H, d, *J* = 8.0 Hz), 6.79 (1H, td, *J* = 7.5, 1.0 Hz), 7.19 (1H, ddd, *J* = 8.0, 7.5, 1.0 Hz), 7.43–7.48 (2H, m), 7.56–7.61 (2H, m), 7.96–7.99 (2H, m). MS *m/z*: 419 (M^+). *Anal*. Calcd for $C_{24}H_{25}N_3O_4$: C, 68.72; H, 6.01; N, 10.02. Found: C, 68.52; H, 5.98; N, 9.93.

(3*S*,6*S*)-(–)-6-(1-Benzoyloxyindol-3-ylmethyl)-3-isobutyl-2,5-piperazinedione (–)-30 from (–)-35a – A solution of (–)-**35a** (106.3 mg, 0.34 mmol) in anhydrous pyridine (10.0 mL) was added to benzoyl chloride (952,6 mg, 6.8 mmol) at 0 °C and stirred at rt for 1 h. Water was added to the reaction mixture, and the whole was extracted with CH_2Cl_2-MeOH (9:1, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil. Purification by column chromatography on SiO_2 with $CHCl_3$-MeOH-30% aq. NH_3 (46:1:0.1, v/v) as an eluent to give (–)-**30** (136.1 mg, 96%). (–)-**30:** colorless oil. $[\alpha]_D^{26}$ –8.2 (c 0.29, MeOH). IR (KBr): 3175, 3044, 2950, 1775, 1665, 1445, 1231, 1003, 730 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 0.29 (1H, ddd, *J* = 13.9, 9.7, 5.0 Hz), 0.55 (3H, d, *J* = 6.5 Hz), 0.67 (3H, d, *J* = 6.5 Hz), 0.95 (1H, ddd, *J* = 13.9, 9.5, 4.4 Hz), 1.24–1.34 (1H, m), 3.15 (1H, dd, *J* = 14.8, 4.8 Hz), 3.49 (1H, dd, *J* = 14.8, 4.0 Hz), 3.67 (1H, ddd, *J* = 9.7, 4.4, 1.1 Hz), 4.33 (1H, ddd, *J* = 4.8, 4.0, 1.1 Hz), 7.11–7.15 (1H, m), 7.20–7.22 (2H, m), 7.26 (1H, s), 7.60–7.65 (2H, m), 7.68 (1H, ddd, *J* = 8.1, 1.0, 0.9 Hz), 7.76–7.80 (1H, m), 8.18–8.21 (2H, m). MS *m/z*: 419 (M^+). *Anal*. Calcd for $C_{24}H_{25}N_3O_4$: C, 68.72; H, 6.01; N, 10.02. Found: C, 68.48; H, 5.99; N, 10.01.

(3*S*,6*S*)-(–)-3-Isobutyl-6-(1-methoxyindol-3-ylmethyl)-2,5-piperazinedione ((–)-35b) from (–)-35a – Excess diazomethane in Et_2O was added to the solution of (–)-**35a** (31.4 mg, 0.10 mmol) in MeOH (3.0 mL) and stirred at rt for 10 min. After evaporation of the solvent under reduced pressure, the residual oil was purified by column chromatography on SiO_2 with CH_2Cl_2-MeOH (95:5, v/v) as an eluent to afford (–)-**35b** (30.3 mg, 93%). (–)-**35b:** mp 200–202 °C (colorless prisms, recrystallized from MeOH-CH_2Cl_2-hexane). $[\alpha]_D^{26}$ –47.5 (c 0.30, DMF). IR (KBr): 3190, 3055, 2975, 1633, 1450, 1324, 1093, 736

cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 0.12 (1H, ddd, J = 13.7, 9.0, 3.7 Hz), 0.42 (3H, d, J = 6.6 Hz), 0.53 (3H, d, J = 6.6 Hz), 0.75 (1H, ddd, J = 13.7, 9.0, 4.6 Hz), 1.19–1.27 (1H, m), 2.97 (1H, dd, J = 14.4, 4.6 Hz), 3.24 (1H, dd, J = 14.4, 3.9 Hz), 3.42–3.46 (1H, m), 4.01 (3H, s), 4.11–4.13 (1H, m), 7.01 (1H, td, J = 8.1, 1.0 Hz), 7.17 (1H, td, J = 8.1, 1.0 Hz), 7.28 (1H, s), 7.37 (1H, d, J = 8.1 Hz), 7.59 (1H, d, J = 8.1 Hz), 8.00 (1H, d, J = 2.7 Hz), 8.08 (1H, d, J = 2.0 Hz). MS *m/z*: 329 (M^+). *Anal*. Calcd for $C_{18}H_{23}N_3O_3$: C, 65.63; H, 7.04; N, 12.76. Found: C, 65.71; H, 7.14; N, 12.74.

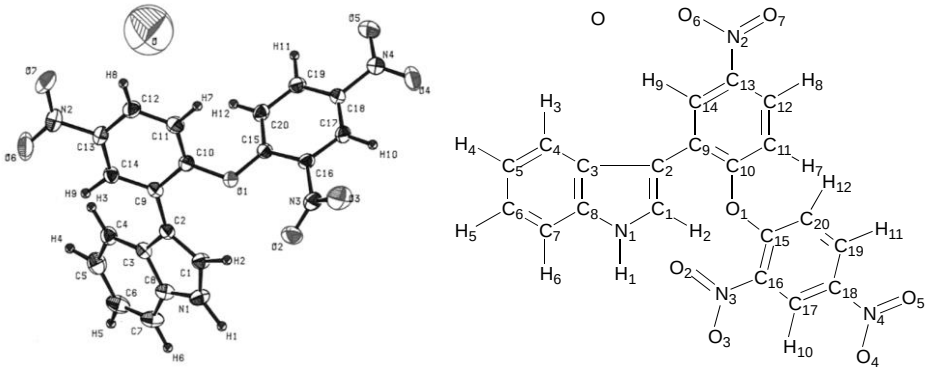
(3*S*,6*S*)-(–)-6-(1-Hydroxyindol-3-ylmethyl)-3-isobutyl-2,5-piperazinedione ((–)-35a) from 34 – A solution of $Na_2WO_4 \cdot 2H_2O$ (10.7 mg, 0.03 mmol) in H_2O (0.9 mL) was added to a solution of **34** (48.7 mg, 0.16 mmol) in MeOH (5.0 mL) and CH_2Cl_2 (3.0 mL), and then a solution of 30% H_2O_2 (184.6 mg, 1.63 mmol) in MeOH (1.0 mL) was added to the reaction mixture at 0 °C. After stirring at rt for 1 h, water was added and the whole was extracted with CH_2Cl_2-MeOH (9:1, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil. Purification by column chromatography on SiO_2 with $CHCl_3$-MeOH-30% aq. NH_3 (46:5:0.5, v/v) as an eluent to give (–)-**35a** (32.3 mg, 63%). (–)-**35a:** colorless oil. $[\alpha]_D^{29}$ –46.6 (c 0.30, DMF). IR (film): 3164, 2950, 1659, 1446, 1316, 1093, 730 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: –0.03 (1H, ddd, J = 13.8, 9.9, 5.0 Hz), 0.47 (3H, d, J = 6.6 Hz), 0.61 (3H, d, J = 6.6 Hz), 0.77 (1H, ddd, J = 13.8, 9.5, 4.4 Hz), 1.13–1.22 (1H, m), 3.08 (1H, dd, J = 14.7, 4.6 Hz), 3.44 (1H, dd, J = 14.7, 3.8 Hz), 3.60 (1H, ddd, J = 9.9, 4.4, 1.1 Hz), 4.25 (1H, ddd, J = 4.6, 3.8, 1.1 Hz), 6.99 (1H, ddd, J = 8.1, 7.0, 1.0 Hz), 7.10 (1H, s), 7.13 (1H, ddd, J = 8.1, 7.0, 1.0 Hz), 7.34 (1H, ddd, J = 8.1, 1.0, 0.9 Hz), 7.56 (1H, ddd, J = 8.1, 1.0, 0.9 Hz). MS *m/z*: 315 (M^+). *Anal*. Calcd for $C_{17}H_{21}N_3O_3 \cdot 1/4H_2O$: C, 63.83; H, 6.77; N, 13.13. Found: C, 63.72; H, 6.70; N, 12.83.

(3*S*,6*S*)-6-[(3*RS*)-2,3-Dihydroindol-3-ylmethyl]-3-isobutyl-2,5-piperazinedione 34 from (+)-33 – Et_3SiH (0.11 mL, 0.69 mmol) was added to a solution of (+)-**33** (99.4 mg, 0.33 mmol) in CF_3CO_2H (3 mL) at rt. After stirring for 15 min at 60 °C, additional Et_3SiH (0.22 mL, 1.38 mmol) was added and the whole was continuously stirred for 2 h at 60 °C. The solvent was evaporated under reduced pressure. Water was added to the residue and the resultant solution was made alkaline by addition of sat. aqueous $HaHCO_3$ under ice cooling. The whole was extracted with CH_2Cl_2-MeOH (9:1, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to column chromatography on SiO_2 with $CHCl_3$-MeOH-30% aq. NH_3 (46:2:0.2, v/v) as an eluent to give **34** (1:1 mixture of diastereomers at the position 3 of 2,3-dihydroindole nucleus, 82.6 mg, 83%). **34:** colorless oil. ^{1}H-NMR (CD_3OD) δ: 0.97 (3H, d, J = 6.6 Hz), 0.98 (3H, d, J = 6.6 Hz), 0.99 (3H, d, J = 6.6 Hz), 1.00 (3H, d, J = 6.6 Hz), 1.63–1.70 (2H, m), 1.72–1.80 (2H, m), 1.83–1.92 (2H, m), 1.97 (1H, ddd, J = 13.7, 8.6, 7.5 Hz), 2.09–2.20 (2H, m), 2.33 (1H, ddd, J = 13.7, 6.0, 5.3 Hz), 3.19–3.24 (2H, m), 3.43–3.50 (2H, m), 3.66 (1H, dd, J = 9.1, 8.6 Hz), 3.70 (1H, dd, J = 9.1, 8.6 Hz), 3.88 (1H, ddd, J =

8.6, 4.6, 0.9 Hz), 3.94 (2H, ddd, *J* = 9.1, 4.6, 0.9 Hz), 4.06 (1H, ddd, *J* = 6.8, 6.0, 0.9 Hz), 6.67–6.74 (4H, m), 6.98–7.03 (2H, m), 7.10–7.13 (2H, m).

(3*S*,6*S*)-(+)-6-(Indol-3-ylmethyl)-3-isobutyl-2,5-piperazinedione (+)-33 from (+)-32 – A solution of benzyloxycarbonyl-L-tryptophyl-L-leucine methyl ester (+)-**32** (401.6 mg, 0.86 mmol) in MeOH (100 mL) was hydrogenated over 10% Pd/C (201.3 mg) at rt for 40 min. After removal of the catalyst by filtration, the solvent was evaporated off under reduced pressure. The residue was dissolved in MeOH (100 mL) and the whole was heated at reflux for 48 h. After evaporation of the solvent, the residue was purified by column chromatography on SiO_2 with CH_2Cl_2-MeOH (98:2, v/v) as an eluent to afford (+)-**33** (156.1 mg, 60%). (+)-**33:** mp 270–271 °C (decomp., colorless prisms, recrystallized from MeOH–H_2O, lit.,[9ab] mp 265–268 °C (decomp.)). $[\alpha]_D^{32}$ +54.4 (c 0.4, AcOH), lit.,[9ab] $[\alpha]_D^{25\text{-}28}$ +48.0 (c 0.4, AcOH). IR (KBr): 3178, 3040, 2959, 1664, 1458, 743 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: –0.17 (1H, ddd, *J* = 13.7, 9.7, 4.8 Hz), 0.46 (3H, d, *J* = 6.6 Hz), 0.60 (3H, d, *J* = 6.6 Hz), 0.67 (1H, ddd, *J* = 13.7, 9.5, 4.2 Hz), 1.10–1.19 (1H, m), 3.11 (1H, dd, *J* = 14.7, 4.6 Hz), 3.48 (1H, dd, *J* = 14.7, 3.7 Hz), 3.57 (1H, ddd, *J* = 9.7, 4.2, 0.9 Hz), 4.26 (1H, ddd, *J* = 4.6, 3.7, 0.9 Hz), 6.99 (1H, td, *J* = 8.1, 1.0 Hz), 7.05 (1H, s), 7.07 (1H, td, *J* = 8.1, 1.0 Hz), 7.31 (1H, dd, *J* = 8.1, 1.0 Hz), 7.59 (1H, dd, *J* = 8.1, 1.0 Hz). We determined that (+)-**33** was the same as the reported sample.[9ab]

X-Ray Analysis of 8, 13, 25, and 29



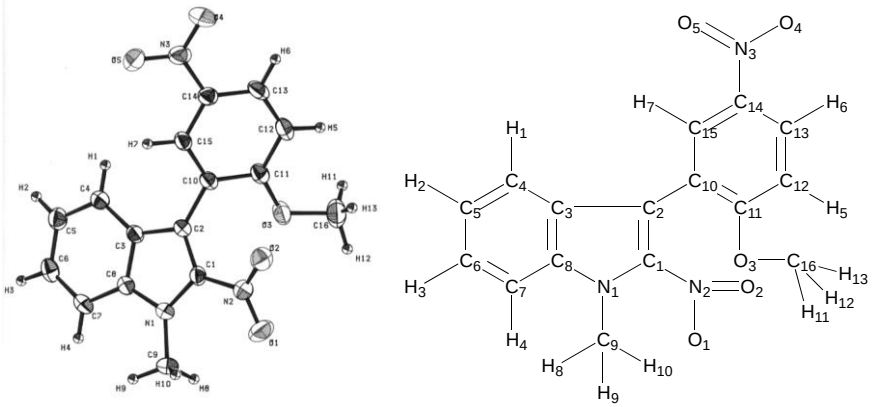
Numbering

Figure 2. X-Ray Analysis of **8**, R= 0.063 and Rw= 0.078

A single crystal (1.00x0.50x0.40 mm) of **8** was obtained by recrystallization from CH_2Cl_2-MeOH. All measurements were made on a Rigaku AFC5R diffractometer with graphite monochromated Mo-$K\alpha$ radiation (λ=0.71069 Å). Crystal data: $C_{20}H_{12}N_4O_7$, M=420.34, monoclinic, space group $P2_1/c$ (#14), a=10.728 (3)Å, b=18.543 (5)Å, c=10.903 (2)Å, β=116.40 (2)°, V=1943 (1)Å^3, Z=4, D_{calc}=1.437 g/cm^3, F(000)=864, and μ(Mo$K\alpha$)=1.04 cm^{-1}. The structure was solved by direct methods using MITHRIL.[11]

The non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 2367 observed reflections ($I>3.00\sigma(I)$, $2\theta<55.0°$) and 284 variable parameters. The final refinement converged with R= 0.063 and Rw= 0.078.

atom	x	y	z	B (eq)	atom	x	y	z	B (eq)
O	0.576 (1)	0.0270 (7)	0.529 (1)	30.1 (5)	C (11)	0.3959 (4)	0.0901 (2)	0.7646 (4)	4.0 (2)
O (1)	0.8134 (3)	0.0848 (3)	1.1619 (4)	7.7 (2)	C (12)	0.5395 (4)	0.0915 (2)	0.8283 (4)	4.0 (2)
O (2)	0.8199 (3)	0.1038 (2)	0.9731 (4)	7.6 (2)	C (13)	0.6036 (4)	0.0951 (2)	0.9700 (4)	3.6 (2)
O (3)	0.1772 (3)	0.0919 (2)	0.7746 (3)	3.8 (1)	C (14)	0.5312 (4)	0.0979 (2)	1.0465 (4)	3.2 (1)
O (4)	–0.0582 (3)	0.0223 (2)	0.7046 (3)	6.6 (2)	C (15)	0.1037 (4)	0.1337 (2)	0.6633 (4)	3.0 (1)
O (5)	–0.1577 (4)	0.0073 (2)	0.4869 (4)	7.4 (2)	C (16)	–0.0283 (4)	0.1101 (2)	0.5698 (4)	3.2 (1)
O (6)	–0.2589 (4)	0.2373 (2)	0.2386 (4)	8.5 (2)	C (17)	–0.1094 (4)	0.1490 (2)	0.4547 (4)	3.7 (2)
O (7)	–0.0845 (4)	0.3056 (2)	0.2832 (4)	7.2 (2)	C (18)	–0.0566 (4)	0.2134 (2)	0.4343 (4)	3.4 (2)
N (1)	0.1445 (4)	0.0876 (2)	1.1376 (4)	4.1 (1)	C (19)	0.0719 (4)	0.2384 (2)	0.5240 (4)	3.5 (2)
N (2)	0.7560 (4)	0.0955 (2)	1.0408 (4)	4.8 (2)	C (20)	0.1509 (4)	0.1987 (2)	0.6389 (4)	3.5 (2)
N (3)	–0.0850 (4)	0.0421 (2)	0.5906 (4)	4.5 (2)	H (1)	0.0504	0.0663	1.1388	5
N (4)	–0.1392 (4)	0.2545 (2)	0.3091 (4)	4.9 (2)	H (2)	0.1049	0.0465	0.9411	4.1
C (1)	0.1789 (4)	0.0757 (2)	1.0327 (4)	3.5 (2)	H (3)	0.551	0.1967	1.2689	4.5
C (2)	0.3079 (4)	0.1043 (2)	1.0647 (4)	3.0 (1)	H (4)	0.5696	0.2346	1.459	5.5
C (3)	0.3545 (4)	0.1376 (2)	1.1984 (4)	3.2 (1)	H (5)	0.3713	0.2159	1.5337	6.2
C (4)	0.4707 (4)	0.1793 (2)	1.2833 (4)	3.8 (2)	H (6)	0.1825	0.1402	1.389	5.2
C (5)	0.4764 (5)	0.2054 (3)	1.4060 (4)	5.0 (2)	H (7)	0.3503	0.0863	0.6627	4.4
C (6)	0.3722 (6)	0.1908 (3)	1.4446 (4)	5.1 (2)	H (8)	0.5912	0.0849	0.7768	4.6
C (7)	0.2578 (5)	0.1509 (3)	1.3641 (5)	4.8 (2)	H (9)	0.587	0.1001	1.1548	3.7
C (8)	0.2497 (4)	0.1251 (2)	1.2403 (4)	3.8 (2)	H (10)	–0.2064	0.1275	0.391	4.3
C (9)	0.3858 (4)	0.0995 (2)	0.9827 (4)	2.9 (1)	H (11)	0.1089	0.2848	0.5015	4.1
C (10)	0.3221 (4)	0.0953 (2)	0.8397 (4)	3.3 (2)	H (12)	0.2405	0.2196	0.7023	3.9

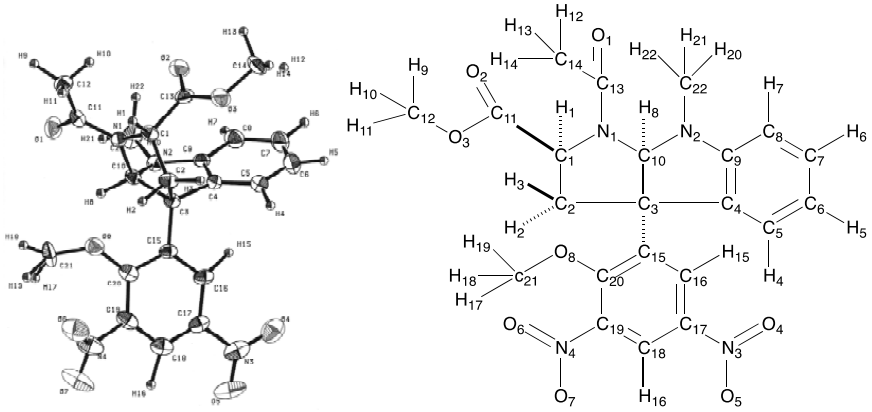


Numbering

Figure 3. X-Ray Analysis of **13**, R= 0.043 and Rw= 0.044

A single crystal (0.30x0.30x0.20 mm) of **13** was obtained by recrystallization from CH_2Cl_2-hexane. All measurements were made on a Rigaku AFC5R diffractometer with graphite monochromated Mo-$K\alpha$ radiation (λ=0.71069 Å). Crystal data: $C_{16}H_{13}N_3O_5$, M=327.30, monoclinic, space group $C2/c$ (#15), a=17.843 (6)Å, b=11.928 (5)Å, c=15.225 (1)Å, β=111.04 (3)°, V=3024 (2)Å^3, Z=8, D_{calc}=1.438 g/cm^3, F(000)=1360, and μ(Mo$K\alpha$)=1.02 cm^{-1}. The structure was solved by direct methods using MITHRIL.[11] The non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 1298 observed reflections (I>3.00σ(I), 2θ<55.1°) and 269 variable parameters. The final refinement converged with R= 0.043 and Rw= 0.044.

atom	x	y	z	B (eq)	atom	x	y	z	B (eq)
O (1)	0.6944 (2)	0.0789 (3)	0.7704 (3)	7.6 (2)	C (12)	0.6064 (3)	0.4971 (3)	0.6166 (3)	4.3 (2)
O (2)	0.6575 (2)	0.2449 (2)	0.7907 (2)	5.0 (1)	C (13)	0.5484 (3)	0.5682 (3)	0.6233 (3)	4.3 (2)
O (3)	0.6475 (2)	0.3059 (2)	0.6060 (2)	4.6 (1)	C (14)	0.4796 (2)	0.5245 (3)	0.6312 (3)	3.6 (2)
O (4)	0.4298 (2)	0.7004 (2)	0.6434 (3)	7.5 (2)	C (15)	0.4685 (2)	0.4100 (3)	0.6336 (3)	3.4 (2)
O (5)	0.3543 (2)	0.5595 (2)	0.6366 (3)	6.8 (2)	C (16)	0.7259 (3)	0.3417 (6)	0.6112 (6)	6.9 (3)
N (1)	0.5370 (2)	0.0278 (2)	0.6583 (2)	3.4 (1)	H (1)	0.359 (2)	0.265 (3)	0.491 (2)	3.6 (8)
N (2)	0.6448 (2)	0.1531 (3)	0.7524 (2)	4.2 (2)	H (10)	0.595 (3)	–0.074 (4)	0.769 (4)	10 (2)
N (3)	0.4173 (2)	0.5992 (3)	0.6376 (2)	4.8 (2)	H (11)	0.716 (3)	0.393 (4)	0.562 (3)	8 (2)
C (1)	0.5668 (2)	0.1350 (3)	0.6819 (3)	3.2 (2)	H (12)	0.761 (3)	0.271 (4)	0.615 (3)	9 (2)
C (2)	0.5148 (2)	0.2150 (3)	0.6301 (2)	3.0 (2)	H (13)	0.750 (3)	0.380(4)	0.668 (3)	7 (1)
C (3)	0.4457 (2)	0.1547 (3)	0.5713 (3)	3.1 (2)	H (2)	0.271 (2)	0.128 (3)	0.414 (3)	5 (1)
C (4)	0.3717 (2)	0.1876 (4)	0.5049 (3)	3.8 (2)	H (3)	0.298 (2)	–0.061 (3)	0.438 (2)	4.2 (9)
C (5)	0.3179 (3)	0.1058 (4)	0.4594 (3)	4.4 (2)	H (4)	0.419 (2)	–0.119 (3)	0.552 (2)	2.1 (7)
C (6)	0.3361 (2)	–0.0081 (4)	0.4765 (3)	4.4 (2)	H (5)	0.656 (2)	0.522 (3)	0.613 (3)	5 (1)
C (7)	0.4072 (2)	–0.0426 (3)	0.5416 (3)	4.0 (2)	H (6)	0.556 (2)	0.649 (3)	0.627 (2)	4.2 (9)
C (8)	0.4620 (2)	0.0401 (3)	0.5902 (3)	3.2 (2)	H (7)	0.420 (2)	0.383 (2)	0.642 (2)	2.3 (7)
C (9)	0.5732 (3)	–0.0800 (4)	0.6985 (4)	4.5 (2)	H (8)	0.617 (3)	–0.098 (4)	0.679 (3)	7 (1)
C (10)	0.5264 (2)	0.3370 (3)	0.6279 (3)	3.3 (2)	H (9)	0.530 (3)	–0.138 (3)	0.677 (3)	7 (1)
C (11)	0.5955 (2)	0.3823 (3)	0.6173 (3)	3.7 (2)					

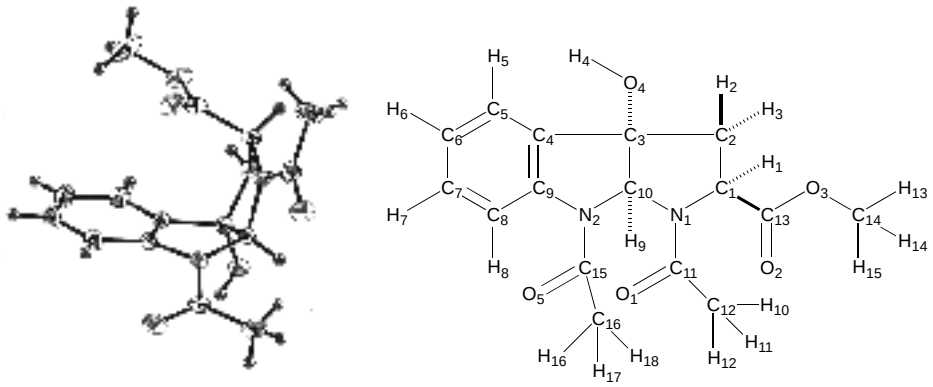


Numbering

Figure 4. X-Ray Analysis of **25,** R= 0,052 and Rw= 0.053

X-Ray analysis of 25 – A single crystal (0.50x0.30x0.20 mm) of **25** was obtained by recrystallization from MeOH. All measurements were made on a Rigaku AFC5R diffractometer with graphite monochromated Mo-$K\alpha$ radiation (λ=0.71069 Å). Crystal data: $C_{22}H_{22}N_4O_8$, M=470.44, monoclinic, space group $P2_1/n$ (#14), a=9.978 (3)Å, b=12.818 (4)Å, c=17.562 (5)Å, β=90.28 (2)°, V=2246 (1)Å^3, Z=4, D_{calc}=1.391 g/cm^3, F(000)=984, and μ(Mo$K\alpha$)=1.01 cm^{-1}. The structure was solved by direct methods using MITHRIL[11]. The non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 1479 observed reflections (I>3.00σ (I), 2θ <55.0°) and 307 variable parameters. The final refinement converged with R= 0.052 and Rw= 0.053.

atom	x	y	z	B (eq)	atom	x	y	z	B (eq)
O (1)	0.5271 (3)	0.1035 (3)	0.2176 (2)	4.7 (2)	C (17)	0.9459 (5)	–0.2436 (4)	0.4419 (3)	3.8 (3)
O (2)	0.8734 (3)	0.2890 (3)	0.2499 (2)	4.8 (2)	C (18)	0.8304 (6)	–0.2778 (4)	0.4739 (3)	4.3 (3)
O (3)	0.9654 (3)	0.3016 (3)	0.3659 (2)	5.1 (2)	C (19)	0.7201 (5)	–0.2118 (4)	0.4701 (3)	4.1 (3)
O (4)	1.1736 (4)	–0.2722 (3)	0.4267 (2)	6.7 (2)	C (20)	0.7225 (5)	–0.1154 (4)	0.4310 (3)	3.6 (3)
O (5)	1.0507 (5)	–0.4004	0.4656 (2)	7.8 (3)	C (21)	0.4912 (5)	–0.0927 (5)	0.3982 (3)	5.7 (3)
O (6)	0.5402 (4)	–0.1754 (3)	0.5482 (2)	6.8 (2)	C (22)	0.7912 (5)	0.0260 (5)	0.1473 (3)	5.5 (3)
O (7)	0.5748 (5)	–0.3365 (3)	0.5163 (2)	8.7 (3)	H (1)	0.7011	0.2562	0.3883	4.1
O (8)	0.6156 (3)	–0.0521 (2)	0.4224 (2)	4.4 (2)	H (2)	0.7337	0.0931	0.4499	4.2
N (1)	0.6975 (4)	0.1374 (3)	0.2985 (2)	3.1 (2)	H (3)	0.9010	0.1460	0.4461	4.2
N (2)	0.8411 (4)	0.0172 (3)	0.2241 (2)	3.4 (2)	H (4)	1.1295	0.0577	0.4182	5.4
N (3)	1.0661 (5)	–0.3104 (4)	0.4448 (2)	5.3 (3)	H (5)	1.3094	0.1008	0.3196	6.3
N (4)	0.6015 (5)	–0.2444 (4)	0.5132 (2)	5.8 (3)	H (6)	1.2874	0.0935	0.1846	6.2
C (1)	0.7683 (5)	0.1998 (4)	0.3552 (3)	3.2 (2)	H (7)	1.0702	0.0339	0.1376	5.5
C (2)	0.8195 (5)	0.1178 (4)	0.4113 (3)	3.4 (3)	H (8)	0.6681	–0.0199	0.2802	3.7
C (3)	0.8546 (4)	0.0237 (4)	0.3601 (2)	3.0 (2)	H (9)	0.4407	0.2946	0.2422	4.5
C (4)	0.9889 (4)	0.0425 (4)	0.3213 (3)	3.2 (2)	H (10)	0.5939	0.3238	0.2722	4.5
C (5)	1.1125 (5)	0.0647 (4)	0.3540 (3)	4.3 (3)	H (11)	0.4999	0.2914	0.3368	4.5
C (6)	1.2202 (5)	0.0821 (4)	0.3060 (4)	5.5 (3)	H (12)	1.1340	0.4070	0.3940	6.8
C (7)	1.2055 (5)	0.0785 (4)	0.2283 (3)	5.3 (3)	H (13)	1.0374	0.4248	0.2947	7.1
C (8)	1.0809 (5)	0.0583 (4)	0.1948 (3)	4.7 (3)	H (14)	1.1284	0.3243	0.2821	7.1
C (9)	0.9722 (5)	0.0403 (4)	0.2433 (3)	3.3 (2)	H (15)	1.0386	–0.1106	0.3661	4.3
C (10)	0.7555 (4)	0.0316 (3)	0.2905 (2)	2.8 (2)	H (16)	0.8000	–0.3581	0.5024	5.5
C (11)	0.5809 (5)	0.1645 (4)	0.2623 (3)	3.5 (3)	H (17)	0.4619	–0.1686	0.3832	6.2
C (12)	0.5224 (5)	0.2690 (4)	0.2783 (3)	3.9 (3)	H (18)	0.4132	–0.0730	0.3899	6.2
C (13)	0.8742 (5)	0.2667 (4)	0.3166 (3)	3.7 (3)	H (19)	0.4153	–0.1179	0.4441	6.2
C (14)	1.0734 (5)	0.3664 (4)	0.3367 (3)	5.6 (3)	H (20)	0.8641	0.0112	0.1090	6.1
C (15)	0.8452 (5)	–0.0808 (4)	0.4004 (2)	3.1 (2)	H (21)	0.7083	0.0110	0.1357	6.1
C (16)	0.9571 (5)	–0.1458 (4)	0.4073 (2)	3.5 (2)	H (22)	0.7961	0.1152	0.1290	6.1



Numbering

Figure 5. X-Ray Analysis of **29**, R= 0.045 and Rw= 0.050

X-Ray analysis of 29 – A single crystal (0.50x0.30x0.10 mm) of **29** was obtained by recrystallization from MeOH. All measurements were made on a Rigaku AFC5R diffractometer with graphite monochromated Mo-$K\alpha$ radiation (λ=0.71069 Å). Crystal data: $C_{16}H_{18}N_2O_5$, M=318.33, monoclinic, space group $P2_1/a$ (#14), a=8.230 (5)Å, b=20.75 (1)Å, c=9.607 (6)Å, β=112.86 (5)°, V=1512 (2)Å^3, Z=4, D_{calc}=1.398 g/cm^3, F(000)=672, and μ(Mo$K\alpha$)=0.98 cm^{-1}. The structure was solved by direct methods using MITHRIL[11]. The non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 1830 observed reflections (I>3.00σ (I), 2θ <55.0°) and 280 variable parameters. The final refinement converged with R= 0.045 and Rw= 0.050.

atom	x	y	z	B (eq)	atom	x	y	z	B (eq)
O (1)	0.7200 (3)	0.3296 (1)	0.6974 (2)	4.0 (1)	C (15)	0.9996 (4)	0.4208 (1)	0.5978 (3)	2.8 (1)
O (2)	0.5902 (3)	0.2704 (1)	0.2381 (2)	4.0 (1)	C (16)	0.9947 (6)	0.4357 (2)	0.7470 (4)	4.1 (2)
O (3)	0.3547 (3)	0.3165 (1)	0.0607 (2)	4.4 (1)	H (1)	0.322 (4)	0.329 (1)	0.320 (3)	3.2 (6)
O (4)	0.5443 (3)	0.5186 (1)	0.3237 (2)	2.90 (8)	H (2)	0.313 (4)	0.425 (1)	0.147 (3)	3.4 (7)
O (5)	1.1385 (3)	0.4189 (1)	0.5788 (2)	4.4 (1)	H (3)	0.311 (4)	0.442 (1)	0.309 (3)	3.0 (6)
N (1)	0.5701 (3)	0.3564 (1)	0.4557 (2)	2.35 (9)	H (4)	0.636 (5)	0.536 (2)	0.339 (5)	7 (1)
N (2)	0.8447 (3)	0.4095 (1)	0.4767 (2)	2.17 (8)	H (5)	0.518 (4)	0.445 (1)	0.013 (3)	2.7 (6)
C (1)	0.4226 (4)	0.3501 (1)	0.3092 (3)	2.7 (1)	H (6)	0.726 (4)	0.407 (2)	-0.084 (4)	4.1 (8)
C (2)	0.3816 (4)	0.4200 (1)	0.2592 (4)	2.8 (1)	H (7)	0.993 (4)	0.366 (1)	0.076 (3)	3.8 (7)
C (3)	0.5624 (3)	0.4511 (1)	0.3164 (3)	2.3 (1)	H (8)	1.064 (4)	0.366 (1)	0.339 (3)	2.9 (6)
C (4)	0.6719 (3)	0.4306 (1)	0.2281 (3)	2.2 (1)	H (9)	0.663 (3)	0.441 (1)	0.556 (3)	1.2 (5)
C (5)	0.6286 (4)	0.4306 (1)	0.0741 (3)	3.1 (1)	H (10)	0.458 (5)	0.236 (2)	0.464 (5)	7 (1)
C (6)	0.7498 (5)	0.4080 (2)	0.0188 (4)	3.7 (1)	H (11)	0.375 (7)	0.273 (3)	0.555 (6)	11 (2)

C (7)	0.9106 (5)	0.3847 (2)	0.1172 (4)	3.8 (1)	H (12)	0.531 (6)	0.233 (2)	0.651 (5)	10 (1)
C (8)	0.9556 (4)	0.3835 (2)	0.2708 (4)	3.1 (1)	H (13)	0.341 (6)	0.303 (2)	–0.142 (6)	9 (2)
C (9)	0.8337 (3)	0.4071 (1)	0.3249 (3)	2.3 (1)	H (14)	0.338 (8)	0.239 (3)	–0.065 (6)	12 (2)
C (10)	0.6637 (3)	0.4178 (1)	0.4703 (3)	2.2 (1)	H (15)	0.53 (1)	0.271 (4)	–0.019 (8)	17 (3)
C (11)	0.6016 (4)	0.3174 (1)	0.5763 (3)	2.8 (1)	H (16)	0.925 (8)	0.469 (3)	0.753 (6)	12 (2)
C (12)	0.4885 (6)	0.2587 (2)	0.5560 (5)	4.9 (2)	H (17)	1.099 (6)	0.452 (2)	0.809 (5)	8 (1)
C (13)	0.4696 (4)	0.3075 (1)	0.2007 (3)	2.9 (1)	H (18)	0.954 (6)	0.402 (2)	0.791 (5)	9 (1)
C (14)	0.387 (1)	0.2812 (3)	–0.0562 (5)	6.7 (3)					

REFERENCES AND NOTES

1. a) This is Part 145 of a series entitled “The Chemistry of Indoles”; b) Part 144: K. Nakagawa (Goto), T. Kobayashi, T. Kawasaki, and M. Somei, *Heterocycles*, 2018, **97**, 968.
2. Professor Emeritus of Kanazawa University. Present address: 56-7 Matsuhidai, Matsudo, Chiba 270-2214, Japan.
3. T. Kawasaki, M. Tabata, K. Nakagawa, K. Kobayashi, A. Kodama, T. Kobayashi, M. Hasegawa, K. Tanii, and M. Somei, *Heterocycles*, 2015, **90**, 1038 and references cited therein.
4. M. Somei, T. Kawasaki, Y. Fukui, F. Yamada, T. Kobayashi, H. Aoyama, and D. Shinmyo, *Heterocycles*, 1992, **34**, 1877.
5. Y. Fukui and M. Somei, *Heterocycles*, 2001, **55**, 2055.
6. S. Safe and A. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1972, 427.
7. A. J. Birch and J. J. Wright, *Tetrahedron*, 1970, **26**, 2329.
8. H. Hayashi, T. Fujiwara, S. Murao, and M. Arai, *Agric. Biol. Chem*., 1991, **55**, 3143.
9. a) T. Shiba and K. Nunami, *Tetrahedron Lett*., 1974, 509; b) D. E. Nitecki, B. Halpern, and J. W. Westley, *J. Org. Chem*., 1968, **33**, 864.
10. a) A. E. Lanzilotti, R. Littell, W. J. Fanshawe, T. C. McKenzie, and F. M. Lovell, *J. Org. Chem*., 1979, **44**, 4809; b) M. Somei and T. Kawasaki, *Heterocycles*, 1989, **29**, 1251.
11. C. J. Gilmore, *J. Appl. Cryst*., 1984, **17**, 42.