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1-HYDROXYINDOLES: PRODUCTION OF FERULOYLSEROTONIN, AN ALKALID OF SAFFLOWER SEED, NOVEL RING SYSTEM COMPOUND, 1,10-DIAZA-9,20-DIOXOKABUTANES, 2,2'-BISINDOLES, AND (*dl*)-3a, 3a'-BISPYRROLO[2,3-*b*]INDOLES[1]

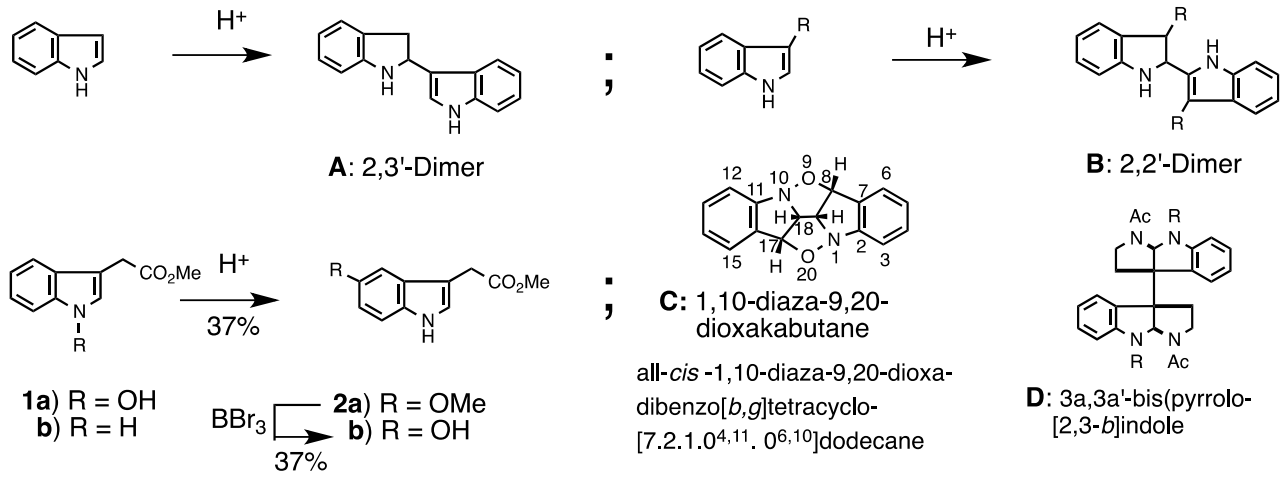
Mutsuko Tabata,[a] Naoki Oshikiri,[a] Masakazu Hasegawa,[a] Keiichi Satoh,[a] Yoshikazu Fukui,[a] Yoshiyuki Nagahama,[a] Harunobu Morikawa,[a] Fumio Yamada,[b] and Masanori Somei,[a,c]*

a Faculty of Pharmaceutical Sciences, Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa, 920-1192, Japan; b Sumika Technoservice Corporation, 2-1-4, Takatsukasa, Takarazuka, Hyogo, 665-0051, Japan; c Someiyakko Kenkyusho, 56-7 Matsuhidai, Matsudo, Chiba, 270-2214, Japan.
Corresponding author: e-mail address: somei.home@topaz.plala.or.jp

Abstract – Methyl 1-hydroxyindole-3-acetate (**1a**) produced novel hexacyclic 8,17-bis(methoxycarbonylmethyl)-1,10-diaza-9,20-dioxakabutane (**3**) as a major product by the reaction with 85% formic acid, while its reaction with trifluoroacetic acid generated exclusively another 2,2'-bisindole dimer, 1-hydroxy-3,3'-di(methoxycarbonylmethyl)-2,2'-bisindole (**4**). Reaction of **1a** with mineral acid such as HCl afforded nucleophile substituted 5-chloroindole derivative (**6**). Products and their distribution changed depending on the structure of 1-hydroxyindole. Species of acid, reaction conditions, side chain structure of 1-hydroxyindole at the 3-position are additional factors for governing the product formation. In the cases that the side chain has a C—C—N structure, nucleophilic substitution reaction occurred effectively, and was applied for the preparation of *N*-feruloylserotonin (**46d**), an alkaloid isolated from safflower seed. 1-Hydroxymelatonin (**69**), having a methoxy group on the benzenoid part, afforded (*dl*)-3a,3a'-bis(pyrrolo[2,3-*b*]indole) compound (**72**) by the treatment with 85% formic acid. Products' structures are unequivocally determined by X-ray single crystallographic analyses.

INTRODUCTION

Indoles are sensitive to acids and generally result in tar formation.[2] Sometimes 2,3'-dimer[2,3] (**A**) and/or 2,2'-dimer (**B**) were isolated (Scheme 1).[2,3] In contrast, we found that 1-hydroxyindoles,[4] having an extra-oxygen atom at the nitrogen, take place regioselective nucleophilic substitution reactions[5] at the 5-position upon treatment with acids. For example, methyl 1-hydroxyindole-3-acetate (**1a**) afforded methyl 5-methoxyindole-3-acetate[6] (**2a**) in 37% yield upon reaction with $BF_3 \cdot (MeOH)_2$ in refluxing MeOH. Treatment of **2a** with BBr_3 produced 37% yield of methyl 5-hydroxyindole-3-acetate (**2b**). Thus, a biologically interesting metabolite of methyl indole 3-acetate, plant growth hormone, is now readily available. Based on these results, we have interested in the chemical behavior of 1-hydroxyindoles toward acids, and discovered novel two types of dimerization to occur generating either hexacyclic 1,10-diaza-9,20-dioxakabutanes[7] (**C**) or (*dl*)-3a,3a'-bispyrrolo[2,3-*b*]indole compounds[8] (**D**) depending on the 1-hydroxyindole structures. In the particular case that the side chain at the 3-position has a C—C—N structure,[5,9] nucleophilic substitution reaction occurred effectively, and it was applied for the preparation of *N*-feruloylserotonin[10] (**46d**), an alkaloid isolated from safflower seed. This is the full report of the previous communications[7,8] with new results.



Scheme 1

RESULTS AND DISCUSSIONS

Methyl 1-hydroxyindole-3-acetate (**1a**) was prepared from methyl indole-3-acetate (**1b**) according to our 1-hydroxyindole synthetic method.[4] The reaction of **1a** with acids resulted in the formation of tar together with various products. The results are summarized in Table 1. Treatment of **1a** with 85% formic acid

Table 1. Products upon the change of acid

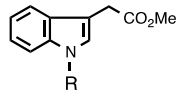
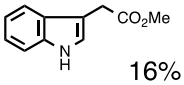
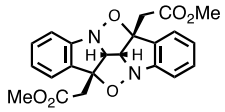
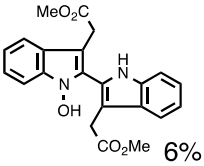
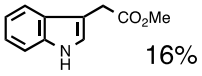
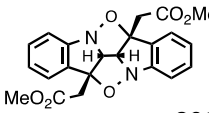
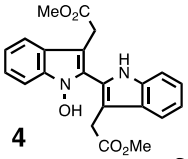
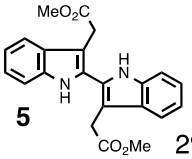
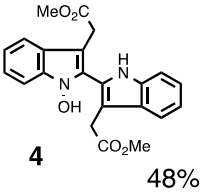
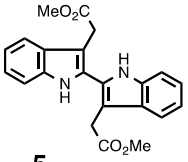
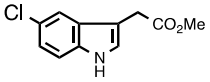
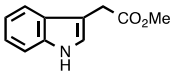
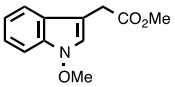
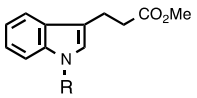
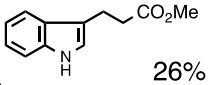
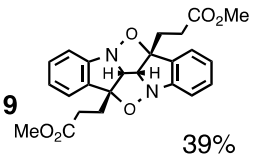
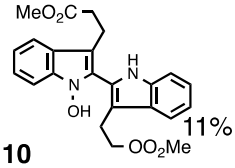
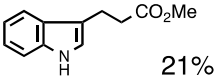
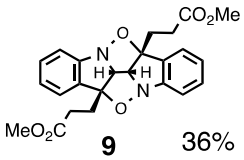
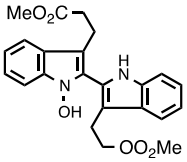
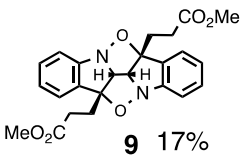
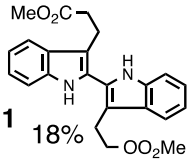
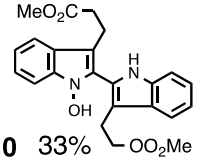
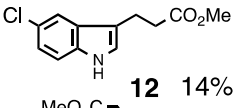
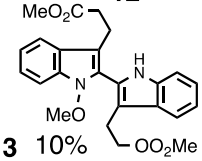
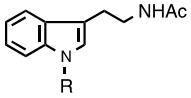
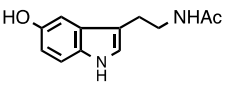
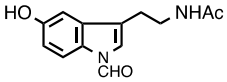
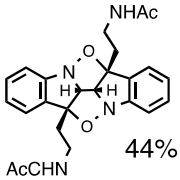
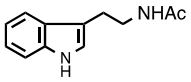
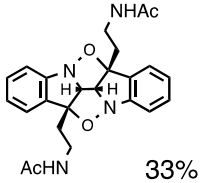
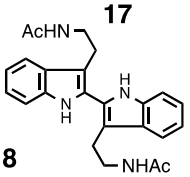
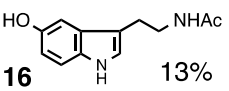
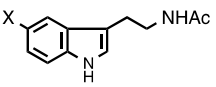
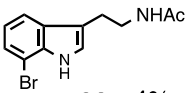
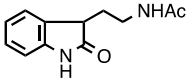
1-Hydroxyindole	HCO_2H (pKa 3.7)	H_3PO_4 (pKa 2.2)	TFA (pKa 0.2)	HCl (pKa -7.0) HBr (pKa -9.0)
 **1a**) R = OH **b**) R = H	 **1b** 16%  **3** 21%  **4** 6%	 16% **1b**  29% **3**  **4** 3%  **5** 2%	 **4** 48%  **5** 17%	HCl, then CH_2N_2  **6** 19%  15% **1b**  **7** 20%
 **8a**) R = OH **b**) R = H **c**) R = OMe	 **8b** 26%  **9** 39%  **10** 11%	 21% **8b**  **9** 36%  **10** 8%	 **9** 17%  **11** 18%  **10** 33%	HCl then CH_2N_2 **8b** 12% **8c** 9%  **12** 14%  **13** 10%
 **14a**) R = OH **b**) R = H	 **15** 41%  **16** 6%	 44% **17** **14a** 5%  **14b** 16%	 **17** 33%  **18** 21%  **16** 13%	 **19a**) X=Cl, 35% **b**) X=Br, 5%  **20** 4%  **21** 19%(HBr) **14b** 24% (HCl) 3% (HBr) **14a** 13%

Table 2. Products upon the change of acid

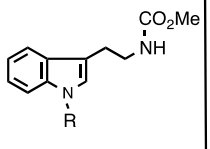
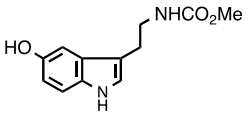
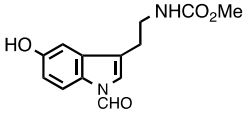
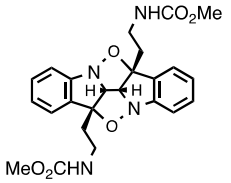
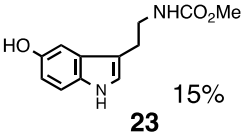
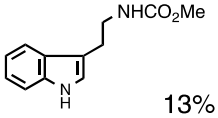
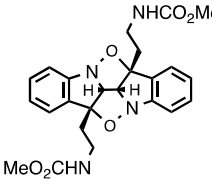
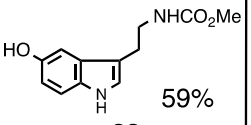
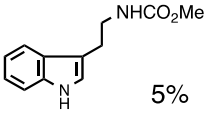
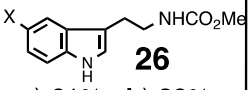
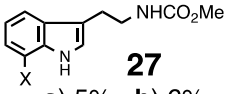
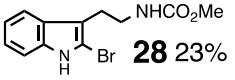
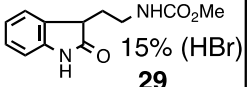
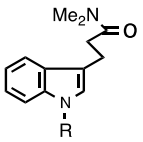
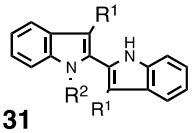
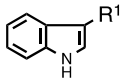
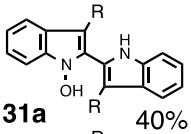
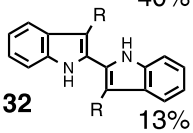
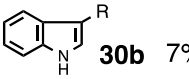
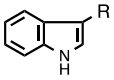
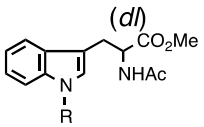
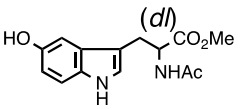
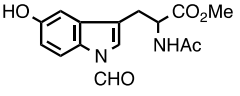
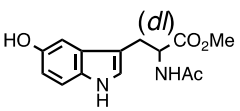
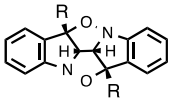
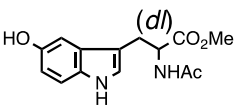
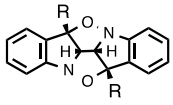
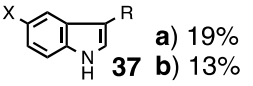
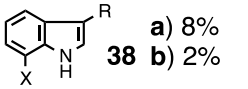
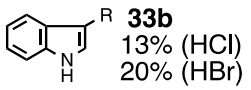
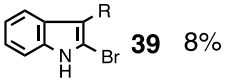
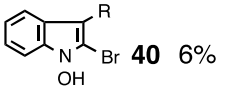
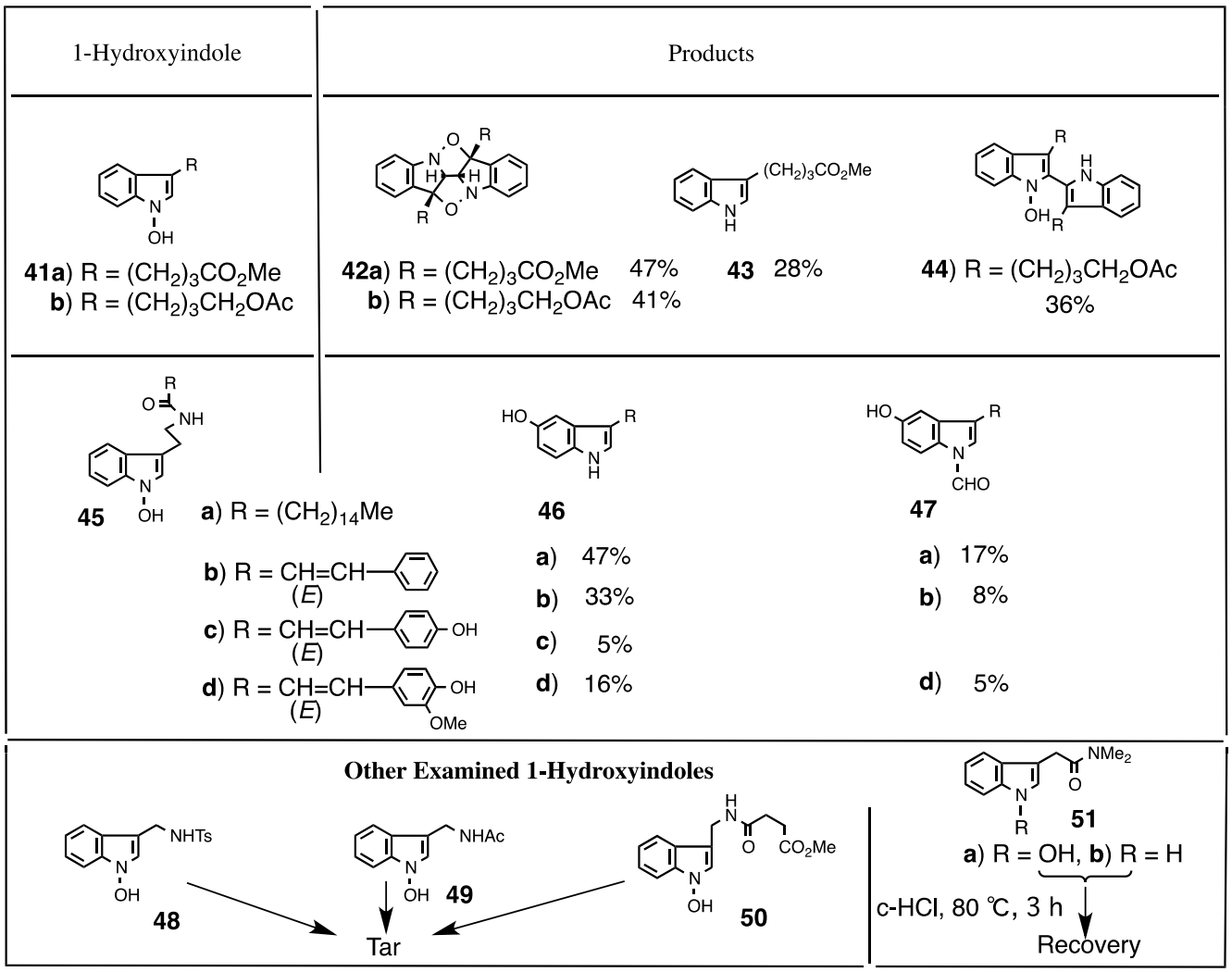
1-Hydroxyindole	HCO_2H (pKa 3.7)	H_3PO_4 (pKa 2.2)	TFA (pKa 0.2)	HBr (pKa -9.0) HCl (pKa -7.0)
 **22a**) R = OH **b**) R = H	 **23** 8%  **24** 54%	 **25** 11%  15% **23**  13% **22b**	 **25** 5%  59% **23**  5% **22b**	**a**) X=Cl; **b**) X=Br  **26** **a**) 61% ; **b**) 39%  **27** **a**) 5% ; **b**) 6%  **28** 23%  15% (HBr) **29** **23** 18% **22b** 4% (HCl)10%(HBr)
 **30a**) R = OH **b**) R = H	$R^1 = (CH_2)_2CONMe_2$  **31** **a**) R^2 = OH 21% **b**) R^2 = OMe  **30b** 11%		R = $(CH_2)_2CONMe_2$  **31a** 40%  **32** 13%  **30b** 7%	R = $(CH_2)_2CONMe_2$  **30b** 29%
 **33a**) R = OH **b**) R = H	 46% **34**  27% **35**	**33b** 8%  5% **34** (*dl*) R = CH_2CHCO_2Me NHAc  **36**, 4% mixture of diastereoisomers	 44% **34** (*dl*) R = CH_2CHCO_2Me NHAc  **36**, 9% mixture of diastereoisomers	R = CH_2CHCO_2Me NHAc **a**) X=Cl; **b**) X=Br  **37** **a**) 19% **b**) 13%  **38** **a**) 8% **b**) 2%  **33b** 13% (HCl) 20% (HBr)  **39** 8%  **40** 6%

Table 3. Products upon treatment with 85% HCO_2H



(HCO_2H) at rt produced tar together with **1b**, 8,17-bis(methoxycarbonylmethyl)-1,10-diaza-9,20-dioxakabutane[7] (**3**), and 1-hydroxy-3,3'-di(methoxycarbonylmethyl)-2,2'-bisindole (**4**) in 16, 21, and 6% yields, respectively. Instead of using HCO_2H, upon reaction with phosphoric acid (H_3PO_4), **1a** afforded **1b**, **3**, **4**, and 3,3'-di(methoxycarbonylmethyl)-2,2'-bisindole (**5**), in the respective yields of 16, 29, 3, and 2%. Trifluoroacetic acid (TFA), stronger acid than the former acids, changed the distribution of products so as to give 2,2'-dimers, **4** and **5**, as the major products in the respective yields of 48 and 17%, but the formation of 1,10-diaza-9,20-dioxakabutane was not observed at all.

When organic acids were changed to stronger mineral acids, nucleophilic substitution occurred instead of dimerization. Treatment of **1a** with HCl, followed by methylation of the resulted carboxylic acids with diazomethane, afforded methyl 5-chloroindole-3-acetate (**6**), methyl 1-methoxyindole-3-acetate (**7**), and **1b** in the respective yields of 19, 20, and 15% except for tar.

Similar set of products were isolated when methyl 1-hydroxyindole-3-propionate (**8a**) was employed as a substrate. Thus, the reaction of **8a** with 85% HCO_2H at rt produced methyl indole-3-propionate (**8b**), 8,17-bis[2-(methoxycarbonyl)ethyl]-1,10-diaza-9,20-dioxakabutane (**9**), and 1-hydroxy-2,2'-dimer (**10**) in 26, 39, and 11% yields, respectively. In the reaction with H_3PO_4, **8a** afforded **8b**, **9**, and **10** in the respective yields of 21, 36, and 8%. When TFA was employed as an acid, **9**, **10**, and 2,2'-dimer (**11**) were produced in 17, 33, and 18% yields, respectively. The reaction of **8a** with HCl and subsequent treatment with CH_2N_2 again produced nucleophilic substitution product, methyl 5-chloroindole-3-propionate (**12**) together with **8b**, **8c**, and **13** in the respective yields of 14, 12, 9, and 10%.

Side-chain structure at the 3-position of 1-hydroxyindole caused different appearance of the products towards each acid. *N*b-Acetyl-1-hydroxytryptamine[4] (**14a**), prepared from *N*b-acetyltryptamine (**14b**), generated nucleophilic substituted products, *N*b-acetyl-5-hydroxytryptamine (**15**) and *N*b-acetyl-1-formyl-5-hydroxytryptamine (**16**) in the respective yields of 41 and 6% upon the reaction with 85% HCO_2H. Treatment of **14a** with H_3PO_4 produced 44% yield of 8,17-bis[2-(acetamino)ethyl]-1,10-diaza-9,20-dioxakabutane (**17**) together with **14a** (5%) and **14b** (16%). The reaction of **14a** with TFA generated **17**, 2,2'-dimer (**18**), and **15** in 33, 21, and 13% yields, respectively. Upon reaction with HCl, *N*b-acetyl-5-chlorotryptamine (**19a**), **14a**, and **14b** were isolated in 35, 13, and 24% yields, respectively. While the reaction with HBr generated complex mixture of products, such as *N*b-acetyl-5-bromotryptamine (**19b**), *N*b-acetyl-7-bromotryptamine (**20**), **14b**, and *N*b-acetyl-2-oxo-tryptamine (**21**) in 5, 4, 3, and 19% yields, respectively.

Interestingly the change of *N*b-substituent of 1-hydroxytryptamine from acetyl to methoxycarbonyl group makes nucleophilic substitution occur more easily in every acid treatment (Table 2). In fact, 1-hydroxy-*N*b-methoxycarbonyltryptamine (**22a**) generated 5-hydroxy- (**23**) and 1-formyl-5-hydroxy-*N*b-methoxycarbonyltryptamine (**24**) in 8 and 54% yields, respectively. H_3PO_4 reacted with **22a** to afford **23** in 15% yield together with 11% yield of 8,17-bis[2-(methoxycarbonylamino)ethyl]-1,10-diaza-9,20-dioxakabutane (**25**) and 13% yield of *N*b-methoxycarbonyltryptamine (**22b**). On the other hand, treatment of **22a** with TFA afforded predominantly **23** in 59% yield in addition to **25** and **22b** in 5 and 5% yields, respectively.

The reactions of **22a** with mineral acids formed complex mixture of products. Thus, treatment of **22a** with HCl afforded 5-chloro- (**26a**), 7-chloro-*N*b-methoxycarbonyltryptamine (**27a**), and **22b** in 61, 5, and 4% yields, respectively. While upon treatment with HBr,[11] **23**, 5-bromo- (**26b**), 7-bromo- (**27b**), 2-bromo-*N*b-methoxycarbonyltryptamine (**28**), **22b**, and 2-oxo-*N*b-methoxycarbonyltryptamine (**29**) were produced in 18, 39, 6, 23, 10, and 15% yields, respectively.

Acid treatments of *N*,*N*-dimethyl-1-hydroxyindole-3-propionamide (**30a**) afforded only 2,2'-dimer products, and formations of both kabutane and nucleophilic substituted product were not observed. Thus,

upon the reaction with 85% HCO_2H, **31a** and **30b** were isolated in 21 and 11% yields, respectively. TFA converted **30a** to **31a**, **32**, and **30b** in 40, 13, and 7% yields, respectively. Treatment with HCl caused only removal of 1-hydroxy group to give **30b** in 29% yield.

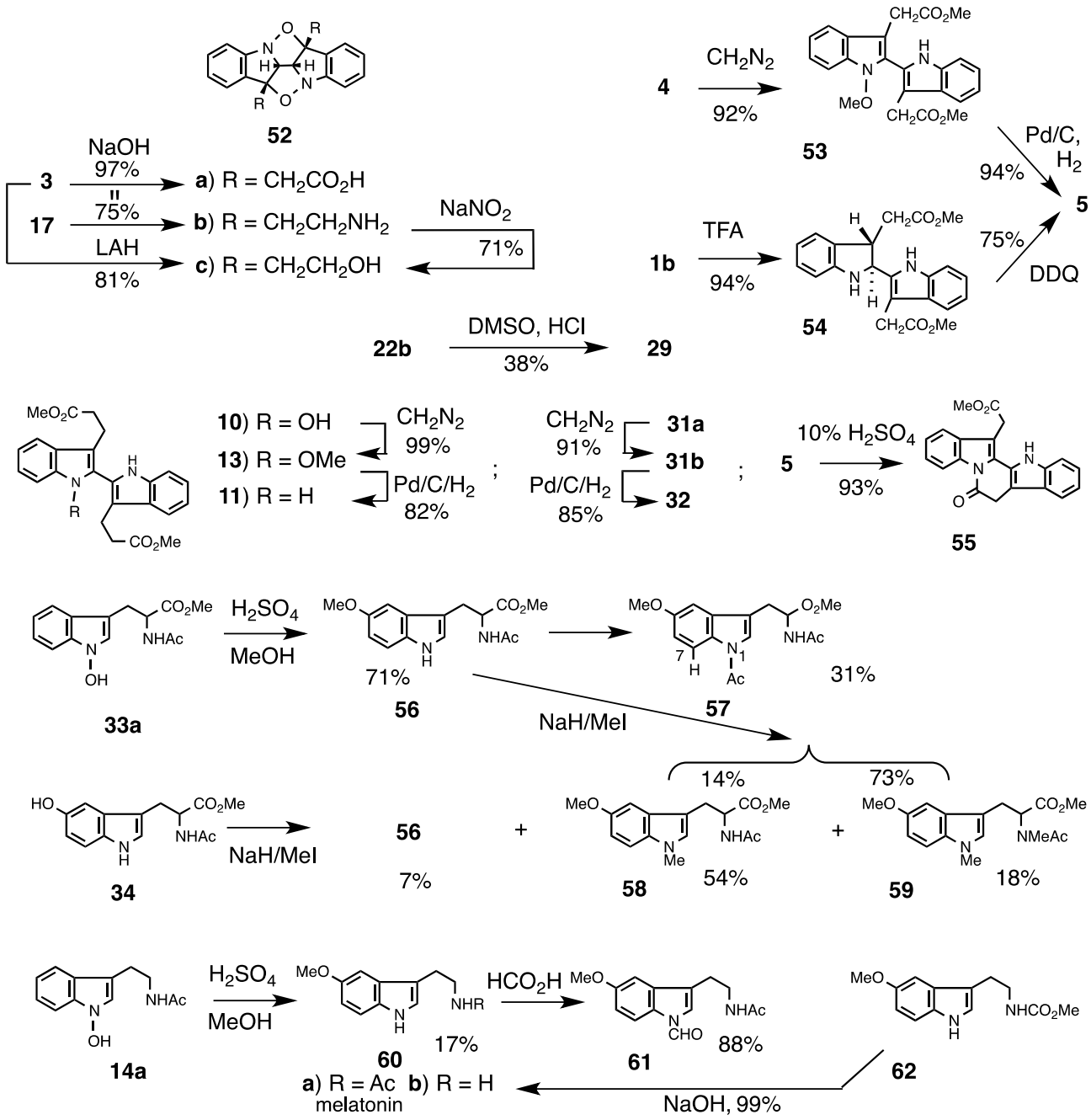
Next, we examined the reactivity of (*dl*)-*N*b-acetyl-1-hydroxytryptophan methyl ester (**33a**), whose side chain structure at the 3-position can be regarded as a superposition of those of **8a** and **14a**. The question is whether the product distribution resembles to one of them or differs. Interestingly major reaction was the nucleophilic substitution reaction similar to **14a** and formation of 2,2'-dimer was not observed at all. Thus, treatment of **33a** with 85% HCO_2H afforded (*dl*)-*N*b-acetyl-5-hydroxytryptophan methyl ester (**34**) and (*dl*)-*N*b-acetyl-1-formyl-5-hydroxytryptophan methyl ester (**35**) in 46 and 27% yields, respectively. When the reaction of **33a** with H_3PO_4 was carried out, **34** was produced in 5% yield in addition to 8% yield of **33b** and 4% yield of kabutane (**36**, a mixture of diastereomers). Treatment of **33a** with TFA gave **34** in 44% yield together with 9% yield of kabutane (**36**). Upon the reaction of **33a** with HCl,[12] (*dl*)-*N*b-acetyl-5-chloro- (**37a**), (*dl*)-*N*b-acetyl-7-chloro- (**38a**), and (*dl*)-*N*b-acetyltryptophan methyl ester (**33b**) were produced in 19, 8, and 13% yields, respectively. HBr reacted with **33a** to give (*dl*)-*N*b-acetyl-5-bromo- (**37b**), (*dl*)-*N*b-acetyl-7-bromotryptophan methyl ester (**38b**), **33b**, (*dl*)-*N*b-acetyl-2-bromotryptophan methyl ester (**39**), and (*dl*)-*N*b-acetyl-1-hydroxy-2-bromotryptophan methyl ester (**40**) in 13, 2, 20, 8, and 6% yields, respectively.

In both cases of methyl 1-hydroxyindole-3-butyrate[13a] (**41a**) and 3-[4-(acetoxy)butyl]-1-hydroxyindole **(41b)** upon the reaction with 85% HCO_2H (Table 3), nucleophilic substitution product was not observed at all. Thus, **41a** produced the corresponding kabutane (**42a**) and **43** in 47 and 28% yields, respectively. **41b** produced 41% yield of **42b** together with 36% yield of 2,2'-dimer (**44**).

On the other hand, upon reactions of **45a**–**45d**[13b] with 85% HCO_2H, only nucleophilic substitution products were isolated in addition to tars. Thus, 1-hydroxy-*N*b-palmitoyltryptamine (**45a**) gave **46a** and **47a** in 47 and 17% yields, respectively. **45b** gave **46b** and **47b** in 33 and 8% yields, respectively. **45c** gave **46c** in 5% yield together with tar. Application of these findings to *N*b-feruloyl-1-hydroxytryptamine (**45d**) afforded *N*-feruloylserotonin (**46d**),[10] an alkaloid isolated from safflower seed, in 16% yield together with 5% yield of its 1-formyl compound (**47d**). **46c** and **46d** were alternatively synthesized in the respective yields of 94 and 99% by the reaction of serotonin with either 4-hydroxycinnamic acid or ferulic acid.

3-Amiomethyl-1-hydroxyindole derivatives, such as **48**, **49**, and **50**, formed tar immediately after treatment with such weak acid as 85% HCO_2H and useful products were not isolated at all. In contrast, similar compound, *N*,*N*-dimethyl-1-hydroxyindole-3-acetamide (**51a**) and *N*,*N*-dimethylindole-3-acetamide (**51b**) were stable against HCl, thus they were totally recovered after treatment with c-HCl at 80 °C for 3 h.

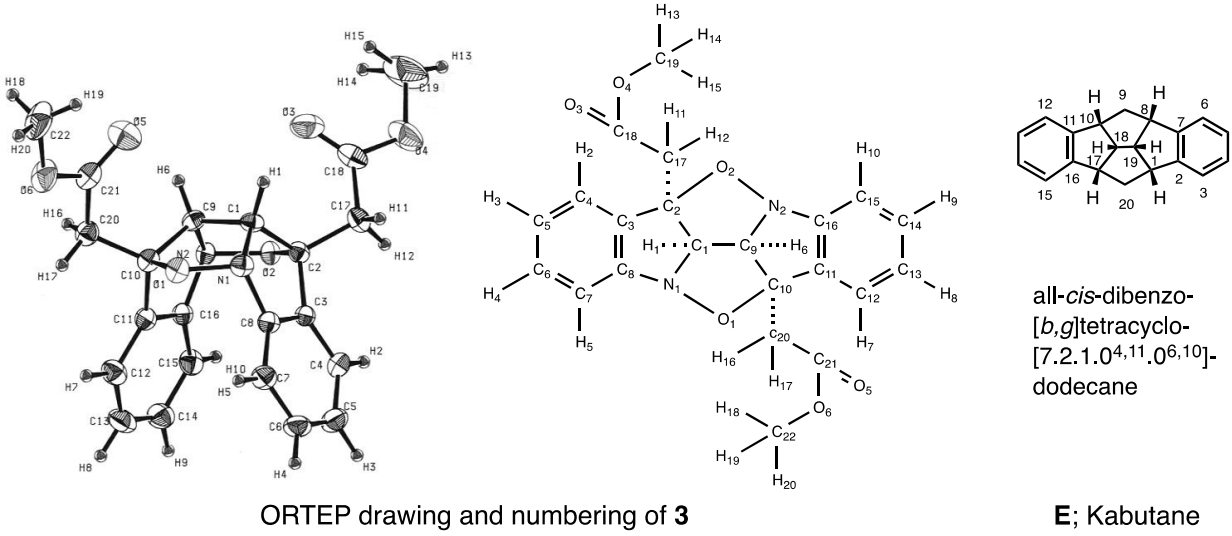
From these experimental results, we can conclude that the reaction products of 1-hydroxyindoles with acids depend on the side chain structure at the 3-position. When the side chain has a C—C—N structure, nucleophilic substitution reaction occurs.[5,14] Specifically when 1-hydroxyindole has a C—C—N side chain at the 3-position, we have proved that the indole nitrogen is sp^3 like atom rather than sp^2 due to the bishomoallylic conjugation,[14] which is the reason for nucleophilic substitution to occur.



Scheme 2

STRUCTURAL DETERMINATION AND CORRELATIONS

Structural correlations among kabutanes were performed as follows. Alkaline hydrolysis of **3** and **17** with aqueous 8% NaOH afforded **52a** and **52b** in the respective yields of 97 and 75% (Scheme 2). Reduction of **3** with $LiAlH_4$ produced **52c** in 81% yield. Diazotization of **52b** with $NaNO_2$-AcOH and subsequent base treatment produced **52c** in 71% yield. Although these chemical correlations and their spectral data were insufficient for determine their structures. Fortunately, the compound (**3**) was found to be suitable crystals for X-ray single crystallographic analysis and its structure was determined unequivocally. It has a novel hexacyclic dimer structure as shown in Figure 1. The shape resembles Japanese ancient soldiers' helmet, Kabuto. Therefore, we gave the corresponding mother skeleton, all-*cis*-dibenzo[*b*,*g*]tetracyclo-[7.2.1.$0^{4,11}$.$0^{6,10}$]dodecane (**E**), a name kabutane as the short name. Accordingly, **3** is one of a family member of 1,10-diaza-9,20-dioxakabutane (**C**), and its name is 8,17-bis(methoxycarbonylmethyl)-1,10-diaza-9,20-dioxakabutane.



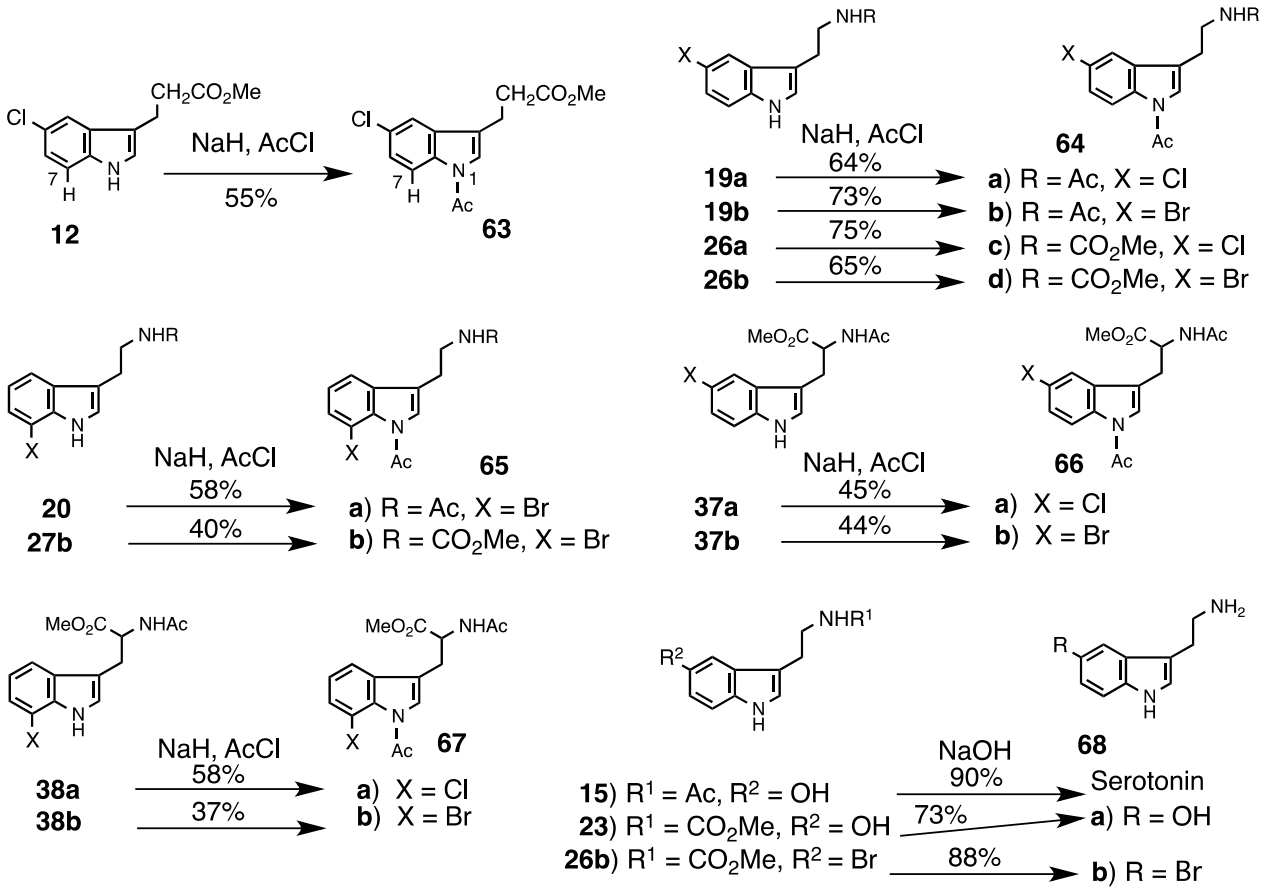
ORTEP drawing and numbering of **3** **E**; Kabutane

Figure 1

The structure of **4** to be a 2,2'-dimer was deduced as follows. Methylation of **4** with diazomethane gave 1-methoxy dimer (**53**) in 92% yield, proving the existences of 1-hydroxy and 1-methoxy group in the respective molecules (**4** and **53**). On the other hand, according to Bergman's report,[15] **1b** was derived to 2,3-*trans*-2,3-dihydro-2,2'-bisindole (**54**) in 94% yield by the reaction with TFA. In the ^{1}H-NMR spectrum, the coupling constant of hydrogens at the 2- and 3-positions are 10.9 Hz, which confirmed their stereochemistry is *trans*. Oxidation of **54** with dichlorodicyanoquinone produced **5** in 75% yield. While catalytic hydrogenation of **53** with 10% Pd/C removed 1-methoxy group to give **5** in 94% yield. Further treatment of **5** with 10% H_2SO_4 took place 6-membered cyclization to produce **55** in 93% yield. These chemical correlations suggested that **4** is a 2,2'-dimer. For getting structural proof of 2,2'-dimer, X-ray

single crystallographic analysis was performed using suitable crystals **53**, and the results proved it unequivocally as shown in Figure 2.

Since the structure of 2,2'-dimer was established, the related structural correlations were performed. Thus, 1-hydroxy-2,2'-dimer (**10**) and **31a** were methylated with CH_2N_2 to afford 1-methoxy-2,2'-dimer (**13**) and **31b** in 99 and 91% yields, respectively. Subsequent palladium catalyzed hydrogenation of **13** and **31b** produced **11** and **32** in the respective yields of 82 and 85% yield. On the other hand, the structure of **29** was proved by the alternative synthesis from **22b** in 38% yield by the reaction with DMSO and HCl.[16]



Scheme 3

When **33a** was reacted with H_2SO_4 in MeOH, nucleophilic substitution at the 5-position occurred predominantly and afforded methyl *N*b-acetyl-5-methoxytryptophan methyl ester (**56**) in 71% yield. The structure was proved by leading it to the corresponding 1-acetyl compound (**57**) in 31% yield by the reaction with NaH/AcCl. Comparison of the ^{1}H-NMR spectra of **56** and **57** showed that the introduction of acetyl group into the 1-position caused deshielding effect to the proton at the 7-position. Thus, the shift of δ-value from 7.24 (1H, d, J=8.8 Hz) to 8.23 (1H, d, J=8.8 Hz), coupling constant and pattern clearly proved that **56** and **57** are 5-substituted compounds.

Methylation of **34** with NaH/MeI produced **56**, **58**, and **59** in 7, 54, and 18% yields, respectively, while the same methylation of **56** produced **58** and **59** in the respective yields of 14 and 73%. Treatment of **14a** with 10% H_2SO_4 afforded melatonin (**60a**) in 17% yield. Further reaction of **60a** with 85% HCO_2H gave *N*-formylmelatonin (**61**) in 92% yield.

The structures of various 5- and 7-substituted indoles,[17] obtained in Tables 1 and 2, were proved by applying the above-mentioned ^{1}H-NMR deshielding effect of the introduced 1-acetyl group to the proton at the 7-position. Thus, **12**, **19a**, **19b**, **26a**, **26b**, **37a**, and **37b** were reacted with NaH/AcCl to afford the corresponding 1-acety compounds, **63**, **64a**, **64b**, **64c**, **64d**, **66a**, and **66b**, respectively, and their structures were proved.

In the ^{1}H-NMR spectra of **20**, **27b**,[17] **38a**, and **38b**, their proton coupling patterns showed to be either 4- or 7-substituted indoles. Their reactions with NaH/AcCl afforded the corresponding 1-acetyl compounds, **65a**, **65b**,[17] **67a**, and **67b**, where 1-acetyl group did not show the deshielding effect on their benzenoid protons. The facts prove that they are 7-substituted indoles.

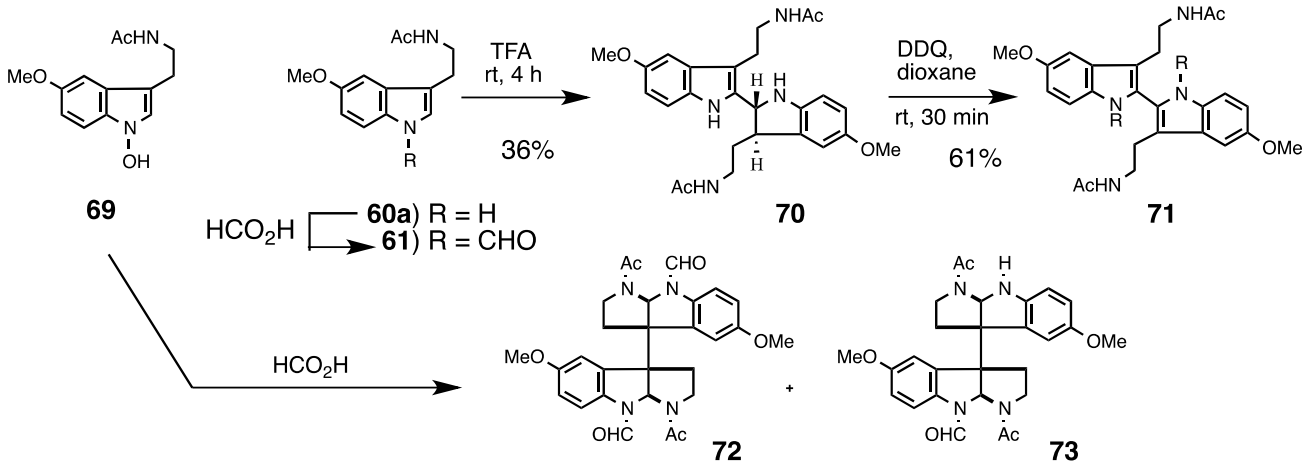
In addition, alkaline hydrolysis of **62**[17] produced 5-methoxytryptamine (**60b**) in 99% yield. *N*-Acetyl- (**15**) and *N*-methoxycarbonylserotonin (**23**) were hydrolyzed with NaOH to give serotonin (**68a**) in 90 and 73% yields, respectively. Hydrolysis of **26b** produced 5-bromotryptamine (**68b**) in 88% yield.

THE REACTION OF 1-HYDROXYMELATONIN

The reaction products of 1-hydroxyindoles with acids change depending on the side chain structure at the 3-position of indole. We are interested in what kind of reaction would occur in the case of 1-hydroxyindole having a functional group on the benzenoid group. As a suitable substrate, we chose 1-hydroxymelatonin[18] (**69**) and prepared it from melatonin (**60a**) according to our 1-hydroxyindole synthetic method. The compound (**69**) was found to be a stable crystalline compound.

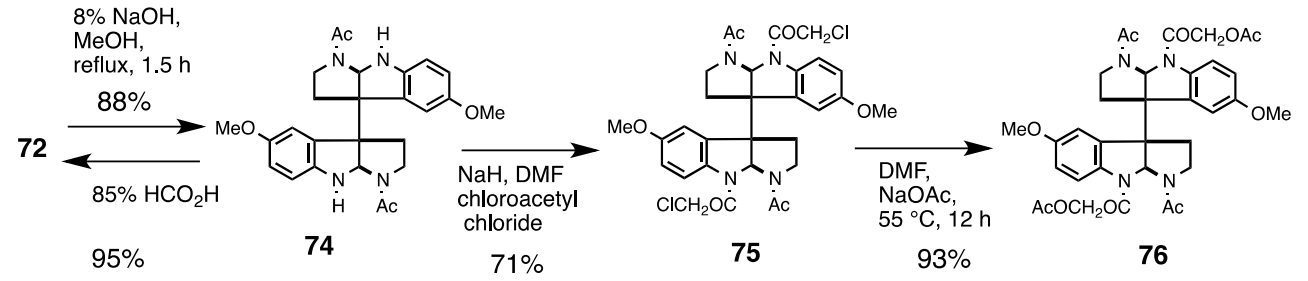
Next, we examined the reaction of **60a** with TFA and found that it produced 2,2'-dimer (**70)** in 36% yield together with 18% yield of recovery (Scheme 4). Subsequent oxidation of **70** with DDQ in dioxane afforded 2,2'-bismelatonin (**71**) in 61% yield. Upon reaction of **60a** with 85% HCO_2H, only *N*-formylation occurred and 1-formylmelatonin (**61**) was isolated in 92% yield as mentioned above.

When we treated 1-hydroxymelatonin (**69**) with 30% HCO_2H in MeOH at rt, we found an interesting result. Contrary to our expectation that either 2,2'-dimer or kabutane would be produced, we isolated (*dl*)-3a,3a'-bispyrrolo[2,3-*b*]indole compound (**73**) in 23% yield together with 18% yield of recovery. When 85% HCO_2H alone was employed at rt, (*dl*)-3a,3a'-bis(1-acetyl-8-formyl-5-methoxypyrrolo-[2,3-*b*]indole) (**72**) was produced predominantly in 44% yield.



Entry	Reaction Conditions	Yield (%) of 72	73	69
1	85% HCO_2H, rt, 1.5 h	44	0	0
2	30% HCO_2H, MeOH, rt, 1.5 h	0	23	18

Scheme 4



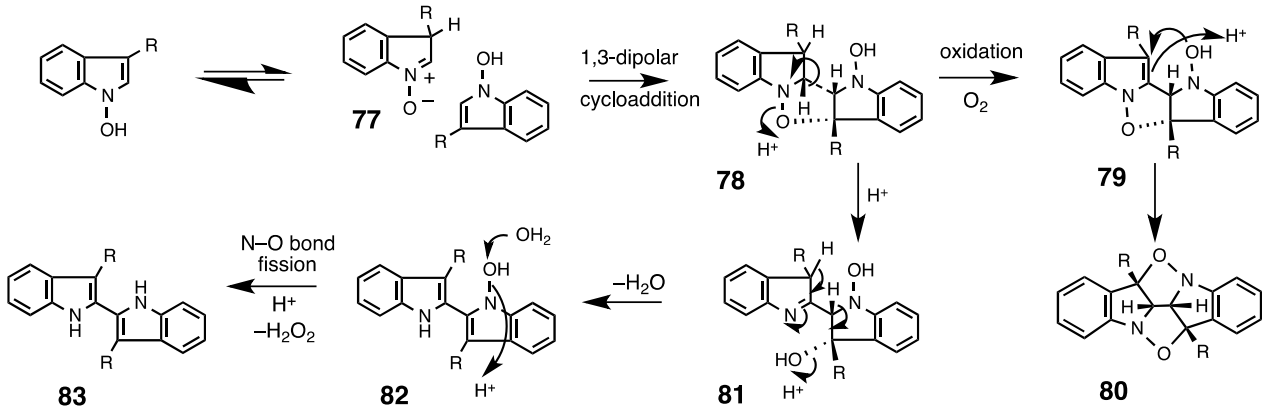
Scheme 5

Alkaline hydrolysis of **72** with 8% NaOH in refluxing MeOH removed formyl group to give 88% yield of **74**, which was reconverted to **72** in 95% yield by the reaction with 85% HCO_2H (Scheme 5). Treatment of **74** with NaH in DMF, followed by acylation with chloroacetyl chloride produced **75** in 71% yield. Further reaction of **75** with NaOAc in DMF at 55 °C gave 93% yield of acetate (**76**). Since it was difficult to determine these structutes by spectral data, X-ray structural analysis was performed employing **76**. The results are shown in Figure 3, and **72** is determined unequivocally to have (*dl*)-3a,3a'-bispyrrolo[2,3-*b*]indole skeleton. Formation of *meso*-isomer was not observed in the reaction mixture of **69**.

Mechanism for the formation of kabutanes and (*dl*)-3a,3a'-bispyrrolo[2,3-*b*]indoles

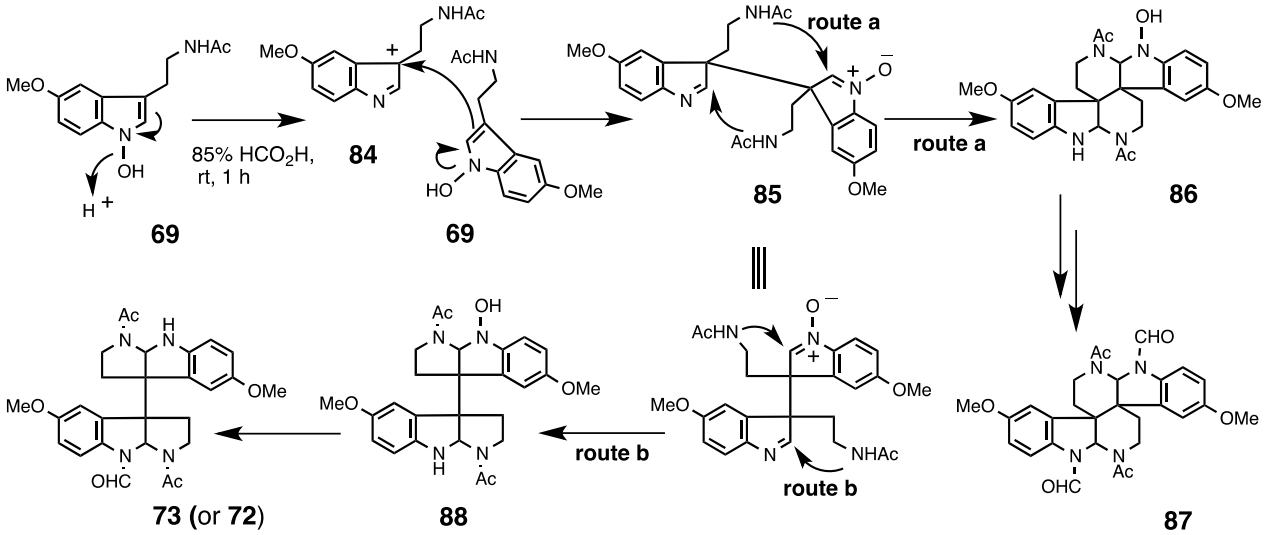
The probable mechanism for the formation of 8,17-disubstituted 1,10-diaza-9,20-dioxakabutane is shown

in Scheme 6. A small amount of nitrone (**77**), which exists in equilibrium with 1-hydroxyindole, occurs 1,3-dipolar cycloaddition to give pentacyclic isoxazolidine intermediate (**78**).



Scheme 6

Subsequent air oxidation produces indole compound (**79**). Protonation at the 2-position of indole part, followed by addition of 1-hydroxy group to the 3-position generates kabutane (**80**). On the other hand, proton assisted ring opening of isoxazolidine ring generates 2,2'-dimer intermediate (**81**). Acid assisted dehydration afford 1-hydroxy-2,2'-dimer (**82**). We have already found that the N-O bond fission of 1-hydroxy indoles readily occur, either homolytic or ionic, upon mild treatment with such as water, acid, heat, and light. Therefore, formation of **83** from **82** proceed under the reaction conditions.



Scheme 7

The mechanism for the formation of (*dl*)-3a,3a'-bispyrrolo[2,3-*b*]indoles can be explained as shown in Scheme 7. Nucleophilic addition of carbon-3' in **69** to the initially generated cation (**84**) at the 3-position

gives imine-nitrone intermediate (**85**). Subsequent intramolecular additions of nucleophiles, *N*b- and *N*b'-nitrogens, to the imine and nitrone carbon atoms has the two possible routes, **a** and **b**. The route **a** generates **86** *via* the 6-membered ring transition state, and finally **87**. On the other hand, route **b** gives 3a,3a'-bispyrrolo[2,3-*b*]indole compound (**88**) *via* 5-membered ring transition state. The sterical congestion of the transition state that gives **86** is larger than that of **88**. In terms of entropy, the 5-membered ring transition state is more advantageous than the 6-membered ring transition state. Based on these two reasons, it can be understood that the route **b** proceeds preferentially. Then, formic acid functions as a reagent for both *N*-formylation and reduction of hydroxylamine to amine to produce **72** and **73**.

In conclusion, we discovered that 1-hydroxyindole compounds are sensitive to acids and undergo five types of competing reactions; **a**) dehydroxylation, **b**) nucleophilic substitution, **c**) 2,2'-dimerization, **d**) production of 1,10-diaza-9,20-dioxakabutanes, and **e**) formation of 3a,3a'-bispyrrolo[2,3-*b*]indoles, which has the similar skeleton with the alkaloids, folicanthine[19] and chimonanthine.[19] Which reaction occurs seems to be governed by the subtle change of such as side-chain structure, substitution of the benzenoid part of 1-hydroxyindole, acid species, and reaction conditions.

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were determined with a Shimadzu IR-420 spectrophotometer, and ^{1}H-NMR spectra with either a JEOL JNM FX100S or JEOL GSX-500 spectrometer with tetramethylsilane as an internal standard. MS spectra were recorded on a JEOL SX-102A spectrometer. Column chromatography was performed on silica gel (SiO_2, 100-200 mesh, from Kanto Chemical Co. Inc.). Preparative thin-layer chromatography (p-TLC) was performed on Merck Kieselgel GF_{254} (Type 60)(SiO_2).

Methyl 5-methoxyindole-3-acetate (2a) from methyl 1-hydroxyindole-3-acetate (1a) — 50% $BF_3 \cdot (MeOH)_2$ (18 mL) was added to a solution of **1a** (246.1 mg, 1.20 mmol) in MeOH (36.0 mL) and refluxed for 6 h with stirring. Under ice cooling, 8% NaOH was added to neutral and the whole was extracted with $CHCl_3$. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–hexane (1:1, v/v) to give **1b** (26.0 mg, 12%), **2a** (97.9 mg, 37%), and **1a** (22.9 mg, 12%) in the order of elution. **2a**: mp 76.0—77.0 °C (lit.[6] mp 73.0—74.0 °C, colorless prisms, recrystallized from $CHCl_3$–hexane). IR (KBr): 3350, 1721, 1623, 1588, 1486, 1240, 1208, 1173, 1096, 1060, 1026, 825, 806 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.71 (3H, s), 3.75 (2H, d, *J*=0.7 Hz), 3.87 (3H, s), 6.87 (1H, dd, *J*=8.8, 2.2 Hz), 7.05 (1H, d, *J*=2.2 Hz), 7.15 (1H, d, *J*=2.2 Hz), 7.24—7.26 (1H, m), 7.98 (1H, brs). High resolution MS *m/z*: Calcd for $C_{12}H_{13}NO_3$: 219.0895. Found: 219.0881. *Anal.* Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.83; H, 5.99; N, 6.45.

Methyl 5-hydroxyindole-3-acetate (2b) from 2a — BBr_3 (1.0M solution in heptane, 0.75 mL) was added to a solution of **2a** (32.0 mg, 0.15 mmol) in anhydrous $CHCl_3$ (3.0 mL) at –19 °C. After the mixture was stirred at rt for 9 h, H_2O was added under ice cooling. The whole was extracted with $CHCl_3$–MeOH (95:5, v/v) and the extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$ to give **2b** (11.3 mg, 37%). **2b**: colorless oil. IR (film): 3390, 1719, 1628, 1585, 1487, 1455, 1435, 1201, 1006, 940, 797 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.70 (3H, s), 3.72 (2H, d, *J*=0.7 Hz), 4.67 (1H, brs, disappeared on addition of D_2O), 6.78 (1H, dd, *J*=8.6, 2.4 Hz), 7.01 (1H, dd, *J*=2.4, 0.6 Hz), 7.14 (1H, d, *J*=2.4 Hz), 7.21 (1H, dd, *J*=8.6, 0.6 Hz), 7.97 (1H, brs, disappeared on addition of D_2O). High resolution MS *m/z*: Calcd for $C_{11}H_{11}NO_3$: 205.0739. Found: 205.0741.

8,17-Bis(methoxycarbonylmethyl)-1,10-diaza-9,20-dioxakabutane (3) and 3,3'-di(methoxycarbonylmethyl)-1-hydroxy-2,2'-bisindole (4) from methyl 1-hydroxyindole-3-acetate (1a) — 85% HCO_2H (80 mL) was added to **1a** (812.6 mg, 3.9 mmol) at rt and stirred for 24 h. After evaporation of the solvent under reduced pressure, water and 8% aq. NaOH were added to pH 7.0, 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 column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (99:1, v/v) to give methyl indole-3-acetate (**1b**) (117.6 mg, 16%), **4** (50.1 mg, 6%), and **3** (165.4 mg, 21%) in the order of elution. **3**: mp 164.0—165.0 °C (colorless prisms recrystallized from MeOH). IR (KBr): 2960, 1738, 1598, 1463, 1433, 1363, 1258, 1197, 1134, 976, 750 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.93 (2H, d, *J*=16.1 Hz), 3.24 (2H, d, *J*=16.1 Hz), 3.71 (6H, s), 5.73 (2H, s), 6.74 (2H, d, *J*=8.0 Hz), 6.78 (2H, ddd, *J*=7.6, 6.7, 1.1 Hz), 6.94 (2H, ddd, *J*=8.0, 6.7, 1.1 Hz), 7.04 (2H, dd, *J*=7.6, 1.1 Hz). MS *m/z*: 408 (M^+). *Anal.* Calcd for $C_{22}H_{20}N_2O_6$: C, 64.70; H, 4.94; N, 6.86. Found: C, 64.51; H, 4.80; N, 6.76. **4**: mp 190.0—192.0 °C (decomp., orange prisms, recrystallized from EtOAc–hexane). IR (KBr): 3230, 1731, 1709, 1445, 1431, 1335, 1215, 1158, 1019, 738 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.65 (2H, s), 3.76 (3H, s), 3.77 (2H, s), 3.83 (3H, s), 7.18–7.22 (2H, m), 7.29 (1H, ddd, *J*=8.0, 7.0, 1.1 Hz), 7.33 (1H, ddd, *J*=8.0, 7.0, 1.1 Hz), 7.48 (1H, d, *J*=8.0 Hz), 7.61 (2H, d, *J*=8.0 Hz), 7.73 (1H, d, *J*=8.0 Hz), 9.73 (1H, brs), 9.89 (1H, s, D_2O exchange). High resolution MS *m/z*: Calcd for $C_{20}H_{20}N_2O_5$: 392.1372. Found: 392.1367; Calcd for $C_{20}H_{20}N_2O_4$: 376.1423. Found: 376.1426.

3,3'-Di(methoxycarbonylmethyl)-2,2'-bisindole (5) from 1a — 85% H_3PO_4 (1.0 mL) was added to a solution of **1a** (40.5 mg, 0.19 mmol) in MeCN (1.0 mL) and stirred at rt for 3.5 h. After evaporation of the solvent under reduced pressure, water and 8% aq. NaOH were added to pH 7.0, 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 column-chromatographed on SiO_2 with

CH_2Cl_2–MeOH (99:1, v/v) to give **5** (0.8 mg, 2%), **1b** (6.0 mg, 16%), **4** (1.3 mg, 3%), and **3** (11.5 mg, 29%) in the order of elution. **5**: mp 207.0—208.0 °C (colorless prisms recrystallized from MeOH). IR (KBr): 3270, 1707, 1433, 1307, 1250, 1190, 1141, 1007, 738 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.83 (6H, s), 3.91 (4H, s), 7.20 (2H, ddd, *J*=8.1, 7.1, 1.1 Hz), 7.26 (2H, ddd, *J*=8.1, 7.1, 1.1 Hz), 7.50 (2H, d, *J*=8.1 Hz), 7.71 (2H, d, *J*=8.1 Hz), 10.81 (2H, br s). MS *m/z*: 376 (M^+). *Anal*. Calcd for $C_{22}H_{20}N_2O_4$: C, 70.20; H, 5.36; N, 7.44. Found: C, 70.07; H, 5.22; N, 7.35.

Formation of 4 and 5 from methyl 1-hydroxyindole-3-acetate (1a) — CF_3CO_2H (TFA, 30 mL) was added to **1a** (319.4 mg, 1.55 mmol) and stirred at rt for 3 h. After evaporation of the solvent under reduced pressure, water and 8% aq. NaOH were added to pH 7.0, 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 column-chromatographed on SiO_2 with CH_2Cl_2 to give **5** (48.3 mg, 17%) and **4** (146.7 mg, 48%).

Methyl 5-chloroindole-3-acetate (6) and methyl 1-methoxyindole-3-acetate (7) from 1a — A mixture of conc. HCl–MeCN (1:2, v/v, 3.0 mL) was added to **1a** (39.7 mg, 0.19 mmol) and stirred at rt for 2 h. After addition of H_2O, the whole was extracted with $CHCl_3$–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 dissolved in MeOH (1.0 mL). Excess ethereal CH_2N_2 was added and stirred at rt for 30 min. Evaporation of the solvent under reduced pressure left an oil, which was column-chromatographed on SiO_2 with EtOAc–hexane (1:4, v/v) to give **7**[4] (8.4 mg, 20%), **1b** (5.5 mg, 15%), and **6** (8.3 mg, 19%) in the order of elution. **6**: pale brown oil. IR (film): 3350, 1721, 1460, 1433, 1199, 1162, 1095, 892, 795 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 3.69 (3H, s), 3.74 (2H, d, *J*=0.7 Hz), 7.06 (1H, dd, *J*=8.6, 2.0 Hz), 7.21 (1H, s), 7.31 (1H, dd, *J*=8.6, 0.6 Hz), 7.49 (1H, dd, *J*=2.0, 0.6 Hz). High resolution MS *m/z*: Calcd for $C_{11}H_{10}{}^{37}ClNO_2$: 225.0371. Found: 225.0388. Calcd for $C_{11}H_{10}{}^{35}ClNO_2$: 223.0340. Found: 223.0397.

Formation of 8,17-bis[2-(methoxycarbonyl)ethyl]-1,10-diaza-9,20-dioxakabutane (9) and 3,3'-di[2-(methoxycarbonyl)ethyl]-1-hydroxy-2,2'-bisindole (10) from methyl 1-hydroxyindole-3-propionate (8a) — 85% HCO_2H (1 mL) was added to **8a** (29.6 mg, 0.13 mmol) and stirred at rt for 2 h. After addition of water and sat. aq. $NaHCO_3$ to the neutral, the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with EtOAc–hexane (1:4, v/v) to give methyl indole-3-propionate (**8b**) (7.0 mg, 26%), **10** (3.0 mg, 11%), and **9** (11.5 mg, 39%) in the order of elution. **9**: mp 83.5—84.5 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3430, 1729, 1460, 1437, 1290, 1201, 1173, 753 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.23—2.34 (4H, m), 2.40—2.51 (4H, m), 3.65 (6H, s), 5.07 (2H, s), 6.75 (2H, d, *J*=8.0 Hz), 6.77 (2H, ddd, *J*=8.0, 6.8, 1.0 Hz), 6.93 (2H, ddd, *J*=8.0, 6.8, 1.0 Hz),

6.99 (2H, d, *J*=8.0 Hz). High resolution MS *m/z*: Calcd for $C_{24}H_{24}N_2O_6$: 436.1634. Found: 436.1646. *Anal*. Calcd for $C_{24}H_{24}N_2O_6$: C, 66.05; H, 5.54; N, 6.42. Found: C, 66.13; H, 5.57; N, 6.35. **10**: yellow oil. IR (film): 3310, 1719, 1711, 1440, 1343, 1210, 1172, 743 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.78 (2H, t, *J*=6.9 Hz), 2.87 (2H, t, *J*=6.9 Hz), 3.00 (2H, br s, changed to t, *J*=6.9 Hz, on addition of D_2O), 3.09 (2H, t, *J*=6.9 Hz), 3.56 (3H, s), 3.60 (3H, s), 7.16 (2H, ddd, *J*=8.0, 7.0, 1.0 Hz), 7.23—7.27 (1H, m), 7.30 (1H, t, *J*=8.0 Hz), 7.47 (1H, d, *J*=8.0 Hz), 7.58 (2H, br d, *J*=7.6 Hz), 7.63 (1H, d, *J*=8.0 Hz), 8.79 (1H, s, disappeared on addition of D_2O), 9.51 (1H, s). High resolution MS *m/z*: Calcd for $C_{24}H_{24}N_2O_5$: 420.1685. Found: 420.1688; Calcd for $C_{24}H_{23}N_2O_4$: 403.1658. Found: 403.1642.

Formation of 9, 10, and 8b from methyl 1-hydroxyindole-3-propionate (8a) — 85% H_3PO_4 (2.0 mL) was added to a solution of **8a** (46.6 mg, 0.21 mmol) in MeCN (2.0 mL) and stirred at rt for 2 h. After addition of water and 8% NaOH to the neutral, the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with EtOAc–hexane (1:4, v/v) to give **8b** (9.1 mg, 21%), **10** (3.5 mg, 8%), and **9** (16.7 mg, 36%) in the order of elution.

Formation of 10, 9, 3,3'-di[2-(methoxycarbonyl)ethyl]-2,2'-bisindole (11) from 8a — TFA (4.0 mL) was added to **8a** (105.8 mg, 0.48 mmol) and the mixture was stirred at rt for 10 min. After evaporation of the solvent, water and 8% NaOH were added to neutral. The whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with EtOAc–hexane (1:4, v/v) to give **11** (17.8 mg, 18%), **10** (33.5 mg, 33%), and **9** (18.0 mg, 17%) in the order of elution. **11**: mp 146.0—147.0 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3300, 1717, 1443, 1430, 1366, 1338, 1248, 1228, 737 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.06 (4H, t, *J*=6.2 Hz), 3.25 (4H, t, *J*=6.2 Hz), 3.65 (6H, s), 7.13 (2H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.23 (2H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.52 (2H, d, *J*=8.1 Hz), 7.59 (2H, d, *J*=8.1 Hz), 10.98 (2H, s). *Anal*. Calcd for $C_{24}H_{24}N_2O_4$: C, 71.27; H, 5.98; N, 6.93. Found: C, 71.04; H, 6.00; N, 6.84.

Methyl 5-chloroindole-3-propionate (12), 3,3'-di[2-(methoxycarbonyl)ethyl]-1-methoxy-2,2'-bisindole (13), and methyl 1-methoxyindole-3-propionate (8c) from 8a — A mixture of conc. HCl–MeCN (1:2, v/v, 6.0 mL) was added to **8a** (105.1 mg, 0.48 mmol) and stirred at rt for 2 h. After addition of H_2O, the whole was extracted with $CHCl_3$–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 dissolved in MeOH (2.0 mL). Excess ethereal CH_2N_2 was added and stirred at rt for 30 min. Evaporation of the solvent under reduced pressure left an oil, which was column-chromatographed on SiO_2 with EtOAc–benzene (1:19, v/v) to give **8c** (10.5 mg, 9%), **13** (10.9 mg, 10%), **8b** (11.2 mg, 12%), and **12**

(15.5 mg, 14%) in the order of elution. **12**: mp 75.0—76.0 °C (pale yellow prisms, recrystallized from ether–hexane). IR (KBr): 3320, 1718, 1435, 1320, 1304, 1198, 1176, 892, 795 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.70 (2H, t, *J*=7.6 Hz), 3.06 (2H, td, *J*=7.6, 0.7 Hz), 3.68 (3H, s), 7.04 (1H, d, *J*=2.4 Hz), 7.14 (1H, dd, *J*=8.6, 2.0 Hz), 7.26 (1H, dd, *J*=8.6, 0.4 Hz), 7.56 (1H, d, *J*=2.0 Hz), 7.99 (1H, brs). *Anal.* Calcd for $C_{12}H_{12}ClNO_2$: C, 60.94; H, 5.09; N, 5.89. Found: C, 60.76; H, 5.11; N, 5.88. **13**: colorless viscous oil. IR (film): 3320, 2940, 1734, 1718, 1434, 1335, 1164, 738 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.51—2.58 (4H, m), 2.94—2.99 (4H, m), 3.47 (3H, s), 3.49 (3H, s), 3.68 (3H, s), 7.07 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.14—7.19 (2H, m), 7.29 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.40 (1H, d, *J*=8.1 Hz), 7.50 (1H, d, *J*=8.1 Hz), 7.64 (1H, d, *J*=8.1 Hz), 7.69 (1H, d, *J*=8.1 Hz), 11.25 (1H, s). High resolution MS *m/z*: Calcd for $C_{25}H_{26}N_2O_5$: 434.1842. Found: 434.1837.

***N*b-Acetylserotonin (15) and *N*b-acetyl-1-formylserotonin (16) from *N*b-acetyl-1-hydroxytryptamine (14a)** — **14a** (101.6 mg, 0.47 mmol) was dissolved in 85% HCO_2H (15.0 mL) at rt and stirred at 50 °C for 30 min. Evaporation of solvent under reduced pressure left an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:2:0.2, v/v) to afford **14a** (4.8 mg, 5%), **15** (42.1 mg, 41%), and unreacted **16** (7.0 mg, 6%) in the order of elution. **15**: colorless oil. IR (film): 3359, 2906, 1623, 1364, 1184, 1090, 932, 792 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.91 (3H, s), 2.85 (2H, dt, *J*=7.3, 1.0 Hz), 3.43 (2H, t, *J*=7.3 Hz), 6.65 (1H, dd, *J*=8.6, 2.4 Hz), 6.92 (1H, dd, *J*=2.4, 0.6 Hz), 7.00 (1H, s), 7.15 (1H, dd, *J*=8.6, 0.6 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{14}N_2O_2$: 218.1054. Found: 218.1046. **16**: mp 209.0—210.0 °C (colorless prisms, recrystallized from MeOH–H_2O). IR (KBr): 3251, 1670, 1628, 1606, 1460, 1400, 1300, 1246, 1197, 779 cm^{-1}. ^{1}H-NMR (DMSO-d_6, 120 °C) δ: 1.80 (3H, s), 2.75 (2H, t, *J*=7.2 Hz), 3.36 (2H, dt, *J*=7.2, 6.2 Hz), 6.80 (1H, dd, *J*=9.0, 2.0 Hz), 6.94 (1H, d, *J*=2.0 Hz), 7.46 (1H, s), 7.49 (1H, brs), 7.92 (1H, d, *J*=9.0 Hz), 8.84 (1H, brs), 9.17 (1H, s). MS *m/z*: 246 (M^+). *Anal.* Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.40; H, 5.80; N, 11.32.

8,17-Bis[(*N*b-acetyl)-2-aminoethyl]-1,10-diaza-9.20-dioxakabutane (17) and 14b from *N*b-acetyl-1-hydroxytryptamine (14a) — 85% H_3PO_4 (1.0 mL) was added to a solution of **14a** (50.0 mg, 0.30 mmol) in MeCN (1.0 mL) and stirred at rt for 1.5 h. After addition of H_2O, the whole was made alkaline by adding 8% NaOH under ice cooling and extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:5:0.5, v/v) to afford **14b** (7.6 mg, 16%), **17** (21.9 mg, 44%), and unreacted **14a** (2.5 mg, 5%) in the order of elution. **17**: mp 171.0—172.0 °C (decomp., colorless powder, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3277, 1640, 1555, 1460, 1365, 1295, 753 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.89 (6H, s), 2.17 (2H, ddd, *J*=6.3, 10.0, 13.1 Hz), 2.32 (2H, ddd, *J*=6.3, 10.0, 13.1 Hz), 3.12 (2H, ddd, *J*=6.3, 10.0, 13.1 Hz), 3.23 (2H, ddd, *J*=6.3,

10.0, 13.1 Hz), 5.27 (2H, s), 6.70 (2H, d, *J*=8.1 Hz), 6.79 (1H, dt, *J*=1.2, 8.1 Hz), 6.93 (2H, ddd, *J*=1.2, 8.1, 8.8 Hz), 7.05 (2H, d, *J*=8.8 Hz). MS *m/z*: 434 (M^+). *Anal.* Calcd for $C_{24}H_{26}N_4O_4 \cdot 1/8H_2O$: C, 66.00; H, 6.06; N, 12.83. Found: C, 65.84; H, 6.02; N, 12.79.

2,2'-Di(*N*b-acetyl)bistryptamine (18), 15, 17 from 14a — TFA (10.0 mL) was added to **14a** (102.0 mg, 0.47 mmol) and stirred at rt for 30 min. After evaporation of solvent, the whole was made alkaline by adding sat. aq. $NaHCO_3$ under ice cooling and extracted with $CHCl_3$–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave **18** (11.6 mg) as crystals. The mother liquor was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:2:0.2, v/v) to afford **18** (8.4 mg), **15** (13.1 mg, 13%), and **17** (33.1 mg, 33%) in the order of elution. Total yield of **18** was 20.0 mg (21%). **18**: mp 282.0—283.0 °C (decomp., pale yellow prisms, recrystallized from MeOH–EtOAc). IR (KBr): 3200, 1653, 1523, 1420, 1330, 745 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.78 (6H, s), 3.05 (4H, t, *J*=7.5 Hz), 3.39 (4H, t, *J*=7.5 Hz), 7.06 (2H, t, *J*=7.5 Hz), 7.14 (2H, t, *J*=7.5 Hz), 7.41 (2H, d, *J*=7.5 Hz), 7.64 (2H, d, *J*=7.5 Hz), 7.88 (2H, brs). MS *m/z*: 402 (M^+). *Anal.* Calcd for $C_{24}H_{26}N_4O_2$: C, 70.05; H, 6.61; N, 13.61. Found: C, 70.09; H, 6.28; N, 13.56.

***N*b-Acetyl-5-chlorotrytryptamine (19a) from 14a** — Conc. HCl (1.0 mL) was added to a solution of **14a** (12.3 mg, 0.05 mmol) in MeCN (2.0 mL) and the mixture was stirred at 80 °C for 5 min. After addition of H_2O, 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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:3:0.3, v/v) to give

14b (2.7 mg, 24%), **19a** (4.6 mg, 35%), and **14a** (1.6 mg, 13%) in the order of elution. **19a**: mp 140.0—141.0 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3253, 3080, 2930, 2855, 1623, 1568, 1457, 1305, 1099, 891, 602 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.91 (3H, s), 2.89 (2H, t, *J*=7.2 Hz), 3.43 (2H, t, *J*=7.2 Hz), 7.04 (1H, dd, *J*=8.6, 2.0 Hz), 7.12 (1H, s), 7,28 (1H, d, *J*=8.6 Hz), 7.53 (1H, d, *J*=2.0 Hz). MS *m/z*: 238 (M^+), 236 (M^+). *Anal.* Calcd for $C_{12}H_{13}ClN_2O$: C, 60.89; H, 5.54; N, 11.84. Found: C, 60.65; H, 5.49; N, 11.72.

***N*b-Acetyl-2-oxytryptamine (21), *N*b-acetyl-7-bromo- (20), *N*b-acetyl-5-bromo- (19b), and *N*b-acetyltryptamine (14b) from 14a** — 47% HBr (50.0 mL) was added to a solution of **14a** (502.2 mg, 2.30 mmol) in MeCN (50.0 mL) and the mixture was stirred at 80 °C for 3 h. After evaporation of solvent under reduced pressure, ice and H_2O were added to the residue, 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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:1:0.1, v/v) to give **20** (25.2 mg, 4%), **14b** (13.7 mg, 3%), **19b** (30.5 mg, 5%), and **21** (90.4 mg, 19%) in the order of elution. **19b**: mp 154.0—155.0 °C (colorless needles, recrystallized from MeOH–CH_2Cl_2). IR (KBr): 3020, 1613, 1563, 1433, 1363, 1208, 1103, 1033, 888, 798 cm^{-1}. ^{1}H-NMR

(CD_3OD) δ: 1.90 (3H, s), 2.89 (2H, t, *J*=7.5 Hz), 3.42 (2H, t, *J*=7.5 Hz), 7.10 (1H, s), 7.16 (1H, dd, *J*=8.1, 2.5 Hz), 7.24 (1H, d, *J*=8.1 Hz), 7.68 (1H, d, *J*=2.5 Hz). *Anal.* Calcd for $C_{12}H_{13}BrN_2O$: C, 51.26; H, 4.66; N, 9.96. Found: C, 51.26; H, 4.69; N, 9.84. **20**: colorless oil. IR (film): 1643, 1543, 1433, 1383, 1333, 1198, 1077, 1037, 872, 772, 727 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.94 (3H, s), 2.95 (2H, dt, *J*=1.3, 7.5 Hz), 3.58 (2H, q, *J*=7.5 Hz), 5.50 (1H, brs), 7.01 (1H, t, *J*=7.5 Hz), 7.11 (1H, t, *J*=1.3 Hz), 7.36 (1H, dd, *J*=7.5, 1.3 Hz), 7.54 (1H, dt, *J*=7.5, 1.3 Hz), 8.25 (1H, brs). High resolution MS *m/z*: Calcd for $C_{12}H_{13}{}^{81}BrN_2O$: 282.0194. Found: 282.0178. Calcd for $C_{12}H_{13}{}^{79}BrN_2O$: 280.0211. Found: 280.0197. **21**: mp 146.0—147.0 °C (colorless prisms, recrystallized from MeOH–CH_2Cl_2). IR (KBr): 3300, 3060, 1693, 1618, 1543, 1225, 940, 740 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.88 (3H, s), 2.00—2.08 (1H, m), 2.10—2.18 (1H, m), 3.21—3.29 (1H, m), 3.32—3.40 (1H, m), 3.49 (1H, t, *J*=6.3 Hz), 6.89 (1H, d, *J*=7.5 Hz), 7.02 (1H, dt, *J*=1.3, 7.5 Hz), 7.20 (1H, t, *J*=7.5 Hz), 7.32 (1H, d, *J*=7.5 Hz). MS *m/z*: 218 (M^+). *Anal.* Calcd for $C_{12}H_{14}N_2O_2$: C, 66.03; H, 6.47; N, 12.84. Found: C, 66.05; H, 6.53; N, 12.80.

***N*b-Methoxycarbonylserotonin (23), 1-formyl-*N*b-methoxycarbonylserotonin (24) from *N*b-methoxycarbonyl-1-hydroxytryptamine (22a)** — **22a** (49.5 mg, 0.21 mmol) was dissolved in 85% HCO_2H (5.0 mL) and stirred at rt for 14 h. evaporation of solvent under reduced pressure afforded an oil. After addition of H_2O, 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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (100:5:0.5, v/v) to give **24** (29.7 mg, 54%) and **23** (4.1 mg, 8%) in the order of elution. **24**: colorless oil. IR (film): 3290, 1692, 1608, 1550, 1464, 1392, 1244 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.74 (2H, t, *J*=7.1 Hz), 3.27 (2H, dt, *J*=7.1, 5.1 Hz), 3.53 (3H, s), 6.80 (1H, dd, *J*=2.3, 8.7 Hz), 6.93 (1H, d, *J*=2.3 Hz), 7.26 (1H, brt, *J*=5.1 Hz), 7.51 (1H, s), 8.03 (1H, d, *J*=8.7 Hz), 9.10 (1H, s). High resolution MS *m/z*: Calcd for $C_{13}H_{14}N_2O_4$: 262.0953. Found: 262.0948. **23**: identical with the commercially available sample.

8,13-Bis[2-(*N*b-methoxycarbonyl)aminoethyl]-1,10-diaza-9,20-dioxakabutane (25), 22b, and 23 from 22a — 85% H_3PO_4 (4.0 mL) was added to a solution of **22a** (200.1 mg, 0.85 mmol) in MeCN (4.0 mL) and stirred at rt for 20 min. After addition of H_2O, the whole was made alkaline by adding 40% NaOH under ice-cooling and extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:1:0.1, v/v) to give **22b** (25.2 mg, 13%), **23** (29.8 mg, 15%), and **25** (22.1 mg, 11%) in the order of elution. **25**: pale brown oil. IR (film): 3330, 2950, 1703, 1533, 1463, 1260, 750 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.20 (2H, dt, *J*=13.8, 6.4 Hz), 2.36 (2H, dt, *J*=13.8, 6.4 Hz), 3.19—3.25 (2H, m), 3.29—3.40 (2H, m), 3.67 (6H, brs), 4.93 (2H, brs), 5.17

(2H, brs), 6.74—6.78 (4H, m), 6.93 (2H, dt, *J*=1.3, 7.5 Hz), 7.00 (2H, d, *J*=7.5 Hz). High resolution MS *m/z*: Calcd for $C_{24}H_{26}N_4O_6$: 466.1852. Found: 466.1861.

5-Hydroxy-*N*b-methoxycarbonyltryptamine (23), *N*b-methoxycarbonyltryptamine (22b), 8,17-bis-[(*N*b-methoxycarbonyl)-2-aminoethyl]-1,10-diaza-9,20-dioxakabutane (25) from 22a — TFA (5.0 mL) was added to **22a** (50.1 mg, 0.21 mmol) and stirred at rt for 5 min. After evaporation of solvent, the whole was made alkaline by adding 8% NaOH under ice cooling and extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:2:0.2, v/v) to afford **22b** (6.4 mg, 5%), **23** (29.5 mg, 59%), and **25** (2.5 mg, 5%) in the order of elution. **25**: brown oil. IR (film): 3330, 2950, 1703, 1533, 1463, 1260, 750 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.20 (2H, dt, *J*=13.8, 6.4 Hz), 2.36 (2H, dt, *J*=13.8, 6.4 Hz), 3.19—3.25 (2H, m), 3.29—3.40 (2H, m), 3.67 (6H, brs), 4.93 (2H, brs), 5.17 (2H, brs), 6.74—6.78 (4H, m), 6.93 (1H, dt, *J*=1.3, 7.5 Hz), 7.00 (2H, d, *J*=7.5 Hz). MS *m/z*: 466 (M^+). High resolution MS *m/z*: Calcd for $C_{24}H_{26}N_4O_6$: 466.1852. Found: 466.1861.

26a, **27a**, **and 23 from 22a** — A conc. HCl (1.0 mL) was added to a solution of **22a** (53.2 mg, 0.23 mmol) in MeCN (2.0 mL) and stirred at 80 °C for 1 h. After addition of sat. aq. $NaHCO_3$, 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 p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (100:1:0.1, v/v) as a developing solvent. Extraction of the bands having *Rf* value of 0.62—0.58, 0.53—0.50, 0.49—0.36, 0.17—0.14, and 0.13—0.11 with $CHCl_3$–MeOH–28% NH_3 (100:10: 1, v/v) afforded **27a** (2.7 mg, 5%), **22b** (2.0 mg, 4%), **26a** (34.8 mg, 61%), **22a** (2.0 mg, 4%), and **23** (9.5 mg, 18%), respectively. **26a**: colorless oil. IR (film): 3320, 2930, 1701, 1524, 1460, 1259, 1096, 794 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.79 (2H, t, *J*=7.4 Hz), 3.22 (2H, dt, *J*=7.4, 5.9 Hz), 3.53 (3H, s), 7.05 (1H, dd *J*=8.6, 2.0 Hz), 7.19 (1H, brt, *J*=5.9 Hz), 7.22 (1H, d, *J*=2.4 Hz), 7.35 (1H, d, *J*=8.6 Hz), 7.54 (1H, d, *J*=2.0 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{13}ClN_2O_2$: 254.0636, 252.0666. Found: 254.0636, 252.0656. **27a**: colorless oil. IR (film): 3420, 3320, 2930, 1704, 1521, 1259, 782 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.82 (2H, t, *J*=7.3 Hz), 3.25 (2H, dt, *J*=7.3, 5.7 Hz), 3.52 (3H, s), 7.00 (1H, t, *J*=7.7 Hz), 7.15 (1H, d, *J*=7.7 Hz), 7.20 (1H, brt, *J*=5.7 Hz), 7.22 (1H, d, *J*=2.4 Hz), 7.51 (1H, d, *J*=7.7 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{13}ClN_2O_2$: 254.0637, 252.0666. Found: 254.0656, 252.0647. **23**: pale yellow oil. IR (film): 3340, 2940, 1686, 1525, 1262, 1186, 796 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.72 (2H, t, *J*=7.7 Hz), 3.21 (2H, dt, *J*=7.7, 5.6 Hz), 3.53 (3H, s), 6.58 (1H, dd, *J*=8.6, 2.4 Hz), 6.81 (1H, d, *J*=2.0 Hz), 7,02 (1H, d, *J*=2.4 Hz), 7.12 (1H, d, *J*=8.6 Hz), 7.18 (1H, brt, *J*=5.6 Hz), 8.60 (1H, s). High resolution MS *m/z*: Calcd for $C_{12}H_{14}N_2O_3$: 234.1004. Found: 234.1019.

26b, **27b**, **28**, **and 29 from 22a** — 47% HBr (3.0 mL) was added to a solution of **22a** (31.5 mg, 0.13 mmol) in $HCONH_2$ (3.0 mL) and stirred at 80 °C for 10 min. After addition of sat. aq. $NaHCO_3$, 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 p-TLC on SiO_2 with EtOAc–hexane (1:2, v/v) as a developing solvent. Extraction of the bands having *Rf* value of 0.64—0.57, 0.50—0.43, 0.43—0.40, 0.40—0.33, and 0.13—0.08 with $CHCl_3$–MeOH–28% NH_3 (100:10:1, v/v) afforded **27b** (2.4 mg, 6%), **22b** (3.0 mg, 10%), **28** (8.8 mg, 23%), **26b** (15.6 mg, 39%), and **29** (4.6 mg, 15%), respectively. **26b**: colorless oil. IR (film): 3290, 2920, 1703, 1540, 1462, 1262, 1025 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.79 (2H, t, *J*=7.2 Hz), 3.22 (2H, dt, *J*=7.2, 5.7 Hz), 3.53 (3H, s), 7.16 (1H, dd, *J*=8.6, 2.0 Hz), 7.19 (1H, brt, *J*=5.7 Hz), 7.21 (1H, d, *J*=2.0 Hz), 7.31 (1H, d, *J*=8.6 Hz), 7.68 (1H, d, *J*=1.5 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{13}{}^{81}BrN_2O_2$: 298.0140. Found: 298.0138. Calcd for $C_{12}H_{13}{}^{79}BrN_2O_2$: 296.0161. Found: 296.0178. **27b**: mp 68.0—69.5 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3420, 3320, 2950, 1703, 1523, 1260, 1085, 1046 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.82 (2H, t, *J*=7.3 Hz), 3.25 (2H, dt, *J*=7.3, 5.7 Hz), 3.52 (3H, s), 6.94 (1H, t, *J*=7.7 Hz), 7.20 (1H, brt, *J*=5.7 Hz), 7,21 (1H, d, *J*=2.4 Hz), 7.29 (1H, t, *J*=7.7 Hz), 7.54 (1H, d, *J*=7.7 Hz). MS *m/z*: 298 (M^+), 296 (M^+). *Anal.* Calcd for $C_{12}H_{13}BrN_2O_2$: C, 48.51; H, 4.41; N, 9.43. Found: C, 48.59; H, 4.42; N, 9.31. **28**: colorless oil. IR (film): 3260, 2950, 1703, 1524, 1446, 1259, 742 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.78 (2H, t, *J*=7.6 Hz), 3.15 (2H, dt, *J*=7.6, 5.6 Hz), 3.53 (3H, s), 7.02 (1H, td, 7.6, 1.2 Hz), 7.08 (1H, td, 7.6, 1.2 Hz), 7.20 (1H, brt, 5.6 Hz), 7.28 (1H, d, 7.8 Hz), 7.50 (1H, d, 7.8 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{13}{}^{81}BrN_2O_2$: 298.0139. Found: 298.0117. Calcd for $C_{12}H_{13}{}^{79}BrN_2O_2$: 296.0160. Found: 296.0151. **29**: mp 123.5—125.0 °C (colorless powder, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3390, 3190, 3090, 1695, 1620, 1538, 1463, 1282, 1264, 1232, 1181, 1142, 743 cm^{-1}. ^{1}H-NMR (pyridine-d_5) δ: 2.21—2.29 (1H, m), 2.29—2.35 (1H, m), 3.57—3.66 (4H, m), 3.67 (3H, s), 7.00 (1H, t, *J*=7.4 Hz), 7.04 (1H, d, *J*=7.8 Hz), 7.20 (1H, t, *J*=7.8 Hz), 7.36 (1H, d, *J*=7.4 Hz). MS *m/z*: 234 (M^+). *Anal.* Calcd for $C_{12}H_{14}N_2O_3 \cdot 1/4H_2O$: C, 60.36; H, 6.12; N, 11.73. Found: C, 60.48; H, 5.95; N, 11.61.

***N*,*N*-Dimethyl-1-hydroxyindole-3-propionamide (30a)** — Prepared according to our 1-hydroxyindole synthetic method from *N*,*N*-dimethylindole-3-propionamide in 66% yield. **30a**: mp 144.0—145.0 °C (colorless prisms, recrystallized from $CHCl_3$–hexane). IR (KBr): 2760, 1598, 1402, 1310, 1140, 1026, 736 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.63 (2H, dd, *J*=8.2, 7.2 Hz), 2.82 (3H, s), 2.88 (2H, dd, *J*=8.2, 7.2 Hz), 2.93 (3H, s), 6.97 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.12 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.23 (1H, s), 7.31 (1H, d, *J*=8.1 Hz), 7.51 (1H, d, *J*=8.1 Hz), 10.98 (1H, s, disappeared on addition of D_2O). *Anal*. Calcd for $C_{13}H_{16}N_2O_2 \cdot 1/4H_2O$: C, 65.94; H, 7.02; N, 11.83. Found: C, 66.14; H, 6.85; N, 11.80.

***N*,*N*-Dimethylindole-3-propionamide (30b) from 30a** — Conc. HCl (2.0 mL) was added to a solution of **30a** (35.0 mg, 0.15 mmol) in MeCN (4.0 mL) at 0 °C. After the mixture was heated at 80 °C with stirring for 5 min, H_2O was added 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 column-chromatographed on SiO_2 with EtOAc–hexane (2:1, v/v) to give **30b** (9.4 mg, 29%). **30b**: mp 145.0—146.0 °C (colorless prisms, recrystallized from $CHCl_3$–hexane). IR (KBr): 3200, 1630, 1415, 1331, 1223, 1077, 734 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.71 (2H, t, *J*=7.6 Hz), 2.91 (3H, s), 2.95 (3H, s), 3.13 (2H, t, *J*=7.6 Hz), 7.04 (1H, d, *J*=2.2 Hz), 7.11 (1H, ddd, *J*=7.9, 7.0, 1.0 Hz), 7.19 (1H, ddd, *J*=8.1, 7.0, 1.0 Hz), 7.36 (1H, d, *J*=8.1 Hz), 7.61 (1H, dd, *J*=7.9, 1.0 Hz), 7.99 (1H, br s). *Anal.* Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.01; H, 7.46; N, 12.91.

1-Hydroxy-3,3'-di[2-(*N*,*N*-dimethylaminocarbonyl)ethyl]-2,2'-bisindole (31a) from 30a — 85% HCO_2H (9 mL) was added to **30a** (208.1 mg, 0.89 mmol) and stirred at rt for 24 h. Water was added and the resultant solution was made neutral by adding 8% NaOH. The whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with EtOAc–hexane (2:1, v/v) to give **31a** (41.5 mg, 21%) and **30b** (20.3 mg, 11%) in the order of elution. **31a**: mp 101.0—107.0 °C (decomp., pale yellow powder, recrystallized from MeOH). IR (KBr): 3160, 2920, 1617, 1494, 1446, 1401, 1337, 1146, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.87-2.92 (2H, m), 2.87 (3H, s), 2.89 (3H, s), 2.92 (3H, s), 2.95 (2H, t, *J*=7.1 Hz), 3.07 (3H, s), 3.10 (2H, br t, *J*=6.2 Hz), 3.15 (2H, t, *J*=7.1 Hz), 7.09—7.14 (2H, m), 7.21 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.24—7.29 (1H, m), 7.54 (1H, d, *J*=8.1 Hz), 7.55 (1H, d, *J*=8.1 Hz), 7.60 (1H, d, *J*=8.1 Hz), 7.63 (1H, d, *J*=8.1 Hz), 10.93 (1H, s, disappeared on addition of D_2O), 11.22 (1H, s). High resolution MS *m/z*: Calcd for $C_{26}H_{30}N_4O_3$: 446.2318. Found: 446.2292; Calcd for $C_{26}H_{30}N_4O_2$: 430.2369. Found: 430.2358.

3,3'-Di[2-(*N*,*N*-dimethylaminocarbonyl)ethyl]-2,2'-bisindole (32) from 30a — TFA (4.0 mL) was added to **30a** (101.7 mg, 0.438 mmol) and stirred at rt for 1 h. The solvent was evaporated under reduced pressure and water was added to the residue. The resultant solution was made neutral by 8% NaOH. The whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$ to give **32** (12.1 mg, 13%), **31a** (39.1 mg, 40%), and **30b** (6.7 mg, 7%) in the order of elution. **32**: mp 232.5—233.5 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3170, 1627, 1492, 1448, 1415, 1395, 1339, 1143, 738 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.90 (6H, s), 2.91 (6H, s), 3.03 (4H, t, *J*=5.9 Hz), 3.34 (4H, t, *J*=5.9 Hz), 7.09 (2H, ddd, *J*=8.1, 7.0, 1.0 Hz), 7.19 (2H, ddd, *J*=8.1, 7.0, 1.0 Hz),

7.57 (2H, d, *J*=8.1 Hz), 7.59 (2H, d, *J*=8.1 Hz), 12.12 (2H, s). *Anal*. Calcd for $C_{26}H_{30}N_4O_2$: C, 72.53; H, 7.02; N, 13.01. Found: C, 72.27; H, 7.05; N, 12.89.

(*dl*)-*N*b-Acetyl-5-hydroxytryptophan methyl ester (34) and (*dl*)-*N*b-acetyl-1-formyl-5-hydroxytryptophan methyl ester (35) from (*dl*)-*N*b-acetyl-1-hydroxytryptophan methyl ester (33a) — **33a** (205.8 mg, 0.74 mmol) was dissolved in 85% HCO_2H (10.0 mL) and stirred at rt for 48 h. Evaporation of solvent under reduced pressure left the residue, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (45:5:0.5, v/v) to afford **35** (61.1 mg, 27%) and **34** (95.2 mg, 46%) in the order of elution. **34**: colorless oil. IR (film): 3368, 1732, 1643, 1438, 1372, 1207 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.92 (3H, s), 3.08 (1H, ddd, *J*=14.8, 7.8, 0.8 Hz), 3.20 (1H, ddd, *J*=14.8, 6.0, 0.8 Hz), 3.53 (3H, s), 4.69 (1H, dd, *J*=7.8, 6.0 Hz), 6.66 (1H, dd, *J*=8.6, 2.4 Hz), 6.88 (1H, dd, *J*=2.4, 0.8 Hz), 7.00 (1H, s), 7.15 (1H, dd, *J*=8.6, 0.8 Hz). High resolution MS *m/z*: Calcd for $C_{14}H_{16}N_2O_4$: 276.1109. Found: 276.1111. **35**: mp 163.0—164 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3324, 3178, 1735, 1686, 1639, 1605, 1551, 1467, 1400, 1249, 1051, 903, 778 cm^{-1}. ^{1}H-NMR (DMSO-d_6, 120 °C) δ: 1.83 (3H, s), 2.89 (1H, ddd, *J*=14.8, 7.8, 0.8 Hz), 3.08 (1H, ddd, *J*=14.8, 6.1, 0.8 Hz), 3.62 (3H, s), 4.61 (1H, dd, *J*=7.8, 6.1 Hz), 6.80 (1H, dd, *J*=8.8, 2.4 Hz), 6.92 (1H, d, *J*=2.4 Hz), 7.46 (1H, s), 7.85 (1H, brs), 7.92 (1H, d, *J*=8.8 Hz), 8.86 (1H, s), 9.19 (1H, s). MS *m/z*: 304 (M^+). *Anal.* Calcd for $C_{15}H_{16}N_2O_5$: C, 59.20; H, 5.30; N, 9.21. Found: C, 58.96; H, 5.22; N, 9.17.

(*dl*)-34 and kabutane (36) from 33a — 85% H_3PO_4 (2.0 mL) was added to a solution of **33a** (200.7 mg, 0.72 mmol) in MeCN (2.0 mL) and stirred at rt for 6 h. After addition of H_2O under ice cooling, the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:2:0.2, v/v) to afford **33b** (15.7 mg, 8%), **36** (17.3 mg, 4%), and **34** (9.5 mg, 5%) in the order of elution. **36**: spectral data showed a mixture of diastereoisomers. MS *m/z*: 550 (M^+).

(*dl*)-34 and kabutane (36) from 33a — TFA (5.0 mL) was added to **33a** (49.9 mg, 0.18 mmol) and stirred at rt for 10 min. After addition of H_2O under ice cooling, the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:2:0.2, v/v) to afford **36** (8.9 mg, 9%), and **34** (22.1 mg, 44%) in the order of elution.

(*dl*)-*N*b-Acetyl-7-chloro- (38a), (*dl*)-*N*b-acetyl-5-chlorotryptophan methyl ester (37a), and (*dl*)-33b from 33a — Conc. HCl (2.0 mL) was added to a solution of **33a** (30.5 mg, 0.11 mmol) in MeCN (4.0 mL) at 0 °C. After the mixture was heated at 88 °C with stirring for 5 min, H_2O was added 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 p-TLC on SiO_2 with

$CHCl_3$–MeOH–28% NH_3 (46:2:0.2, v/v) as a developing solvent. Extraction of the top band with CH_2Cl_2–MeOH (95:5, v/v) gave **38a** (2.5 mg, 8%). Extraction from the middle and lower bands with CH_2Cl_2–MeOH (95:5, v/v) afforded **33b** (3.6 mg, 13%) and **37a** (6.1 mg, 19%), respectively. **37a**: colorless oil. IR (film): 3262, 1735, 1653, 1434, 1217, 887, 791 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.00 (3H, s), 3.25 (1H, dd, *J*=14.8, 4.9 Hz), 3.32 (1H, dd, *J*=14.8, 4.9 Hz), 3.72 (3H, s), 4.94 (1H, dt, *J*=8.0, 4.9 Hz), 6.00 (1H, d, *J*=8.0 Hz, disappeared on addition of D_2O), 7.00 (1H, d, *J*=2.4 Hz), 7.14 (1H, dd, *J*=8.6, 2.0 Hz), 7.27 (1H, d, *J*=8.6 Hz), 7.48 (1H, d, *J*=2.0 Hz), 8.17 (1H, brs, disappeared on addition of D_2O). High resolution MS *m/z*: Calcd for $C_{14}H_{15}{}^{37}ClN_2O_3$: 296.0740. Found: 296.0692. Calcd for $C_{14}H_{15}{}^{35}ClN_2O_3$: 294.0770. Found: 294.0745. **38a**: mp 167.0—168.0 °C (colorless needles, recrystallized from CH_2Cl_2–MeOH). IR (KBr): 3351, 3235, 1725, 1664, 1532, 1437, 1381, 1342, 1233, 1208, 1132, 781 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.91 (3H, s), 3.15 (1H, ddd, *J*=14.7, 7.9, 0.7 Hz), 3.27 (1H, ddd, *J*=14.7, 5.9, 0.7 Hz), 3.65 (3H, s), 4.72 (1H, dd, *J*=7.9, 5.9 Hz), 6.99 (1H, t, *J*=7.9 Hz), 7.11 (1H, dd, *J*=7.9, 2.0 Hz), 7.15 (1H, s), 7.47 (1H, dd, *J*=7.9, 2.0 Hz). MS *m/z*: 296 (M^+), 294 (M^+). *Anal.* Calcd for $C_{14}H_{15}ClN_2O_3$: C, 57.05; H, 5.13; N, 9.50. Found: C, 56.76; H, 5.10; N, 9.39.

(*dl*)-*N*b-Acetyl-5-bromotryptophan methyl ester (37b), 39, 40, (*dl*)-*N*b-acetyl-7-bromotryptophan methyl ester (38b), and 33b from 33a — 47% HBr (15.0 mL) was added to a solution of **33a** (200.1 mg, 0.72 mmol) in MeCN (15 mL) at 0 °C. After the mixture was heated at 80 °C with stirring for 5 min, H_2O was added 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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:1:0.1, v/v) to afford **39** (19.6 mg, 8%), **38b** (5.5 mg, 2%), **33b** (37.4 mg, 20%), **37b** (32.8 mg, 13%), and **40** (14.2 mg, 6%) in the order of elution. **37b**: colorless oil. IR (film): 3299, 1735, 1653, 1528, 1460, 1372, 1216, 1099, 882, 792, 736 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.00 (3H, s), 3.26 (1H, dd, *J*=14.8, 5.1, 0.7 Hz), 3.32 (1H, ddd, *J*=14.8, 5.1, 0.7 Hz), 3.73 (3H, s), 4.94 (1H, dt, *J*=7.7, 5.1 Hz), 5.99 (1H, d, *J*=7.7 Hz, disappeared on addition of D_2O), 6.98 (1H, d, *J*=2.4 Hz), 7.23 (1H, d, *J*=8.6), 7.27 (1H, dd, *J*=8.6, 1.8 Hz), 7.64 (1H, d, *J*=1.8 Hz), 8.13 (1H, brs, disappeared on addition of D_2O). High resolution MS *m/z*: Calcd for $C_{14}H_{15}{}^{81}BrN_2O_3$: 340.0246. Found: 340.0250. Calcd for $C_{14}H_{15}{}^{79}BrN_2O_3$: 338.0264. Found: 338.0262. **38b**: mp 161.0—162.0 °C (yellow prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3359, 3248, 1737, 1663, 1530, 1433, 1380, 1339, 1230, 1115, 777, 737, 710, 551 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.91 (3H, s), 3.14 (1H, ddd, *J*=14.7, 7.9, 0.7 Hz), 3.27 (1H, ddd, *J*=14.7, 5.9, 0.7 Hz), 3.66 (3H, s), 4.72 (1H, dd, *J*=7.9, 5.9 Hz), 6.94 (1H, t, *J*=7.9 Hz), 7.15 (1H, s), 7.26 (1H, dd, *J*=7.9, 0.7 Hz), 7.51 (1H, dd, *J*=7.9, 0.7 Hz). MS *m/z*: 340 (M^+), 338 (M^+). *Anal.* Calcd for $C_{14}H_{15}BrN_2O_3$: C, 49.58; H, 4.46; N, 8.26. Found: C, 49.33; H, 4.46; N, 8.05. **39**: colorless oil. IR (film): 3251, 1737, 1656, 1530, 1437, 1375, 1337, 1217, 1179, 1008, 740 cm^{-1}. ^{1}H-NMR

($CDCl_3$) δ: 1.97 (3H, s), 3.25 (1H, dd, *J*=14.5, 5.1 Hz), 3.31 (1H, dd, *J*=14.5, 6.0 Hz), 3.71 (3H, s), 4.93 (1H, dt, *J*=8.1, 6.0 Hz), 6.05 (1H, d, *J*=8.1 Hz, disappeared on addition of D_2O), 7.12 (1H, t, *J*=8.1 Hz), 7.18 (1H, t, *J*=8.1 Hz), 7.28 (1H, d, *J*=8.1 Hz), 7.48 (1H, d, *J*=8.1 Hz), 8.16 (1H, brs, disappeared on addition of D_2O). High resolution MS *m/z*: Calcd for $C_{14}H_{15}{}^{81}BrN_2O_3$: 340.0246. Found: 340.0246. Calcd for $C_{14}H_{15}{}^{79}BrN_2O_3$: 338.0265. Found: 338.0255. **40**: mp 147.0 °C (decomp., colorless prisms, recrystallized from MeOH–H_2O). IR (KBr): 3350, 2755, 1738, 1626, 1547, 1436, 1359, 1206, 983, 737 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.89 (3H, s), 3.14 (1H, dd, *J*=14.3, 7.0 Hz), 3.25 (1H, dd, *J*=14.3, 7.0 Hz), 3.61 (3H, s), 4.69 (1H, t, *J*=7.0 Hz), 7.04 (1H, ddd, *J*=8.1, 8.1, 1.1 Hz), 7.16 (1H, ddd, *J*=8.1, 8.1, 1.1 Hz), 7.35 (1H, ddd, *J*=8.1, 1.1, 0.9 Hz), 7.47 (1H, ddd, *J*=8.1, 1.1, 0.9 Hz). MS *m/z*: 356 (M^+), 354 (M^+). *Anal.* Calcd for $C_{14}H_{15}BrN_2O_4$: C, 47.34; H, 4.26; N, 7.89. Found: C, 47.07; H, 4.33; N, 7.64.

8,17-Bis[3-(methoxycarbonyl)prop-1-yl])-1,10-diaza-9,20-dioxakabutane (42a) and methyl indole-3-butyrate (43) from methyl 1-hydroxyindole-3-butyrate (41a) — 85% HCO_2H (30.0 mL) was added to **41a** (507.3 mg, 2.17 mmol) and stirred at rt for 1 h. After addition of H_2O, the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with ether–hexane (1:1, v/v) to give **42a** (237 mg, 47%) and **43** (132.1 mg, 28%) in the order of elution. **42a**: pale yellow oil. IR (film): 1735, 1598, 1458, 1435, 1360, 1258, 1172, 748 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.46—1.55 (2H, m), 1.67—1.77 (2H, m), 1.99—2.14 (4H, m), 2.29—2.40 (4H, m), 3.66 (6H, s), 5.12 (2H, s), 6.70—6.80 (4H, m), 6.92 (2H, t, *J*=8.1 Hz), 6.99 (2H, d, *J*=8.1 Hz). High resolution MS *m/z*: Calcd for $C_{26}H_{28}N_2O_6$: 464.1979. Found: 464.1982.

1-Hydroxy-3,3'-di[4-(acetoxy)but-1-yl]-2,2'-bisindole (44) and 8,17-bis[4-(acetoxy)but-1-yl])-1,10-diaza-9,20-dioxakabutane (42b) from 3-[4-(acetoxy)but-1-yl]-1-hydroxyindole (41b) — 85% HCO_2H (15.0 mL) was added to (**41b**, 204.9 mg, 0.83 mmol) and stirred at rt for 1 h. After addition of H_2O, the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with ether-hexane (1:1, v/v) to give **44** (71.4 mg, 36%) and **42b** (80.1 mg, 41%) in the order of elution. **44**: pale yellow oil. IR (film): 3360, 1720, 1450, 1365, 1240, 1040, 740 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.50—1.73 (6H, m), 1.86 (3H, s), 1.82 (3H, s), 1.89—2.01 (2H, m), 2.57—2.90 (4H, m), 3.91 (2H, t, *J*=7.0 Hz), 3.95 (2H, t, *J*=7.0 Hz), 7.04 (1H, t, *J*=8.1 Hz), 7.05 (1H, t, *J*=8.1 Hz), 7.13 (1H, t, *J*=8.1 Hz), 7.19 (1H, t, *J*=8.1 Hz), 7.37 (1H, d, *J*=8.1 Hz), 7.42 (1H, d, *J*=8.1 Hz), 7.58 (1H, d, *J*=8.1 Hz), 7.61 (1H, d, *J*=8.1 Hz). High resolution MS *m/z*: Calcd for $C_{28}H_{32}N_2O_5$: 476.2310. Found: 476.2312. **42b**: pale yellow oil. IR (film): 1735, 1600, 1465, 1368, 1242, 1040, 750 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.10—1.19 (2H, m), 1.35—1.44 (2H, m), 1.59—1.72 (4H, m), 1.98 (6H, s), 2.01—2.13 (4H, m), 4.02 (4H, t, *J*=7.0

Hz), 4.57 (2H, s), 6.71 (2H, d, *J*=8.1 Hz), 6.79 (2H, t, *J*=8.1 Hz), 6.93 (2H, t, *J*=8.1 Hz), 7.02 (2H, d, *J*=8.1 Hz). High resolution MS *m/z*: Calcd for $C_{28}H_{32}N_2O_6$: 492.2261. Found: 492.2289.

46a and 47a from 45a — 85% HCO_2H (30.0 mL) was added to a solution of **45a** (203.6 mg, 0.49 mmol) in CH_2Cl_2 (20 mL) at rt and stirred for 24 h. Evaporation of solvent under reduced pressure afforded oil, which was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:3:0.3, v/v) as a developing solvent. Extraction of the bands having *Rf* value of 0.51–0.41 and 0.40–0.29 with CH_2Cl_2–MeOH (95:5, v/v) gave **47a** (37.0 mg, 17%) and **46a** (95.5 mg, 47%), respectively. **46a**: mp 114.0—117.0 °C (colorless prisms, recrystallized from EtOAc). IR (KBr): 3418, 3318, 2930, 2850, 1640, 1543, 1475, 1423, 1192, 1168, 802, 708 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 0.89 (3H, t, *J*=7.1 Hz), 1.26—1.33 (24H, m), 1.57 (2H, brq, *J*=7.1 Hz), 2.14 (2H, t, *J*=7.1 Hz), 2.86 (2H, t, *J*=7.1 Hz), 3.44 (2H, t, *J*=7.1 Hz), 6.65 (1H, dd, *J*=8.6, 2.4 Hz), 6.93 (1H, d, *J*=2.4 Hz), 6.99 (1H, s), 7.14 (1H, d, *J*=8.6 Hz). MS *m/z*: 414 (M^+). *Anal.* Calcd for $C_{26}H_{42}N_2O_2$: C, 75.31; H, 10.21; N, 6.76. Found: C, 75.24; H, 10.20; N, 6.67. **47a**: mp 114.0—115.0 °C (colorless prisms, recrystallized from EtOAc). IR (KBr): 3300, 2930, 2853, 1673, 1612, 1462, 1400, 1240, 1223, 1203, 1185, 780 cm^{-1}. ^{1}H-NMR (DMSO-d_6, 110 °C) δ: 0.85 (3H, t, *J*=7.2 Hz), 1.23—1.30 (24H, m), 1.45—1.52 (2H, m), 2.05 (2H, t, *J*=7.2 Hz), 2.75 (2H, t, *J*=7.2 Hz), 3.37 (2H, td, *J*=7.2, 5.9 Hz), 6.80 (1H, dd, *J*=8.9, 2.2 Hz), 6.94 (1H, d, *J*=2.2 Hz), 7.46 (2H, s), 7.92 (1H, brd, *J*=8.9 Hz), 8.88 (1H, s), 9.18 (1H, brs). MS *m/z*: 442 (M^+). *Anal.* Calcd for $C_{27}H_{42}N_2O_3$: C, 73.26; H, 9.56; N, 6.33. Found: C, 72.96; H, 9,57; N, 6.24.

46b and 47b from 45b — 85% HCO_2H (6.0 mL) was added to a solution of **45b** (62.3 mg, 0.20 mmol) and stirred at 60 °C for 30 min. Evaporation of solvent under reduced pressure afforded oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:3:0.3, v/v) to afford **46b** (20.8 mg, 33%) and **47b** (5.1 mg, 8%). **46b**: colorless oil. IR (film): 3270, 1652, 1597, 1530, 1212, 796 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.94 (2H, t, *J*=6.3 Hz), 3,58 (2H, t, *J*=6.3 Hz), 6.59 (1H, d, *J*=15.5 Hz), 6.66 (1H, dd, *J*=8.4, 2.3 Hz), 6.96 (1H, d, *J*=2.3 Hz), 7.03 (1H, s), 7.16 (1H, d, *J*=8.4 Hz), 7.32—7.40 (3H, m), 7.52 (1H, d, *J*=15.5 Hz), 7.52—7.56 (2H, m). High resolution MS *m/z*: Calcd for $C_{19}H_{18}N_2O_2$: 306.1368. Found: 306.1386. **47b**: colorless oil. IR (film): 3383, 1690, 1599, 1453, 1261, 796 cm^{-1}. ^{1}H-NMR (DMSO-d_6, 140 °C) δ: 2.85 (2H, t, *J*=6.2 Hz), 3.53 (2H, q, *J*=6.2 Hz, collapsed to t, on addition of D_2O), 6.56 (1H, d, *J*=15.9 Hz), 6.81 (1H, dd, *J*=8.8, 2.4 Hz), 6.98 (1H, d, *J*=2.4 Hz), 7.30—7.39 (3H, m), 7.41 (1H, d, *J*=15.9 Hz), 7.47—7.52 (2H, m), 7.49 (1H, s), 7.70 (1H, brs, disappeared on addition of D_2O), 7.92 (1H, d, *J*=8.8 Hz), 8.74 (1H, brs, disappeared on addition of D_2O), 9.18 (1H, s). High resolution MS *m/z*: Calcd for $C_{20}H_{18}N_2O_3$: 334.1317. Found: 334.1331.

***N*b-(4-Hydroxycinnamoyl)serotonin (46c) from 45c** — **45c** (145.0 mg. 0.45 mmol) was dissolved in 85% HCO_2H (15 mL) and the mixture was stirred at 60 °C for 15 min. Evaporation of solvent under

reduced pressure afforded oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH (95::5, v/v) to give **46c** (7.2 mg, 5%). **46c**: colorless oil. IR (film): 3310, 1650, 1582, 1513, 1214, 1170, 831, 755 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.93 (2H, t, *J*=7.2 Hz), 3.57 (2H, t, *J*=7.2 Hz), 6.40 (1H, d, *J*=15.8 Hz), 6.66 (1H, ddd, *J*=8.6, 2.4, 1.0 Hz), 6.77—6.81(2H, m), 6.96 (1H, dd, *J*=2.4, 1.0 Hz), 7.03 (1H, s), 7.16 (1H, dd, *J*=8.6, 1.0 Hz), 7.38—7.42 (2H, m), 7.45 (1H, d, *J*=15.8 Hz). High resolution MS (FAB^+) *m/z*: Calcd for $C_{19}H_{19}N_2O_3$: 323.1396. Found: 323.1399.

46c from serotonin (68) — *N*-Hydroxybenzotriazole (18.3 mg, 0.14 mmol) was added to a solution of 4-hydroxycinnnamic acid (22.2 mg, 0.13 mmol) and dicyclohexylcarbodiimide (DCC, 28.2 mg, 0.14 mmol) in anhydrous DMF (1.0 mL), and the mixture was stirred at rt for 15 min. To the mixture was added a solution of **68** (20.1 mg, 0.11 mmol) in anhydrous DMF (1.0 mL) and stirred at rt for 10 h under N_2 atmosphere. After addition of H_2O, solvent was evaporated under reduced pressure, and the resulting precipitates were filtered off, washed with EtOAc. The filtrate was evaporated under reduced pressure to leave an oil, which was column-chromatogaphed on SiO_2 with $CHCl_3$–MeOH (99:1, v/v) to give **46c** (46.8 mg, 94%).

***N*b-Feruloylserotonin (46d) and *N*b-feruloyl-1-formylserotonin (47d) from 45d** — **45d** (196.0 mg, 0.56 mmol) was dissolved in 85% HCO_2H (20.0 mL) and stirred at rt for 4 h. After evaporation of solvent under reduced pressure, the residue was column-chromatographed on SiO_2 with $CHCl_3$–MeOH (97:3, v/v) to afford **46d** (32.2 mg, 16%) and **47d** (11.2 mg, 5%). **46d**: mp 101.0—106.0 °C (colorless prisms, recrystallized from $CHCl_3$–MeOH). IR (KBr): 3373, 1653, 1586, 1519, 1270, 1214 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.93 (2H, t, *J*=7.3 Hz), 3.58 (2H, t, *J*=7.3 Hz), 3.38 (3H, s), 6.41 (1H, d, *J*=15.8 Hz), 6.66 (1H, dd, *J*=8.6, 2.2 Hz), 6.79 (1H, d, *J*=8.6 Hz), 6.96 (1H, d *J*=2.2 Hz), 7.02 (1H, dd, *J*=8.6, 2.2 Hz), 7.03 (1H, s), 7.11 (1H, d, *J*=2.2 Hz), 7.16 (1H, d, *J*=8.6 Hz), 7.45 (1H, d *J*=15.8 Hz). MS (FAB^+) *m/z*: 353 (M^++1). *Anal.* Calcd for $C_{20}H_{20}N_2O_4 \cdot 1/8H_2O$: C, 67.74; H, 5.76; N, 7.90. Found: C, 67.98; H, 5.92; N, 7.64. **47d**: colorless oil. ^{1}H-NMR (CD_3OD) δ: 2.83 (2H, t, *J*=7.3 Hz), 3.53 (2H, t, *J*=7.3 Hz), 4.46 (3H, s), 6.31 (1H, d, *J*=15.6 Hz), 6.70 (1H, d, *J*=8.3 Hz), 6.74 (1H, d, *J*=8.3 Hz), 6.91 (1H, s), 6.93 (1H, dd, *J*=8.3, 2.0 Hz), 7.02 (1H, d, *J*=2.0 Hz), 7.28 (1H, s), 7.35 (1H, d, *J*=15.8 Hz), 8.02 (1H, d, *J*=8.3 Hz), 8.94 (1H, s). High resolution MS *m/z*: Calcd for $C_{21}H_{20}N_2O_5$: 380.1372. Found: 380.1371.

***N*b-Feruloylserotonin (46d) from serotonin (68)** — A solution of **68** (22.2 mg, 0.13 mmol) in anhydrous DMF (1.0 mL) was added to a solution of ferulic acid (34.5 mg, 0.17 mmol), DCC (32.5 mg, 0.16 mmol), and *N*-hydroxybenzotriazole (21.2 mg, 0.16 mmol) in anhydrous DMF (1.0 mL), and the mixture was stirred at rt for 15 h under N_2 atmosphere. After addition of H_2O, solvent was evaporated under reduced pressure, and the resulting precipitates were filtered off, washed with EtOAc. The filtrate

was evaporated under reduced pressure to leave an oil, which was column-chromatogaphed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:3:0.3, v/v) to give **46d** (43.9 mg, 99%).

The reaction of *N*,*N*-dimethyl-1-hydroxyindole-3-acetamide (51a) with HCl — Conc. HCl (0.5 mL) was added to a solution of **51a** (20.2 mg, 0.093 mmol) in DMF (1.0 mL) and stirred at 80 °C for 3 h. After addition of sat. aq. $NaHCO_3$ under ice cooling, the whole was extracted with EtOAc. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with EtOAc–hexane (4:1, v/v) to give **51a** (19.8 mg, 98%).

The reaction of *N*,*N*-dimethylindole-3-acetamide (51b) with HCl — Conc. HCl (0.5 mL) was added to a solution of **51b** (20.2 mg, 0.093 mmol) in DMF (1.0 mL) and stirred at 80 °C for 3 h. After addition of sat. aq. $NaHCO_3$ under ice cooling, the whole was extracted with EtOAc. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH (95:5, v/v) to give **51b** (19.8 mg, 98%).

8,17-Bis(carboxymethyl)-1,10-diaza-9,20-dioxakabutane (52a) from 3 — Aqueous 8% NaOH (8.0 mL) was added to a solution of **3** (74.7 mg, 0.13 mmol) in MeOH (32.0 mL) and stirred at rt for 2 h. To the reaction mixture, 6% aq. HCl was added to pH<1, then the whole was extracted with $CHCl_3$. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–AcOH (100:1:0.1, v/v) to give **52a** (67.6 mg, 97%). **52a**: mp 165.5—167.0 °C (decomp., colorless prisms recrystallized from MeOH–H_2O). IR (KBr): 2900, 1743, 1716, 1463, 1327, 1197, 987, 754 cm^{-1}. IR (THF): 1736, 746 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.99 (2H, d, *J*=16.2 Hz), 3.22 (2H, d, *J*=16.2 Hz), 5.69 (2H, s), 6.69 (2H, d, *J*=7.9 Hz), 6.80 (2H, td, *J*=7.6, 1.0 Hz), 6.94 (2H, ddd, *J*=7.9, 7.6, 1.0 Hz), 7.10 (2H, dd, *J*=7.6, 1.0 Hz). MS *m/z*: 380 (M^+). *Anal*. Calcd for $C_{20}H_{16}N_2O_6 \cdot 1/8H_2O$: C, 62.78; H, 4.28; N, 7.32. Found: C, 62.75; H, 4.36; N, 7.26.

8,17-Bis[2-(amino)ethyl]-1,10-diaza-9,20-dioxakabutane (52b) from 17 — 40% NaOH (3.0 mL) was added to a solution of **17** (63.7 mg, 0.15 mmol) in MeOH (3.0 mL) and the mixture was refluxed for 1 h with stirring. After addition of H_2O, the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:5:0.5 v/v) to afford **52b** (38.6 mg, 75%). **52b**: brown oil. IR (film): 3350, 2930, 1593, 1463, 1313, 1170, 750 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.13—2.20 (2H, m), 2.22—2.30 (2H, m), 2.67—2.73 (2H, m), 2.76—2.83 (2H, m), 5.21 (2H, s), 6.73—6.78 (4H, m), 6.92 (2H, dt, *J*=1.3, 6.3 Hz), 7.01 (2H, d, *J*=6.3 Hz). High resolution MS *m/z*: Calcd for $C_{20}H_{22}N_4O_2$: 350.1742. Found: 350.1740.

8,17-Bis[2-(hydroxy)ethyl]-1,10-diaza-9,20-dioxakabutane (52c) from 3 — $LiAlH_4$ (53.2 mg, 1.41 mmol) was added to a solution of **3** (57.5 mg, 0.14 mol) in anhydrous THF (3.0 mL) at 0 °C and stirred at rt for 1 h. After addition of MeOH and 10% aqueous Rochelle salt under ice cooling, the whole was

extracted with $CHCl_3$–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave crystalline solid. Recrystallization from MeOH afforded **52c** (33.6 mg). The mother liquor was column-chromatographed on SiO_2 with $CHCl_3$–MeOH (99:1, v/v) to afford **52c** (6.6 mg). The total yield of **52c** was 40.2 mg (81%). **52c**: mp 177.0—177.5 °C (colorless powder, recrystallized from MeOH). IR (KBr): 3330, 1461, 1085, 1070, 755 cm^{-1}. ^{1}H-NMR (pyridine-d_5) δ: 2.53 (2H, dt, *J*=13.9, 6.6 Hz), 2.71 (2H, dt, *J*=13.9, 6.6 Hz), 3.93 (2H, dt, *J*=10.6, 6.6 Hz), 4.08 (2H, dt, *J*=10.6, 6.6 Hz), 5.93 (2H, s), 6.31 (2H, brs, disappeared on addition of D_2O), 6.84 (2H, ddd, *J*=7.6, 6.5, 1.4 Hz), 6.97—7.02 (4H, m), 7.22—7.23 (2H, m). MS *m/z*: 352 (M^+). *Anal.* Calcd for $C_{20}H_{20}N_2O_4 \cdot 1/8H_2O$: C, 67.74; H, 5.76; N, 7.90. Found: C, 67.67; H, 5.75; N, 7.85.

8,17-Bis[2-(hydroxy)ethyl)-1,10-diaza-9,20-dioxakabutane (52c) from 52b — $NaNO_2$ (519.1 mg, 7.52 mmol) was added to a solution of **52b** (52.3 mg, 0.15 mmol) in AcOH–H_2O (2:1, v/v, 7.5 mL) and the mixture was stirred at rt for 10 min. After addition of H_2O, the whole was made alkaline by adding 40% NaOH under ice cooling and extracted with $CHCl_3$–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. The oil was dissolved in MeOH (3.0 mL). To the solution was added 8% NaOH (3.0 mL) and refluxed for 20 min with stirring. After addition of H_2O, the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH (99:1, v/v) to afford **52c** (37.1 mg, 71%).

3,3'-Di(methoxycarbonylmethyl)-1-methoxy-2,2'-bisindole (53) from 4 — An excess amount of CH_2N_2 (Et_2O solution) was added to a solution of **4** (26.1 mg, 0.067 mmol) in MeOH–$CHCl_3$ (1:1, v/v, 3.0 mL) and stirred at rt for 30 min. After evaporation of the solvent, the residue was column-chromatographed on SiO_2 with CH_2Cl_2–hexane (3:1, v/v) to give **53** (24.8 mg, 92%). **53**: mp 166.5—167.5 °C (colorless prisms recrystallized from MeOH–CH_2Cl_2). IR (KBr): 3330, 1720, 1439, 1337, 1256, 1160, 983, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.63 (3H, s), 3.67 (3H, s), 3.78 (2H, s), 3.82 (3H, s), 3.94 (2H, s), 7.19 (1H, ddd, *J*=8.0, 7.0, 1.0 Hz), 7.21 (1H, ddd, *J*=8.0, 7.0, 1,0 Hz), 7.28 (1H, ddd, *J*=8.2, 7.0, 1.0 Hz), 7.32 (1H, ddd, *J*=8.2, 7.0, 1,0 Hz), 7.48 (1H, d, *J*=8.2 Hz), 7.49 (1H, d, *J*=8.2 Hz), 7.65 (2H, d, *J*=8.0 Hz), 10.41 (1H, br s). MS *m/z*: 406 (M^+), 375. *Anal*. Calcd for $C_{23}H_{22}N_2O_5$: C, 67.97; H, 5.46; N, 6.89. Found: C, 67.71; H, 5.40; N, 6.80.

Preparation of 5 from 53 — 10% Pd/C (40.7 mg) was added to a solution of **53** (78.7 mg, 0.19 mmol) in MeOH (60 mL) and the whole was hydrogenated at rt and 1 atm hydrogen for 1 h. After removal of the catalyst by filtration, the solvent was evaporated under reduced pressure. The residue was column-chromatographed on SiO_2 with CH_2Cl_2–hexane (1:1, v/v) to give **5** (68.5 mg, 94%).

3,3'-Di(methoxycarbonylmethyl)-2,3-dihydro-2,2'-bisindole (54) from 1b — TFA (30.0 mL) was added to **1b** (199.2 mg, 1.05 mmol) and stirred at rt for 3 h. After evaporation of the solvent under

reduced pressure, water and 8% aq. NaOH were added to pH 7.0, 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 column-chromatographed on SiO_2 with CH_2Cl_2 to give **1b** (6%) and **54** (186.2 mg, 94%). **54**: colorless oil. IR (film): 3350, 2950, 1725, 1605, 1482, 1460, 1432, 1230, 1008, 741 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.69 (1H, dd, *J*=16.9, 5.9 Hz), 2.73 (1H, dd, *J*=16.9, 7.6 Hz), 3.51 (3H, s), 3.58 (3H, s), 3.68—3.74 (1H, m), 3.76 (1H, d, *J*=16.1 Hz), 3.81 (1H, d, *J*=16.1 Hz), 4.82 (1H, dd, *J*=10.9, 3.5 Hz), 6.03 (1H, d, *J*=3.5 Hz), 6.60 (1H, d, *J*=7.6 Hz), 6.63 (1H, td, *J*=7.6, 1.0 Hz), 6.95—6.98 (2H, m), 7.02 (1H, t, *J*=7.6 Hz), 7.06 (1H, ddd, *J*=7.9, 7.6, 1.0 Hz), 7.31 (1H, t, *J*=7.9 Hz), 7.42 (1H, t, *J*=7.9 Hz), 11.11 (1H, s, disappeared on addition of D_2O). High resolution MS *m/z*: Calcd for $C_{22}H_{22}N_2O_4$: 378.1579. Found: 378.1592.

Preparation of 13 from 10 — An excess amount of CH_2N_2 (Et_2O solution) was added to a solution of **10** (15.8 mg, 0.038 mmol) in MeOH (1.0 mL) and stirred at rt for 30 min. After evaporation of the solvent, the residue was column-chromatographed on SiO_2 with EtOAc–hexane (1:4, v/v) to give **13** (16.2 mg, 99%).

Formation of 11 from 13 — 10% Pd/C (40.7 mg) was added to a solution of **13** (20.3 mg, 0.047 mmol) in MeOH (2 mL) and the whole was hydrogenated at rt and 1 atm hydrogen for 3 h. After addition of THF to the mixture, the catalyst was removed by filtration. The filtrate was evaporated under reduced pressure. The residue was column-chromatographed on SiO_2 with EtOAc–hexane (1:4, v/v) to give **11** (15.5 mg, 82%).

29 from 22b — Conc. HCl (0.76 mL) was added to a solution of **22b** (106.1 mg, 0.49 mmol) in DMSO (0.40 mL) and stirred at rt for 6 h. The whole was neutralized by adding sat. aq. $NaHCO_3$ 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 column-chromatographed on SiO_2 with EtOAc–benzene (2:1, v/v) to give **29** (43.2 mg, 38%).

3,3'-Di[2-(*N*,*N*-dimethylaminocarbonyl)ethyl]-1-methoxy-2,2'-bisindole (31b) from 31a — An excess amount of CH_2N_2 was added to a solution of **31a** (36.1 mg, 0.081 mmol) in MeOH (2.0 mL) and stirred at rt for 30 min. After evaporation of the solvent, the residue was column-chromatographed on SiO_2 with EtOAc–hexane (4:1, v/v) to give **31b** (33.9 mg, 91%). **31b**: pale yellow hard oil. IR (KBr): 3180, 2930, 1622, 1444, 1399, 1335, 1139, 743 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.65 (2H, t, *J*=8.3 Hz), 2.81 (3H, s), 2.87 (3H, s), 2.89—2.94 (2H, m), 2.92 (3H, s), 2.94 (3H, s), 3.13 (2H, brt, *J*=5.8 Hz), 3.25 (2H, t, *J*=8.3 Hz), 3.57 (3H, s), 7.13 (1H, t, *J*=8.1 Hz), 7.16 (1H, t, *J*=8.1 Hz), 7.25—7.30 (1H, m), 7.48 (1H, t, *J*=8.1 Hz), 7.53 (1H, t, *J*=8.1 Hz), 7.59 (1H, t, *J*=8.1 Hz), 7.71 (1H, t, *J*=8.1 Hz), 11.54 (1H, s). High resolution MS *m/z*: Calcd for $C_{27}H_{32}N_4O_3$: 460.2475. Found: 460.2473; Calcd for $C_{26}H_{29}N_4O_2$: 429.2291. Found: 429.2291.

3,3'-Di[2-(*N*,*N*-dimethylaminocarbonyl)ethyl]-2,2'-bisindole (32) from 31b — 10% Pd/C (10.1 mg) was added to a solution of **31b** (20.6 mg, 0.045 mmol) in MeOH (2.0 mL) and the whole was hydrogenated at rt and 1 atm hydrogen for 1 h. After removal of the catalyst by filtration, the solvent was evaporated under reduced pressure. The residue was column-chromatographed on SiO_2 with EtOAc–hexane (1:2, v/v) to give **32** (16.4 mg, 85%).

Preparation of 5 from 54 — 96% DDQ (28.3 mg, 0.12 mmol) was added to a solution of **54** (30.8 mg, 0.081 mmol) in benzene (3.0 mL) and the mixture was refluxed for 30 min. After evaporation of the solvent, the residue was dissolved in dioxane. The precipitates were removed by filtration through Al_2O_3 layer and the solvent was removed under reduced pressure. The residue was column-chromatographed on SiO_2 with CH_2Cl_2–Hexane (1:1, v/v) to give **5** (23.1 mg, 75%).

6,7-Dihydro-13-(methoxycarbonylmethyl)-6-oxo-12*H*-pyrido[1,2-*a*:3,4-*b*']diindole (55) from 5 — Aq. 27% H_2SO_4 (4.0 mL) was added to a solution of **5** (39.9 mg, 0.10 mmol) in MeOH (16.0 mL) and the mixture was refluxed for 14 h. After addition of water, the whole was extracted with $CHCl_3$. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with EtOAc–hexane (1:1, v/v) to give **5** (2.5 mg, 6%) and **55** (34.0 mg, 93%). **55**: mp 235.0—237.0 °C (decomp., colorless needles, recrystallized from $CHCl_3$–MeOH). IR (KBr): 3340, 1704, 1685, 1359, 1324, 1212, 1178, 737 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.74 (3H, s), 3.99 (2H, s), 4.16 (2H, s), 7.19 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.30 (1H, ddd, *J*=8.3, 7.1, 1.0 Hz), 7.36—7.42 (2H, m), 7.53 (1H, d, *J*=8.1 Hz), 7.56 (1H, d, *J*=8.1 Hz), 7.63 (1H, dd, *J*=7.1, 1.5 Hz), 8.60 (1H, dd, *J*=7.1, 1.5 Hz), 10.00 (1H, s). *Anal*. Calcd for $C_{21}H_{16}N_2O_3 \cdot 1/8H_2O$: C, 72.77; H, 4.73; N, 8.08. Found: C, 72.88; H, 4.67; N, 8.09.

(*dl*)-*N*b-Acetyl-5-methoxytryptophan methyl ester (56) from 33a — Conc. H_2SO_4 (2.0 mL) was added to a solution of **33a** (33.0 mg, 0.12 mmol) in MeOH (7.0 mL) at 0 °C and heated under reflux for 30 min. H_2O was added 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 column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (97:3, v/v) to give **56** (24.7 mg, 71%). **56**: colorless oil. IR (film): 3374, 2950, 1730, 1658, 1483, 1438, 1211, 1060, 1022, 920, 800 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.97 (3H, s), 3.27 (1H, dd, *J*=14.7, 4.9 Hz), 3.32 (1H, dd, *J*=14.7, 4.9 Hz), 3.71 (1H, s), 3.85 (3H, s), 4.95 (1H, dt, *J*=7.5, 4.9 Hz), 6.00 (1H, d, *J*=7.5 Hz, disappeared on addition of D_2O), 6.86 (1H, dd, *J*=8.8, 2.4 Hz), 6.95 (1H, d, *J*=2.4 Hz), 6.98 (1H, d, *J*=2.4 Hz), 7.24 (1H, d, *J*=8.8 Hz), 8.00 (1H, brs, disappeared on addition of D_2O). High resolution MS *m/z*: Calcd for $C_{15}H_{18}N_2O_4$: 290.1275. Found: 290.1280.

(*dl*)-1,*N*b-Diacetyl-5-methoxytryptophan methyl ester (57) from 56 — A solution of **56** (16.0 mg, 0.06 mmol) in DMF (2.0 mL) was added to 60% NaH (4.5 mg, 0.11 mmol) at 0 °C with stirring. After stirring

for 5 min, a solution of AcCl (13.0 mg, 0.17 mmol) in anhydrous DMF (1.0 mL) was added and stirred at rt for 1 h. After addition of H_2O, 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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:1:0.1, v/v) to give **57** (5.6 mg, 31%) and **56** (4.1 mg, 26%) in the order of elution. **57**: mp 158.0—159.0 °C (colorless needles, recrystallized from MeOH). IR (KBr): 3303, 1740, 1631, 1554, 1478, 1392, 1331, 1260, 1249, 1178, 1047, 1007, 945, 814 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.93 (3H, s), 2.59 (3H, s), 3.10 (1H, ddd, *J*=14.8, 8.0, 0.9 Hz), 3.23 (1H, ddd, *J*=14.8, 5.9, 0.9 Hz), 3.69 (3H, s), 3.85 (3H, s), 4.80 (1H, dd, *J*=8.0, 5.9 Hz), 6.92 (1H, dd, *J*=8.8, 2.4 Hz), 7.05 (1H, d, *J*=2.4 Hz), 7.48 (1H, s), 8.23 (1H, d, *J*=8.8 Hz). MS *m/z*: 332 (M^+). *Anal.* Calcd for $C_{17}H_{20}N_2O_5$: C, 61.43; H, 6.07; N, 8.43. Found: C, 61.48; H, 6.07; N, 8.38.

(*dl*)-*N*b-Acetyl-5-methoxy- (56), (*dl*)-*N*b-acetyl-5-methoxy-1-methyl- (58), (*dl*)-*N*b-acetyl-5-methoxy-1,*N*b-dimethyltryptophan methyl ester (59) from 34 — A solution of **34** (87.4 mg, 0.32 mmol) in DMF (2.5 mL) was added to 60% NaH (26.8 mg, 0.67 mmol) at 0 °C with stirring. After stirring for 5 min, MeI (0.1 mL) was added and stirred at rt for 1 h. After addition of H_2O, 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 column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (99:1, v/v) to afford **59** (18.3 mg, 18%), **58** (51.7 mg, 54%), and **56** (6.1 mg, 7%) in the order of elution. **58**: mp 134.0—135.0 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3270, 2952, 2908, 1737, 1644, 1548, 1490, 1423, 1225, 1170, 1037, 1009, 849, 783 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.97 (3H, s), 3.25 (1H, dd, *J*=14.6, 5.3 Hz), 3.29 (1H, dd, *J*=14.6, 5.3 Hz), 3.72 (6H, s), 3.85 (3H, s), 4.93 (1H, dt, *J*=7.9, 5.3 Hz), 5.97 (1H, d, *J*=7.9 Hz), 6.78 (1H, s), 6.88 (1H, dd, *J*=8.8, 2.2 Hz), 6.98 (1H, d, *J*=2.2 Hz), 7.17 (1H, d, *J*=8.8 Hz). *Anal.* Calcd for $C_{16}H_{20}N_2O_4$: C, 63.14; H, 6.62; N, 9.21. Found: C, 62.84; H, 6.64; N, 9.16. **59**: colorless oil. IR (film): 2945, 1738, 1645, 1491, 1427, 1403, 1224, 1033, 790 cm^{-1}. ^{1}H-NMR ($CDCl_3$, rotational isomers exist) δ: 1.78 (6/5H, s), 2.06 (3H, s), 2.84 (3H, s), 2.92 (6/5H, s), 3.09 (2/5H, dd, *J*=15.2, 9.7 Hz), 3.19 (1H, dd, *J*=15.4, 10.3 Hz), 3.39 (1H, dd, *J*=15.4, 5.5 Hz), 3.44 (2/5H, dd, *J*=15.2, 5.2 Hz), 3.70 (3H, s), 3.71 (6/5H, s), 3.74 (3H, s), 3.79 (6/5H, s), 3.87 (21/5H, s), 4.65 (2/5H, dd, *J*=9.7, 5.2 Hz), 5.39 (1H, dd, *J*=10.3, 5.5 Hz), 6.80 (2/5H, s), 6.85 (1H, s), 6.88 (1H, dd, *J*=8.8, 2.2 Hz), 6.90 (2/5H, dd, *J*=8.8, 2.2 Hz), 6.98 (2/5H, d, *J*=2.2 Hz), 7.03 (1H, d, *J*=2.2 Hz), 7.17 (1H, d, *J*=8.8 Hz), 7.19 (2/5H, dd, *J*=8.8 Hz). High resolution MS *m/z*: Calcd for $C_{17}H_{22}N_2O_4$: 318.1578. Found: 318.1587.

58 and 59 from 56 — A solution of **56** (53.1 mg, 0,18 mmol) in DMF (2.0 mL) was added to 60% NaH (11.8 mg, 0.29 mmol) at 0 °C with stirring. After stirring for 5 min, MeI (0.5 mL) was added and stirred at rt for 30 min. After addition of H_2O, 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 column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (99:1, v/v) to give **59** (42.4 mg, 73%) and **58** (8.0 mg, 14%) in the order of elution.

Melatonin (60a) from *N*b-acetyl-1-hydroxytryptamine (14a) — Conc. H_2SO_4 (2.0 mL) was added to a solution of **14a** (29.7 mg, 0.13 mmol) in MeOH (7.0 mL) at 0 °C and stirred for 24 h. H_2O was added under ice cooling 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 column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (98:2, v/v) to give *N*b-acetyltryptamine (**14b**) (2.8 mg, 10%) and **60a** (5.3 mg, 17%) in the order of elution.

***N*b-Acetyl-1-formyl-5-methoxytryptamine (61) from 60a** — **60a** (23.2 mg, 0.10 mmol) was dissolved in 85% HCO_2H (5.0 mL) at rt and stirred for 94 h. After evaporation of solvent under reduced pressure, the residual oil was column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (97:3, v/v) to give **61** (23.9 mg, 92%) and **60a** (1.2 mg, 5%) in the order of elution. **61**: colorless oil. IR (film): 3275, 1705, 1635, 1603, 1477, 1386, 1240, 1100, 1040, 783 cm^{-1}. ^{1}H-NMR (DMSO-d_6, 120 °C) δ: 1.80 (3H, s), 2.81 (2H, dd, *J*=5.8, 1.0 Hz), 3.38 (2H, dt, *J*=5.8, 4.8 Hz), 3.82 (3H, s), 6.94 (1H, dd, *J*=7.5, 2.4 Hz), 7.14 (1H, d, *J*=2.4 Hz), 7.51 (1H, brs), 7.52 (1H, s), 8.03 (1H, d, *J*=7.5 Hz), 9.23 (1H, s). High resolution MS *m/z*: Calcd for $C_{14}H_{16}N_2O_3$: 260.1159. Found: 260.1151.

5-Methoxytryptamine (60b) from *N*b-methoxycarbonyl-5-methoxytryptamine (62) — 20% NaOH (1.0 mL) was added to a solution of **62** (51.2 mg, 0.21 mmol) in MeOH (1.0 mL) and refluxed for 4 h with stirring. After addition of ice and H_2O, 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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:5:0.5, v/v) to give **60b** (38.8 mg, 99%). **60b**: mp 124.0—126.0 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 2850, 1586, 1490, 1436, 1306, 1216, 1010, 790 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.88 (2H, t, *J*=6.7 Hz), 3.03 (2H, t, *J*=6.7 Hz), 3.87 (3H, s), 6.86 (1H, dd, *J*=8.6, 2.4 Hz), 7.03 (1H, d, *J*=2.2 Hz), 7.05 (1H, d *J*=2.4 Hz), 7.26 (1H, d, *J*=2.2 Hz), 7.91 (1H, brs). *Anal.* Calcd for $C_{11}H_{14}N_2O$: C, 69.44; H, 7.42; N, 14.73. Found: C, 69.14; H, 7.43; N, 14.50.

Methyl 1-acetyl-5-chloro-3-propionate (63) from 12 — General procedure for introduction of acetyl group into the indole 1-position: A solution of **12** (25.8 mg, 0.10 mmol) in anhydrous DMF (2.0 mL) was added to 60% NaH (10.8 mg, 0.26 mmol) at 0 °C with stirring. After stirring for 10 min, a solution of AcCl (29.8 mg, 0.38 mmol) in anhydrous DMF (1.0 mL) was added and stirred at rt for 2 h. After addition of H_2O, the whole was extracted with EtOAc–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 column-chromatographed on SiO_2 with EtOAc–hexane (1:4, v/v) to afford **12** (11.0 mg, 43%) and **63** (16.6 mg, 55%) in the order of elution. **63**: mp 127.0—128.0 °C (colorless prisms, recrystallized from

MeOH). IR (KBr): 1717, 1695, 1443, 1382, 1325, 1265, 1016, 937, 817 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.60 (3H, s), 2.71 (2H, t, *J*=7.5 Hz), 3.01 (2H, td, *J*=7.5, 1.0 Hz), 3.70 (3H, s), 7.25 (1H, s), 7.31 (1H, dd, *J*=8.8, 2.1 Hz), 7.49 (1H, d, *J*=2.1 Hz), 8.36 (1H, d, *J*=8.8 Hz). *Anal.* Calcd for $C_{14}H_{14}ClNO_3$: C, 60.11; H, 5.04; N, 5.01. Found: C, 60.08; H, 5.01; N, 4.93.

1,*N*b-Diacetyl-5-chlorotryptamine (64a) from 19a — Following the general procedure for introduction of acetyl group into the indole 1-position, **19a** (52.7 mg, 0.22 mmol), anhydrous DMF (2.0 mL), 60% NaH (22.6 mg, 0.56 mmol), and AcCl (54.6 mg, 0.70 mmol) in anhydrous DMF (1.0 mL) were used. After the same work-up and separation, **64a** (39.4 mg, 64%) and **19a** (16.5 mg, 31%) were obtained in the order of elution. **64a**: mp 190—191 °C (colorless prisms, recrystallized from MeOH–CH_2Cl_2). IR (KBr): 3254, 3088, 2950, 1718, 1637, 1443, 1380, 1300, 933, 796 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.81 (3H, s), 2.62 (3H, s), 2.79 (2H, t, *J*=7.1 Hz), 3.32—3.37 (2H, m), 7.35 (1H, dd, *J*=8.8, 2.2 Hz), 7.69 (1H, d, *J*=2.2 Hz), 7.75 (1H, s), 7.98 (1H, brt, *J*=5.0 Hz), 8.30 (1H, d, *J*=8.8 Hz). MS *m/z*: 280 (M^+), 278 (M^+). *Anal.* Calcd for $C_{14}H_{15}ClN_2O_2$: C, 60.33; H, 5.42; N, 10.05. Found: C, 60.35; H, 5.41; N, 10.01.

***N*a,*N*b-Diacetyl-5-bromotryptamine (64b) from 19b** — Following the general procedure for introduction of acetyl group into the indole 1-position, **19b** (35.6 mg, 0.12 mmol) in anhydrous DMF (2.0 mL), 60% NaH (10.0 mg, 0.25 mmol), and AcCl (30.0 mg, 0.38 mmol) in anhydrous DMF (1.0 mL) were used. After the same work-up and separation, **64b** (29.9 mg, 73%) and **19b** (4.0 mg, 11%) were obtained in the order of elution. **64b**: mp 176.0—178.0 °C (colorless powder, recrystallized from CH_2Cl_2). IR (KBr): 3250, 3080, 1710, 1630, 1442, 1375, 930, 795 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.98 (3H, s), 2.61 (3H, s), 2.89 (2H, dt, *J*=1.3, 6.3 Hz), 3.60 (2H, q, *J*=6.3 Hz), 5.56 (1H, brs), 7.30 (1H, s), 7.46 (1H, dd, *J*=7.5, 2.5 Hz), 7.66 (1H, d, *J*=2.5 Hz), 8.32 (1H, brd, *J*=7.5 Hz). *Anal.* Calcd for $C_{14}H_{15}BrN_2O_2$: C, 52.03; H, 4.68; N, 8.67. Found: C, 51.91; H, 4.60; N, 8.53.

64c from 26a — Following the general procedure for introduction of acetyl group into the indole 1-position, **26a** (28.1 mg, 0.11 mmol) in anhydrous DMF (2.0 mL), 60% NaH (8.7 mg, 0.22 mmol), and AcCl (29.6 mg, 0.33 mmol) in anhydrous DMF (1.0 mL) were used. After the same work-up and separation, **64c** (24.6 mg, 75%) was obtained. **64c**: mp 127.5—129.5 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3330, 2950, 1688, 1542, 1446, 1392, 1344, 1254, 1242, 1206, 1016, 940, 822 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.61 (3H, s), 2.80 (2H, t, *J*=7.0 Hz), 3.30 (2H, dt, *J*=7.0, 5.0 Hz), 3.53 (3H, s), 7.27 (1H, br t, *J*=5.0 Hz), 7.35 (1H, dd, *J*=8.8, 2.3 Hz), 7.67 (1H, d, *J*=2.3 Hz), 7.74 (1H, s), 8.30 (1H, d, *J*=8.8 Hz). MS *m/z*: 296 (M^+), 294 (M^+). *Anal.* Calcd for $C_{14}H_{15}ClN_2O_3 \cdot 1/4H_2O$: C, 56.19; H, 5.22; N, 9.36. Found: C, 56.23; H, 5.00; N, 9.40.

64d from 26b — Following the general procedure for introduction of acetyl group into the indole 1-position, **26b** (28.5 mg, 0.09 mmol) in anhydrous DMF (3.0 mL), 60% NaH (9.5 mg, 0.19 mmol), and

AcCl (24.3 mg, 0.28 mmol) in anhydrous DMF (2.0 mL) were used. After the same work-up and separation, **64d** (21.1 mg, 65%) was obtained. **64d**: mp 131.0—132.0 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3420, 1726, 1701, 1539, 1446, 1390, 1263, 1243, 1056 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.61 (3H, s), 2.80 (2H, t, *J*=6.9 Hz), 3.29 (2H, dt, *J*=6.9, 5.7 Hz), 3.53 (3H, s), 7.27 (1H, br t, *J*=5.7 Hz), 7.47 (1H, dd, *J*=8.8, 1.9 Hz), 7.73 (1H, s), 7.81 (1H, d, *J*=1.9 Hz), 8.25 (1H, d, *J*=8.8 Hz). MS *m/z*: 340 (M^+), 338 (M^+). *Anal.* Calcd for $C_{14}H_{15}BrN_2O_3 \cdot 1/8H_2O$: C, 49.25; H, 4.43; N, 8.20. Found: C, 49.21; H, 4.44; N, 8.14.

***N*a,*N*b-Diacetyl-7-bromotryptamine (65a) from 20** — Following the general procedure for introduction of acetyl group into the indole 1-position, **20** (32.5 mg, 0.11 mmol) in anhydrous DMF (3.0 mL), 60% NaH (10.0 mg, 0.25 mmol), and AcCl (30.1 mg, 0.38 mmol) in anhydrous DMF (1.0 mL) were used. After the same work-up and separation, **20** (13.5 mg, 41.5%) and **65a** (21.8 mg, 58%) were obtained in the order of elution. **65a**: mp 133.0—135.0 °C (colorless cotton like crystals, recrystallized from CH_2Cl_2). IR (KBr): 3305, 3115, 1713, 1646, 1563, 1410, 1368, 1335, 1225, 1185, 1100, 733, 600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.96 (3H, s), 2.65 (3H, s), 2.91 (2H, dt, *J*=1.3, 6.9 Hz), 3.59 (2H, q, *J*=6.9 Hz), 5.55 (1H, brs), 7.17 (1H, t, *J*=7.5 Hz), 7.31 (1H, s), 7.52 (1H, dd, *J*=7.5, 1.3 Hz), 7.58 (1H, dd, *J*=7.5, 1.3 Hz). *Anal.* Calcd for $C_{14}H_{15}BrN_2O_2$: C, 52.03; H, 4.68; N, 8.67. Found: C, 52.08; H, 4.69; N, 8.45.

65b from 27b — Following the general procedure for introduction of acetyl group into the indole 1-position, **27b** (20.5 mg, 0.07 mmol) in anhydrous DMF (2.0 mL), 60% NaH (6.6 mg, 0.14 mmol), and AcCl (20.8 mg, 0.21 mmol) in anhydrous DMF (1.0 mL) were used. After the same work-up and separation, **65b** (9.4 mg, 40%) was obtained. **65b**: colorless oil. IR (film): 3340, 2950, 1717, 1526, 1410, 1258, 1222, 1008 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.65 (3H, s), 2.80 (2H, t, *J*=7.0 Hz), 2.32 (2H, dt, *J*=7.0, 5.7 Hz), 3.53 (3H, s), 7.23 (1H, t, *J*=7.7 Hz), 7.30 (1H, brt, *J*=5.7 Hz), 7.54 (1H, d, *J*=7.7 Hz), 7.64 (1H, d, *J*=7.7 Hz), 7.74 (1H, s). High resolution MS *m/z*: Calcd for $C_{14}H_{15}{}^{81}BrN_2O_3$: 340.0245. Found: 340.0241. Calcd for $C_{14}H_{15}{}^{79}BrN_2O_3$: 338.0266. Found: 338.0278.

(*dl*)-1,*N*b-Diacetyl-5-chlorotryptophan methyl ester (66a) from 37a — Following the general procedure for introduction of acetyl group into the indole 1-position, **37a** (51.7 mg, 0.17 mmol) in anhydrous DMF (2.0 mL), 60% NaH (14.8 mg, 0.37 mmol), and AcCl (35.1 mg, 0.45 mmol) in anhydrous DMF (1.0 mL) were used. After the same work-up and separation, **66a** (26.6 mg, 45 %) and **37a** (8.4 mg, 16%) were obtained in the order of elution. **66a**: mp 203.0—204.0 °C (colorless needles, recrystallized from CH_2Cl_2). IR (KBr): 3270, 1735, 1646, 1548, 1450, 1383, 1324, 1245, 1018, 941, 805 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.02 (3H, s), 2.60 (3H, s), 3.17 (1H, ddd, *J*=15.0, 5.5, 0.7 Hz), 3.29 (1H, ddd, *J*=15.0, 5.5, 0.7 Hz), 3.74 (3H, s), 4.97 (1H, dt, *J*=7.3, 5.5 Hz), 6.06 (1H, d, *J*=7.3 Hz), 7.27 (1H, s), 7.31

(1H, dd, *J*=8.8, 2.2 Hz), 7.43 (1H, d, *J*=2.2 Hz), 8.34 (1H, d, *J*=8.8 Hz). MS *m/z*: 338(M^+), 336 (M^+). *Anal.* Calcd for $C_{16}H_{17}ClN_2O_4$: C, 57.06; H, 5.09; N, 8.32. Found: C, 57.00; H, 5.09; N, 8.32.

(*dl*)-1,*N*b-Diacetyl-5-bromotryptophan methyl ester (66b) from 37 — Following the general procedure for introduction of acetyl group into the indole 1-position, **37b** (65.1 mg, 0.19 mmol) in anhydrous DMF (1.0 mL), 60% NaH (23.0 mg, 0.57 mmol), and AcCl (53.0 mg, 0.67 mmol) in anhydrous DMF (1.0 mL) were used. After the same work-up and separation, **66b** (32.0 mg, 44 %) and **37b** (16.0 mg, 25%) were obtained in the order of elution. **66b**: mp 200.5—201.5 °C (colorless needles, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3278, 3100, 1738, 1703, 1648, 1550, 1445, 1389, 1324, 1237, 1180, 1016, 938, 803, 610 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.03 (3H, s), 2.60 (3H, s), 3.17 (1H, ddd, *J*=14.8, 5.5, 0.7 Hz), 3.28 (1H, ddd, *J*=14.8, 5.7, 0.7 Hz), 3.74 (3H, s), 4.97 (1H, dt, *J*=7.7, 5.7 Hz), 6.06 (1H, d, *J*=7.7 Hz), 7.25(1H, s), 7.44 (1H, dd, *J*=8.8, 1.8 Hz), 7.44 (1H, d, *J*=1.8 Hz), 8,29 (1H, d, *J*=8.8 Hz). MS *m/z*: 382(M^+), 380 (M^+). *Anal.* Calcd for $C_{16}H_{17}BrN_2O_4$: C, 50.41; H, 4.49; N, 7.31. Found: C, 50.54; H, 4.39; N, 7.41.

(*dl*)-1,*N*b-Diacetyl-7-chlorotryptophan methyl ester (67a) from 38a — Following the general procedure for introduction of acetyl group into the indole 1-position, **38a** (26.4 mg, 0.09 mmol) in anhydrous DMF (1.0 mL), 60% NaH (8.9 mg, 0.22 mmol), and AcCl (22.0 mg, 0.28 mmol) in anhydrous DMF (1.0 mL) were used. After the same work-up and separation, **38a** (8.5 mg, 32%) and **67a** (17.6 mg, 58%) were obtained in the order of elution. **67a**: mp 131.0—132.0 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3352, 3098, 1746, 1713, 1662, 1603, 1520, 1370, 1210, 1026, 779 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.92 (3H, s), 2.65 (3H, s), 3.13 (1H, ddd, *J*=15.0, 8.3, 0.9 Hz), 3.26 (1H, ddd, *J*=15.0, 5.9, 0.9 Hz), 3.68 (3H, s), 4.79 (1H, dd, *J*=8.3, 5.9 Hz), 7.24 (1H, t, *J*=7.7 Hz), 7.34 (1H, dd, *J*=7.7, 1.1 Hz), 7.53 (1H, dd, *J*=7.6, 1.1 Hz), 7.58 (1H, s). MS *m/z*: 338(M^+), 336 (M^+). *Anal.* Calcd for $C_{16}H_{17}ClN_2O_4$: C, 57.06; H, 5.09; N, 8.32. Found: C, 57.04; H, 5.10; N, 8.33.

(*dl*)-1,*N*b-Diacetyl-7-bromotryptophan methyl ester (67b) from 38b — Following the general procedure for introduction of acetyl group into the indole 1-position, **38b** (12.4 mg, 0.03 mmol) in anhydrous DMF (1.0 mL), 60% NaH (3.1 mg, 0.07 mmol), and AcCl (9.6 mg, 0.12 mmol) in anhydrous DMF (1.0 mL) were used. After the same work-up and separation, **38b** (6.7 mg, 54%) and **67b** (5.2 mg, 37%) were obtained in the order of elution. **67b**: colorless oil. IR (film): 3280, 3059, 1724, 1652, 1540, 1370, 1220, 1011, 783 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.92 (3H, s), 2.64 (3H, s), 3.12 (1H, ddd, *J*=14.8, 8.2, 0.9 Hz), 3.26 (1H, ddd, *J*=14.8, 5.7, 0.9 Hz), 3.68 (3H, s), 4.79 (1H, dd, *J*=8.2, 5.7 Hz), 7.20 (1H, t, *J*=7.7 Hz), 7.54 (1H, dd, *J*=7.7, 0.9 Hz), 7.58 (1H, dd, *J*=7.7, 0.9 Hz), 7.58 (1H, s). High resolution MS *m/z*: Calcd for $C_{16}H_{17}{}^{79}BrN_2O_4$: 380.0371. Found: 380.0302. Calcd for $C_{16}H_{17}{}^{81}BrN_2O_4$: 382.0350. Found: 382.0255.

Serotonin (68a) from 15 — 40% NaOH (1.0 mL) was added to a solution of **23** (60.5 mg, 0.27 mmol) in MeOH (3.0 mL) and refluxed with stirring for 4 h. After addition of H_2O, the whole was made neutral by adding 6% HCl and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:10:1, v/v) to give **68a** (43.9 mg, 90%) in the order of elution. **68a**: colorless oil. IR (film): 3332, 1579, 1455, 1200, 936, 800 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.83 (2H, t, *J*=6.2 Hz), 2.92 (2H, t, *J*=6.2, Hz), 6.66 (1H, dd, *J*=8.6, 2.4 Hz), 6.92 (1H, dd, *J*=2.4, 1.1 Hz), 7.01 (1H, s), 7.16 (1H, d, *J*=8.6, 1.1 Hz). High resolution MS *m/z*: Calcd for $C_{10}H_{12}N_2O$: 176.0950. Found: 176.0947.

Serotonin (68a) from 23 — 40% NaOH (1.0 mL) was added to a solution of **23** (51.5 mg, 0.22 mmol) in MeOH (3.0 mL) and refluxed with stirring for 4 h. After addition of H_2O, the whole was made neutral by adding 6% HCl and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:10:1, v/v) to give **23** (8.9 mg, 17%) and **68a** (28.2 mg, 73%) in the order of elution.

5-Bromotryptamine 68b from 26b — 10% NaOH (7.0 mL) was added to a solution of **26b** (132.4 mg, 0.44 mmol) in MeOH (7.0 mL) and refluxed for 7 h with stirring. After addition of H_2O, 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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (100:20:2, v/v) to afford **68b** (94.0 mg, 88%). **68b**: colorless oil. IR (film): 3130, 2940, 2870, 1582, 1564, 1459, 1094, 880, 792 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.72—2.82 (4H, m), 7.16 (1H, dd, *J*=8.4, 1.9 Hz), 7.20 (1H, d, *J*=8.4 Hz), 7.30 (1H, d, *J*=8.4 Hz), 7.69 (1H, d, *J*=1.9 Hz). High resolution MS *m/z*: Calcd for $C_{10}H_{11}{}^{81}BrN_2$: 240.0086. Found: 240.0092. Calcd for $C_{10}H_{11}{}^{79}BrN_2$: 238.0104. Found: 238.0104.

1-Formylmelatonin (61) from 60a — 60a (52.5 mg, 0.22 mmol) was dissolved in 85% aqueous HCO_2H (1.0 mL) and the mixture was stirred for 4.5 days at rt. After addition of H_2O, the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with EtOAc to give **61** (51.7 mg, 88%). **61**: colorless oil. IR (film): 3590, 2900, 1700, 1650, 1600, 1550, 1480, 1390, 1240, 1040, 800 cm^{-1}. ^{1}H-NMR (DMSO-d_6, 90 °C) δ: 1.80 (3H, s), 2.80 (2H, t, *J*=7.08 Hz), 3.37 (2H, q, *J*=7.08 Hz), 3.82 (3H, s), 6.94 (1H, dd, *J*=8.79 and 2.44 Hz), 7.15 (1H, dd, *J*=2.44 Hz), 7.54 (1H, s), 7.65 (1H, brs), 8.03 (1H, d, *J*=8.79 Hz), 9.25 (1H, s). High resolution MS *m/z*: Calcd for $C_{14}H_{16}N_2O_3$: 260.1161. Found: 260.1172.

2,3-Dihydro-2,2'-bismelatonin (70) from 60a —60a (20.4 mg, 0.88 mmol) was dissolved in TFA (1.0 mL) and the mixture was stirred for 2.5 h at rt. After evaporation of solvent, the whole was made alkaline

by adding 8% aqueous NaOH under ice cooling and extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH (97:3, v/v) to give unreacted **60a** (3.7 mg, 18%) and **70** (7.4 mg, 36%) in the order of elution. **70**: colorless viscous oil. IR (film): 3280, 1640, 1550, 1490, 1370, 1300, 1215, 1025, 803 cm^{-1}. ^{1}H-NMR (5% CD_3OD in $CDCl_3$) δ: 1.88 (3H, s), 1.95 (3H, s), 1.97—2.05 (2H, m), 2.88—3.03 (2H, m), 3.25—3.32 (2H, m), 3.37—3.50 (2H, m), 3.79 (3H, s), 3.86 (3H, s), 4.84 (1H, d, *J*=8.30 Hz), 6.65 (1H, d, *J*=8.54 Hz), 6.70 (1H, dd, *J*=8.54, 2.44 Hz), 6.79 (1H, d, *J*=2.44 Hz), 6.82 (1H, dd, *J*=8.54, 2.44 Hz), 6.94 (1H, brs), 7.02 (1H, d, *J*=2.44 Hz), 7.19 (1H, d, *J*=8.54 Hz), 8.87 (1H, brs). High resolution MS *m/z*: Calcd for $C_{26}H_{32}N_4O_4$: 464,2423. Found: 464.2419.

2,2'-Bismelatonin (71) from 70 — A solution of **70** (40.6 mg, 0.08 mmol) in dioxane (2.0 mL) was added to DDQ (23.1 mg, 0.10 mmol) and the mixture was stirred at rt for 30 min. After evaporation of the solvent, the residue was column-chromatographed on SiO_2 with $CHCl_3$–MeOH (95:5, v/v) to give **71** (24.7 mg, 61%). **71**: pale yellow powder, recrystallized from MeOH–EtOAc. mp 260—261 °C. IR (KBr): 3300, 1650, 1530, 1442, 1310, 1288, 1210, 1178, 1022, 940, 835, 792, 615 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.77 (6H, s), 2.86 (4H, t, *J*=8.30 Hz), 3.22 (4H, q, *J*=8.30 Hz), 3.80 (6H, s), 6.80 (2H, dd, *J*=8.79, 2.45 Hz), 7.15 (2H, d, *J*=2.45 Hz), 7.31 (2H, d, *J*=8.79 Hz), 8.03 (2H, s), 10.90 (2H, s). MS *m/z*: 462 (M^+). *Anal*. Calcd for $C_{26}H_{30}N_4O_4 \cdot 1/2H_2O$: C, 66.22; H, 6.49; N, 11.88. Found: C, 66.32; H, 6.49; N, 11.83.

(*dl*)-1,1'-Diacetyl-8,8'-diformyl-5,5'-dimethoxy-3a,3a'-bis(1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]-indole) (72) from 69 —**69** (204.8 mg, 0.82 mmol) was dissolved in 85% aqueous HCO_2H (3.0 mL) and the mixture was stirred at rt for 1.5 h, and the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28%NH_3 (46:1:0.1, v/v) to give **72** (93.3 mg, 44%). **72**: colorless fine needles, recrystallized from $CHCl_3$–MeOH (95:5, v/v). mp >300 °C. IR (KBr): 3000, 1670, 1480, 1400, 1280, 1230, 1170, 1055, 1035, 875, 840, 795, 750, 563 cm^{-1}. ^{1}H-NMR (5% CD_3OD in $CDCl_3$) δ: 2.04 (6H, s), 2.17—2.20 (2H, m), 2.33—2.40 (2H, m), 3.06—3.13 (2H, m), 3.63—3.67 (2H, m), 3.80 (6H, s), 5.90 (2H, s), 6.75 (2H, d, *J*=2.4 Hz), 6.85 (2H, dd, *J*=8.7, 2.4 Hz), 7.91 (2H, d, *J*=8.7 Hz), 8.97 (2H, s). MS *m/z*: 518 (M^+). High resolution MS *m/z*: Calcd for $C_{28}H_{30}N_4O_6$: 518.2165. Found: 518.2167. *Anal*. Calcd for $C_{28}H_{30}N_4O_6 \cdot CHCl_3$: C, 54.60; H, 4.90; N, 8.78. Found: C, 54.45; H, 4.89; N, 8.84.

(*dl*)-1,1'-Diacetyl-8-formyl-5,5'-dimethoxy-3a,3a'-bis(1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole) (73) from 69 — **69** (51.2 mg, 0.20 mmol) was dissolved in 30% HCO_2H (85% aqueous HCO_2H in MeOH, 1.0 mL) and the mixture was stirred at rt for 1.5 h. After addition of H_2O, the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH (99:1, v/v) to give **73** (12.9 mg, 23%) and unreacted **69** (9.7 mg, 18%) in the order of elution. **73**: pale brown powder, recrystallized from EtOAc–hexane. mp 235—236 °C. IR (KBr): 3350, 2930, 2870, 1678, 1638, 1488, 1415, 1275, 1223, 1210, 1163, 1043, 865, 807 cm^{-1}. ^{1}H-NMR (DMSO-d_6, 120 °C) δ: 1.85 (3H, s), 1.91 (3H, s), 2.20—2.60 (4H, m), 2.80—3.00 (2H, m), 3.65 (3H, s), 3.75 (3H, s), 3.56—3.76 (2H, m), 4.95 (1H, s), 5.77 (1H, s), 6.50 (1H, brs), 6.61 (1H, dd, *J*=8.7, 2.4 Hz), 6.82 (1H, dd, *J*=8.7, 2.4 Hz), 6.82 (1H, d, *J*=2.4 Hz), 7.05 (1H, d, *J*=2.4 Hz), 7.67 (1H, br s), 8.76 (1H, s). High resolution MS *m/z*: Calcd for $C_{27}H_{30}N_4O_5$: 490.2216. Found: 490.2213.

(*dl*)-1,1'-Diacetyl-5,5'-dimethoxy-3a,3a'-bis(1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole) (74) from 72 — A solution of **72** (41.8 mg, 0.08 mmol) in MeOH (7.0 mL) was added to 8% aqueous NaOH (7.0 mL) and the mixture was refluxed for 1.5 h with stirring. After addition of ice and H_2O, the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH (97:3, v/v) to give **74** (32.9 mg, 88%). **74**: mp 188—189 °C (colorless needles, recrystallized from $CHCl_3$–hexane). IR (KBr): 3360, 2980, 1625, 1490, 1430, 1200, 1025, 850, 800, 750 cm^{-1}. ^{1}H-NMR (DMSO-d_6, 120 °C) δ: 1.84 (6H, s), 2.01—2.12 (2H, m), 2.35—2.52 (2H, m), 2.85—2.98 (2H, m), 3.55—3.65 (2H, m), 3.68 (6H, s), 5.10 (2H, s), 6.48 (2H, d, *J*=8.3 Hz), 6.63 (2H, dd, *J*=8.3, 2.6 Hz), 6.85 (2H, d, *J*=2.6 Hz). MS *m/z*: 462 (M^+). High resolution MS *m/z*: Calcd for $C_{26}H_{30}N_4O_4$: 462.2267. Found: 462.2262. *Anal*. Calcd for $C_{26}H_{30}N_4O_4 \cdot 1/4H_2O$: C, 66.81; H, 6.58; N, 11.99. Found: C,66.55; H, 6.47; N, 11.80.

72 from 74 — **74** (20.6 mg, 0.04 mmol) was dissolved in 85% aqueous HCO_2H (2.0 mL) and the mixture was stirred at rt for 2 h. After evaporation of the solvent, the whole was made alkaline by adding 8% aqueous NaOH under ice cooling and extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with $CHCl_3$–MeOH (97:3, v/v) to give **72** (22.0 mg, 95%).

(*dl*)-8,8'-Chloroacetyl-1,1'-diacetyl-5,5'-dimethoxy-3a,3a'-bis(1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole) (75) from 74 — 60% NaH (8.2 mg, 0.20 mmol, washed with dry benzene) was added to a solution of **74** (20.4 mg, 0.04 mmol) in abs. DMF (2.0 mL) at 0 °C with stirring and AcCl (41.4 mg, 0.367 mmol) was added to the resultant solution. The mixture was stirred at rt for 40 min. After addition of H_2O under ice cooling the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with EtOAc–hexane (2:3, v/v) to give **75** (19.2 mg, 71%). **75**: mp 246—247 °C (colorless powder, recrystallized from $CHCl_3$–hexane). IR (KBr): 2960, 1665, 1645, 1485,

1415, 1390, 1250, 1160, 1025, 858, 819, 795 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.78—1.82 (2H, m), 2.00 (6H, s), 2.29—2.34 (2H, m), 2.94—3.00 (2H, m), 3.45—3.52 (2H, m), 3.84 (6H, s), 4.21 (2H, d, *J*=11.7 Hz), 5.80 (2H, d, *J*=11.7 Hz), 6.35 (2H, s), 6.84 (2H, d, *J*=2.6 Hz), 6.91 (2H, dd, *J*=8.7, 2.6 Hz), 8.04 (2H, d, *J*=8.7 Hz). 500 MHz ^{13}C-NMR ($CDCl_3$) δ: 23.26 (2C), 31.95 (2C), 42.84 (2C), 46.91 (2C), 55.74 (2C), 60.18 (2C), 79.56 (2C), 110.8 (2C), 114.1 (2C), 120.7 (2C), 133.1 (2C), 135.9 (2C), 157.3 (2C), 165.5 (2C), 170.5 (2C). MS *m/z*: 614, 616 (M^+). High resolution MS *m/z*: Calcd for $C_{30}H_{32}Cl_2N_4O_6$: 614.1699, 616.1670, 618.1640. Found: 614.1688, 616.1677, 618.1657. *Anal.* Calcd for $C_{30}H_{32}Cl_2N_4O_6 \cdot 1/4CHCl_3$: C, 56.30; H, 5.04; N, 8.68. Found: C, 56.11; H, 5.06; N, 8.69.

(*dl*)-8,8'-Acetoxyacetyl-1,1'-diacetyl-5,5'-dimethoxy-3a,3a'-bis(1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole) (76) from 75 — A solution of **75** (70.1 mg, 1.11 mmol) in DMF (3.0 mL) was added to a solution of sodium acetate (38.2 mg, 0.46 mmol) in H_2O (0.3 mL) and the mixture was stirred at 55 °C for 12 h. After evaporation of solvent, the whole was extracted with $CHCl_3$–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 column-chromatographed on SiO_2 with EtOAc–hexane (2:1, v/v) to give **76** (69.9 mg, 93%). **76**: mp 274—275 °C (colorless prisms, recrystallized from EtOAc–MeOH). IR (KBr): 2940, 1740, 1665, 1487, 1420, 1280, 1225, 1070, 1030, 860, 820 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.70—1.73 (2H, m), 2.03 (6H, s), 2.15 (6H, s), 2.21—2.27 (2H, m), 2.90—2.94 (2H, m), 3.63—3.66 (2H, m), 3.82 (6H, s), 5.05 (2H, d, *J*=15.3 Hz), 5.51 (2H, d, *J*=15.3 Hz), 6.30 (2H, s), 6.77 (2H,d, *J*=2.4 Hz), 6.91 (2H, dd, *J*=8.7, 2.4 Hz), 7.92 (2H d, *J*=8.7 Hz). MS *m/z*: 662 (M^+). *Anal*. Calcd for $C_{34}H_{38}N_4O_{10}$: C, 61.62; H, 5.78; N, 8.46. Found: C, 61.41; H, 5.86; N, 8.29.

X-Ray analysis: All measurements were made on a Rigaku AFC5R diffractometer with graphite monochromated Mo-$K\alpha$ radiation (λ=0.71069 Å). The structure was solved by direct methods using MITHRIL.[20] The non-hydrogen atoms were refined anisotropically.

Crystal data for 3: $C_{22}H_{20}N_2O_6$, *M*=408.41, monoclinic, space group $P2_1/n$ (#14), *a*=11.5779 (9)Å, *b*=10.7941 (9)Å, *c*=16.488 (2)Å, β=106.068 (6)°, *V*=1980.0 (3)Å^3, *Z*=4, D_{calc}=1.370 g/cm^3, *F*(000)=856, and μ(Mo$K\alpha$)=0.94 cm^{-1}. The final cycle of full-matrix least-squares refinement was based on 2292 observed reflections ($I>3.00\sigma(I)$, $2\theta<55.1°$) and 351 variable parameters. The final refinement converged with *R*=0.046 and *R*w=0.049.

Crystal data for 53: $C_{23}H_{22}N_2O_5$, *M*=406.44, triclinic, space group $P\bar{1}$ (#2), *a*=11.299 (2)Å, *b*=12.045 (2)Å, *c*=8.241 (2)Å, α=105.89 (2)°, β=96.25 (2)°, γ=71.96 (1)°, *V*=1025.3 (3)Å^3, *Z*=2, D_{calc}=1.316 g/cm^3, *F*(000)=428, and μ(Mo$K\alpha$)=0.87 cm^{-1}. The final cycle of full-matrix least-squares refinement was based on 2169 observed reflections ($I>3.00\sigma(I)$, $2\theta<55.1°$) and 359 variable parameters. The final refinement converged with *R*=0.045 and *R*w=0.047.

Table 4. Positional Parameters and B (eq) for **3**

ORTEP drawing and numbering of **3** are reported in Figure 1.

atom	x	y	z	B (eq)	atom	x	y	z	B (eq)
O (1)	0.7448 (2)	–0.2464 (2)	0.4884 (1)	3.55 (8)	C (18)	0.6852 (3)	0.2571 (3)	0.5065 (2)	4.6 (2)
O (2)	0.8470 (2)	0.0867 (2)	0.6112 (1)	3.04 (7)	C (19)	0.660 (1)	0.4623 (5)	0.4554 (5)	10.9 (4)
O (3)	0.7454 (3)	0.2354 (2)	0.4597 (2)	6.5 (1)	C (20)	0.9286 (3)	–0.2610 (3)	0.4518 (2)	3.8 (1)
O (4)	0.6379 (3)	0.3683 (2)	0.5127 (2)	7.1 (1)	C (21)	0.8656 (3)	–0.2444 (3)	0.3599 (2)	4.0 (1)
O (5)	0.8188 (2)	–0.1515 (2)	0.3278 (1)	6.0 (1)	C (22)	0.8157 (5)	–0.3443 (7)	0.2267 (3)	7.5 (3)
O (6)	0.8688 (2)	–0.3491 (2)	0.3180 (1)	6.0 (1)	H (1)	0.679 (2)	0.007 (2)	0.444 (2)	2.97 (1)
N (1)	0.6670 (2)	–0.1533 (2)	0.5081 (1)	3.3 (1)	H (2)	0.692 (2)	0.049 (3)	0.744 (2)	4.36 (2)
N (2)	0.9233 (2)	–0.0033 (2)	0.5869 (1)	2.85 (9)	H (3)	0.643 (3)	–0.120 (3)	0.814 (2)	6.48 (2)
C (1)	0.7210 (2)	–0.0308 (3)	0.4980 (2)	3.0 (1)	H (4)	0.603 (3)	–0.313 (3)	0.742 (2)	5.71 (2)
C (2)	0.7221 (2)	0.0475 (3)	0.5766 (2)	3.0 (1)	H (5)	0.620 (3)	–0.337 (3)	0.607 (2)	4.81 (2)
C (3)	0.6842 (2)	–0.0448 (3)	0.6327 (2)	3.0 (1)	H (6)	0.881 (2)	–0.021 (2)	0.460 (2)	3.19 (1)
C (4)	0.6749 (3)	–0.0299 (3)	0.7142 (2)	4.0 (1)	H (7)	0.953 (3)	–0.409 (3)	0.617 (2)	5.54 (2)
C (5)	0.6447 (3)	–0.1314 (4)	0.7551 (2)	4.8 (2)	H (8)	1.045 (3)	–0.388 (3)	0.764 (2)	5.49 (2)
C (6)	0.6247 (3)	–0.2452 (4)	0.7156 (2)	4.7 (2)	H (9)	1.069 (3)	–0.198 (3)	0.836 (2)	5.94 (2)
C (7)	0.6327 (3)	–0.2613 (3)	0.6340 (2)	4.1 (1)	H (10)	1.019 (3)	–0.018 (3)	0.756 (2)	5.01 (2)
C (8)	0.6628 (2)	–0.1586 (3)	0.5940 (2)	3.1 (1)	H (11)	0.568 (3)	0.148 (3)	0.543 (2)	4.37 (2)
C (9)	0.8530 (2)	–0.0555 (3)	0.5043 (2)	3.0 (1)	H (12)	0.656 (3)	0.206 (3)	0.619 (2)	4.88 (2)
C (10)	0.8678 (2)	0.1976 (3)	0.5110 (2)	3.1 (1)	H (13)	0.631 (5)	0.530 (6)	0.470 (4)	13 (2)
C (11)	0.9321 (2)	–0.2168 (3)	0.6035 (2)	3.2 (1)	H (14)	0.759 (7)	0.448 (7)	0.460 (5)	18 (3)
C (12)	0.9669 (3)	–0.3258 (3)	0.6481 (2)	4.3 (1)	H (15)	0.675 (8)	0.418 (7)	0.400 (5)	19 (3)
C (13)	1.0184 (3)	–0.3179 (4)	0.7341 (2)	4.9 (2)	H (16)	1.008 (3)	–0.228 (3)	0.462 (2)	4.37 (2)
C (14)	1.0355 (3)	–0.2048 (4)	0.7749 (2)	4.8 (2)	H (17)	0.936 (3)	–0.352 (3)	0.465 (2)	4.87 (2)
C (15)	1.0037 (3)	–0.0959 (3)	0.7305 (2)	4.0 (1)	H (18)	0.874 (5)	–0.326 (5)	0.202 (3)	11 (2)
C (16)	0.9526 (2)	–0.1045 (3)	0.6445 (2)	3.0 (1)	H (19)	0.747 (5)	–0.296 (5)	0.211 (3)	10 (2)
C (17)	0.6495 (3)	0.1671 (3)	0.5638 (2)	3.8 (1)	H (20)	0.790 (5)	–0.432 (6)	0.210 (4)	15 (2)

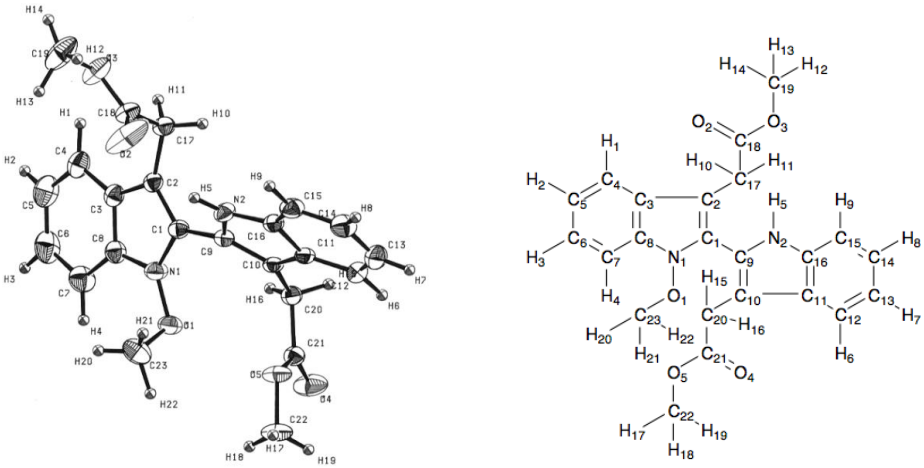


Figure 2. ORTEP drawing and numbering of **53**

Table 5. Positional Parameters and B (eq) for **53**

atom	x	y	z	B (eq)	atom	x	y	z	B (eq)
O (1)	0.4323 (2)	0.3558 (2)	0.7304 (3)	4.4 (1)	C (20)	0.2261 (3)	0.2463 (3)	0.7518 (4)	3.3 (2)
O (2)	0.1970 (3)	0.4588 (2)	0.1294 (3)	9.7 (2)	C (21)	0.3367 (3)	0.1601 (3)	0.8150 (4)	3.4 (2)
O (3)	0.0916 (2)	0.6469 (2)	0.1642 (3)	6.1 (1)	C (22)	0.5249 (4)	0.0025 (4)	0.7445 (6)	5.3 (2)
O (4)	0.3533 (2)	0.1580 (2)	0.9594 (3)	6.4 (2)	C (23)	0.5420 (5)	0.3000 (5)	0.6297 (7)	6.8 (3)
O (5)	0.4140 (2)	0.0878 (2)	0.6961 (2)	4.5 (1)	H (1)	0.149 (3)	0.792 (3)	0.580 (4)	6.01 (2)
N (1)	0.3487 (2)	0.4445 (2)	0.6644 (3)	3.9 (1)	H (2)	0.279 (4)	0.886 (4)	0.775 (5)	7.92 (3)
N (2)	0.2074 (2)	0.2674 (2)	0.3091 (3)	3.6 (1)	H (3)	0.455 (3)	0.777 (3)	0.917 (5)	7.70 (3)
C (1)	0.2573 (3)	0.4259 (2)	0.5427 (3)	3.1 (1)	H (4)	0.498 (3)	0.573 (3)	0.884 (4)	5.53 (2)
C (2)	0.1961 (3)	0.5356 (2)	0.5099 (3)	3.1 (1)	H (5)	0.226 (3)	0.298 (3)	0.232 (4)	4.79 (2)
C (3)	0.2518 (3)	0.6228 (3)	0.6141 (4)	3.6 (2)	H (6)	0.151 (3)	0.015 (3)	0.564 (4)	5.47 (2)
C (4)	0.2252 (4)	0.7484 (3)	0.6418 (4)	4.7 (2)	H (7)	0.108 (3)	–0.108 (3)	0.316 (4)	6.16 (2)
C (5)	0.2993 (5)	0.8053 (4)	0.7551 (5)	6.2 (3)	H (8)	0.109 (3)	–0.072 (3)	0.048 (4)	5.55 (2)
C (6)	0.3977 (5)	0.7428 (4)	0.8419 (5)	6.5 (3)	H (9)	0.147 (3)	0.104 (3)	0.031 (4)	5.05 (2)
C (7)	0.4261 (4)	0.6200 (4)	0.8214 (4)	5.4 (2)	H (10)	0.042 (3)	0.500 (3)	0.367 (3)	4.41 (2)
C (8)	0.3501 (3)	0.5624 (3)	0.7074 (4)	3.9 (2)	H (11)	0.036 (3)	0.640 (3)	0.423 (4)	4.58 (2)
C (9)	0.2323 (2)	0.3098 (2)	0.4801 (3)	3.0 (1)	H (12)	0.131 (5)	0.567 (5)	–0.084 (7)	13 (2)
C (10)	0.2157 (2)	0.2329 (2)	0.5659 (3)	2.9 (1)	H (13)	0.224 (4)	0.618 (4)	0.025 (5)	9 (1)
C (11)	0.1801 (2)	0.1388 (2)	0.4435 (3)	3.1 (1)	H (14)	0.075 (6)	0.711 (5)	–0.032 (7)	15 (2)
C (12)	0.1520 (3)	0.0358 (3)	0.4531 (5)	4.1 (2)	H (15)	0.153 (3)	0.234 (2)	0.790 (3)	3.77 (2)
C (13)	0.1235 (4)	–0.0406 (3)	0.3058 (5)	5.1 (2)	H (16)	0.227 (3)	0.323 (3)	0.812 (4)	5.39 (3)
C (14)	0.1229 (3)	–0.0164 (3)	0.1504 (5)	4.9 (2)	H (17)	0.552 (4)	–0.051 (3)	0.643 (5)	8.95 (4)
C (15)	0.1490 (3)	0.0848 (3)	0.1362 (4)	4.2 (2)	H (18)	0.575 (4)	0.051 (3)	0.811 (5)	8.45 (4)
C (16)	0.1796 (3)	0.1623 (2)	0.2849 (4)	3.3 (2)	H (19)	0.512 (4)	–0.038 (3)	0.816 (5)	8.78 (4)
C (17)	0.0895 (3)	0.5612 (3)	0.3865 (4)	3.7 (2)	H (20)	0.585 (4)	0.358 (4)	0.629 (5)	7.53 (3)
C (18)	0.1325 (3)	0.5486 (3)	0.2147 (4)	3.9 (2)	H (21)	0.518 (4)	0.262 (4)	0.509 (5)	8.75 (3)
C (19)	0.1249 (7)	0.6423 (5)	–0.0050 (7)	8.1 (4)	H (22)	0.600 (3)	0.238 (3)	0.701 (5)	7.58 (3)

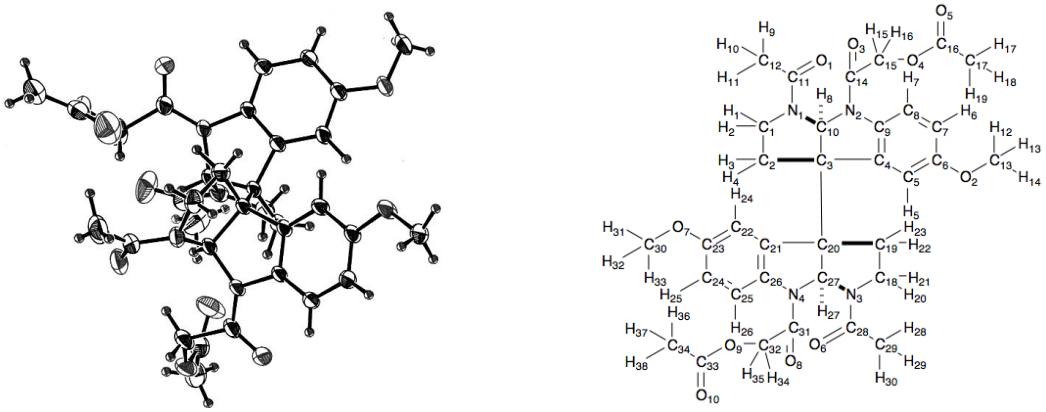


Figure 3. ORTEP drawing and numbering of **76**

Table 6. Positional Parameters and B (eq) for **76**

atom	x	y	z	B (eq)	atom	x	y	z	B (eq)
O (1)	0.4779 (3)	1.1281 (3)	0.3474 (3)	8.4 (3)	C (30)	0.4107 (6)	0.3626 (5)	0.0402 (4)	6.7 (3)
O (2)	0.5319 (2)	0.4176 (2)	0.3966 (2)	5.9 (2)	C (31)	0.3084 (4)	0.9434 (4)	0.1246 (3)	4.7 (2)
O (3)	0.7563 (2)	0.8866 (3)	0.4170 (2)	6.1 (2)	C (32)	0.3174 (5)	1.0668 (5)	0.1477 (5)	7.1 (4)
O (4)	0.7582 (3)	1.1052 (3)	0.3642 (2)	6.1 (2)	C (33)	0.1922 (5)	1.0970 (5)	0.2136 (4)	6.4 (3)
O (5)	0.7148 (3)	1.0309 (4)	0.2562 (2)	9.0 (3)	C (34)	0.1112 (7)	1.1678 (8)	0.2215 (6)	8.7 (5)
O (6)	0.4951 (3)	1.1051 (3)	0.1038 (3)	9.2 (3)	H (1)	0.394 (4)	0.813 (4)	0.416 (3)	6.96 (4)
O (7)	0.4511 (3)	0.4275 (2)	0.0997 (2)	6.3 (2)	H (2)	0.324 (3)	0.896 (4)	0.385 (3)	5.64 (3)
O (8)	0.2352 (2)	0.9058 (3)	0.0994 (2)	6.2 (2)	H (3)	0.348 (3)	0.735 (4)	0.309 (2)	4.97 (3)
O (9)	0.2310 (3)	1.1183 (3)	0.1531 (2)	6.2 (2)	H (4)	0.338 (4)	0.849 (4)	0.266 (3)	7.17 (5)
O (10)	0.2251 (4)	1.0294 (4)	0.2566 (3)	11.5 (3)	H (5)	0.454 (3)	0.566 (4)	0.319 (3)	5.88 (4)
N (1)	0.4473 (3)	0.9480 (3)	0.3753 (2)	4.6 (2)	H (6)	0.654 (3)	0.524 (4)	0.482 (3)	5.69 (3)
N (2)	0.6039 (3)	0.8719 (3)	0.3830 (2)	4.3 (2)	H (7)	0.699 (4)	0.715 (4)	0.475 (3)	7.85 (6)
N (3)	0.5472 (3)	0.9328 (3)	0.1290 (2)	4.5 (2)	H (8)	0.544 (2)	0.970 (3)	0.302 (2)	3.67 (2)
N (4)	0.3861 (3)	0.8807 (3)	0.1318 (2)	4.0 (2)	H (9)	0.342 (5)	1.058 (6)	0.459 (4)	10.69 (6)
C (1)	0.3777 (5)	0.8606 (5)	0.3778 (3)	5.3 (3)	H (10)	0.350 (6)	1.152 (6)	0.413 (5)	10.76 (8)
C (2)	0.3811 (4)	0.8011 (4)	0.3052 (3)	4.6 (2)	H (11)	0.28 (1)	1.084 (7)	0.384 (5)	20.8 (2)
C (3)	0.4830 (3)	0.7997 (3)	0.2955 (2)	3.7 (2)	H (12)	0.558 (5)	0.377 (5)	0.498 (4)	11.46 (9)
C (4)	0.5323 (3)	0.7080 (3)	0.3427 (2)	3.9 (2)	H (13)	0.645 (3)	0.347 (4)	0.450 (3)	6.28 (3)
C (5)	0.5098 (4)	0.5958 (4)	0.3455 (3)	4.5 (2)	H (14)	0.535 (4)	0.278 (5)	0.445 (3)	8.29 (5)
C (6)	0.5602 (3)	0.5286 (3)	0.3974 (2)	4.4 (2)	H (15)	0.674 (5)	1.086 (5)	0.438 (3)	9.96 (7)
C (7)	0.6275 (4)	0.5722 (4)	0.4459 (3)	4.6 (2)	H (16)	0.624 (4)	1.084 (4)	0.352 (3)	7.91 (5)
C (8)	0.6488 (4)	0.6858 (4)	0.4433 (3)	4.7 (2)	H (17)	0.873 (4)	1.119 (5)	0.228 (4)	8.28 (5)
C (9)	0.5995 (3)	0.7526 (3)	0.3916 (2)	4.1 (2)	H (18)	0.824 (5)	1.215 (6)	0.261 (3)	10.62 (7)
C (10)	0.5212 (4)	0.9088 (3)	0.3354 (2)	4.0 (2)	H (19)	0.902 (5)	1.139 (5)	0.300 (4)	9.10 (6)
C (11)	0.4272 (4)	1.0609 (5)	0.3754 (3)	6.0 (3)	H (20)	0.676 (2)	0.887 (4)	0.135 (2)	3.96 (2)
C (12)	0.3465 (7)	1.0986 (7)	0.4095 (5)	8.4 (5)	H (21)	0.609 (4)	0.794 (4)	0.098 (3)	7.03 (4)
C (13)	0.5756 (5)	0.3452 (4)	0.4508 (4)	5.8 (3)	H (22)	0.639 (3)	0.725 (4)	0.207 (2)	5.35 (3)
C (14)	0.6837 (4)	0.9306 (4)	0.3958 (3)	4.9 (2)	H (23)	0.645 (3)	0.837 (4)	0.246 (2)	5.97 (4)
C (15)	0.6775 (5)	1.0588 (4)	0.3891 (4)	6.0 (3)	H (24)	0.530 (3)	0.565 (4)	0.184 (2)	4.61 (3)
C (16)	0.7697 (4)	1.0872 (4)	0.2931 (4)	6.3 (3)	H (25)	0.332 (4)	0.547 (4)	0.018 (3)	6.98 (5)
C (17)	0.8476 (7)	1.1466 (6)	0.2693 (5)	7.6 (4)	H (26)	0.293 (3)	0.733 (4)	0.032 (2)	4.20 (2)
C (18)	0.6180 (4)	0.8465 (4)	0.1339 (3)	4.9 (3)	H (27)	0.459 (3)	0.969 (4)	0.207 (2)	4.88 (3)
C (19)	0.6079 (4)	0.7930 (4)	0.2074 (3)	4.5 (2)	H (28)	0.656 (5)	0.997 (6)	0.029 (4)	10.89 (7)
C (20)	0.5067 (3)	0.7990 (3)	0.2151 (2)	3.7 (2)	H (29)	0.631 (6)	1.114 (7)	0.044 (5)	12.07 (8)
C (21)	0.4544 (3)	0.7119 (3)	0.1657 (2)	4.0 (2)	H (30)	0.70 (1)	1.082 (7)	0.107 (5)	20.8 (2)
C (22)	0.4747 (4)	0.5996 (4)	0.1583 (3)	4.5 (2)	H (31)	0.447 (4)	0.312 (5)	0.040 (3)	6.92 (4)
C (23)	0.4249 (3)	0.5384 (4)	0.1036 (2)	4.6 (2)	H (32)	0.426 (7)	0.399 (6)	–0.002 (4)	14.4 (1)
C (24)	0.3586 (4)	0.5881 (4)	0.0564 (3)	4.7 (2)	H (33)	0.333 (4)	0.358 (5)	0.044 (3)	8.49 (5)
C (25)	0.3385 (4)	0.7007 (4)	0.0638 (2)	4.6 (2)	H (34)	0.354 (5)	1.110 (6)	0.118 (4)	10.17 (7)
C (26)	0.3877 (3)	0.7618 (3)	0.1182 (2)	4.0 (2)	H (35)	0.34 (1)	1.072 (6)	0.199 (5)	19.4 (2)
C (27)	0.4741 (3)	0.9089 (3)	0.1736 (3)	3.9 (2)	H (36)	0.097 (7)	1.168 (8)	0.260 (4)	10.73 (8)
C (28)	0.5552 (4)	1.0351 (5)	0.0984 (3)	6.2 (3)	H (37)	0.119 (7)	1.241 (7)	0.221 (5)	15.0 (1)
C (29)	0.6354 (7)	1.0587 (8)	0.0614 (6)	9.3 (5)	H (38)	0.070 (6)	1.179 (6)	0.173 (4)	12 (3)

Crystal data for 76: $C_{34}H_{38}N_4O_{10}$, M=662.70, monoclinic, space group $P2_1/a$ (#14), a=14.75 (4)Å, b=11.90 (1)Å, c=18.41 (3)Å, β=96.1 (2)°, V=0000 (1)Å^3, Z=4, D_{calc}=1.369 g/cm^3, F(000)=1400, and μ(Cu$K\alpha$)=8.06 cm^{-1}. The final cycle of full-matrix least-squares refinement was based on 3070 observed reflections (I>3.00σ (I), 2θ <120.4°) and 585 variable parameters. The final refinement converged with R=0.070 and Rw=0.079.

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